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Current Health Studies
During the Pandemic Process

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Current

Health Studies

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PREFACE

On February 11, 2020, the World Health Organization defined the disease caused by the novel coronavirus that was first detected in December, 2019 in Wuhan, the capital of Hubei Province in China, as COVID-19 Pandemic Influenza. The importance of technology, quality and quantity of researchers, and scientific research in the detection, control, and treatment of the disease has since been better appreciated. It is the responsibility of all scientists to ensure that all scientific research adds value to scientific developments, the economy of the countries, and the comfort of human life. Every piece of new information revealed in the scientific and technological field contributes to making human life more comfortable life. We hope that this book, which includes the chapters prepared by valuable scientists on the subject, will be useful to our country, all our colleagues, students, and all people who are going through difficult times due to the COVID-19 pandemic.

We sincerely thank everyone who contributed to the creation of this book, those who helped in conveying up-to-date information, our colleagues who peer-reviewed the book, and the publishing house and its staff who contributed to the publication of the book.

Best Regards

Assoc. Prof. Dr. Hakan Kamalak
Assoc. Prof. Dr. Aykut Urfalıoğlu
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CHAPTER I

BRONCHIECTASIS

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INTRODUCTION

Bronchiectasis is a disease with chronic cough and sputum complaints accompanied by recurrent sinopulmonary infections, characterized by enlargement of the airways and thickening of the bronchial wall. When the word's origin is examined, it is derived from the words bronchos and ectasis (dilatation and enlargement) in Ancient Greek. Laennec first described it in 1819. After Sicard started to apply bronchography in 1922, permanent destructive changes in the bronchi began to be seen more clearly. In 1950, Reid showed the relationship between bronchography and pathological changes, and in this study defined bronchiectasis as a permanent dilatation of the bronchi with irreversible damage to the lung.

EPIDEMIOLOGY

Although there are different studies on the incidence and prevalence of bronchiectasis, there is no definite information about its rates worldwide. Infections and vaccination programs in childhood are another factor affecting the frequency of bronchiectasis. On the other hand, some of the bronchiectasis is dry bronchiectasis without symptoms. In the USA, it is calculated as 52 per 100,000 adults. Although the prevalence of bronchiectasis is 10-50 / 10,000 in developing countries, its absolute prevalence is unknown.

ETYMOLOGY

Approximately 40% of bronchiectasis is still defined as idiopathic. While some of the causes that can be detected are lung-localized factors, some have bronchiectasis as a systemic disease component. Recurrent lung infections are still in the first place in the etiology of bronchiectasis. Although the exact figures regarding the incidence of bronchiectasis in the world are unknown, the incidence of bronchiectasis decreases in developed countries due to childhood vaccination programs, early diagnosis and treatment of lung diseases, and decreases in tuberculosis rates. However, as these risk factors persist in developing countries, the incidence of
Bronchiectasis is higher. Bronchiectasis developing secondary to systemic diseases is only 4% of all cases. It is recommended to explore the underlying cause of all patients. The most frequently accused cause is acquired bronchiectasis with recurrent sinopulmonary infections such as adenovirus, pneumonia, pertussis, measles, and tuberculosis, which affect the respiratory tract in childhood. In addition to acquired etiology such as bronchial obstruction due to foreign body and tumor, recurrent aspirations, tracheobronchomegaly, congenital diseases (such as alpha-1 antitrypsin deficiency, immotile cilia syndrome, cystic fibrosis, young syndrome), immune deficiencies are among the other causes of congenital bronchiectasis. While acquired bronchiectasis tends to remain local, congenital bronchiectasis mostly develops diffuse. Death might occur via respiratory failure in diffuse bronchiectasis with worse clinical symptoms. Bacterial, viral, and fungal infections are at the forefront in developing countries, while immunodeficiency syndromes, genetic and metabolic defects take the first place in developed countries.

PHYSIOPATHOLOGY

Two main pathologies play a role in the development of bronchiectasis. The first mechanism is an obstruction or abnormal dilatation of the bronchi, while the second is recurrent and chronic infections. The standard mucociliary mechanism is disrupted by respiratory tract obstruction or dilatation and recurrent infections. With chronic infections, bronchial wall damage occurs, bronchial dilatation develops with the weakening of the bronchial walls. Bronchiectasis is usually seen in medium-diameter bronchi, as well as in more distal bronchi. With the loss of muscle and elastic ducts in the bronchial walls, scar tissue may develop. Even in severe bronchiectasis, secretions cannot be discharged due to ciliary activity disorder, and a dilated bony structure occurs. Reid categorized bronchiectasis into three groups according to the radiological or pathological appearance of the airways. It is divided into three as 1) Fusiform, 2) Varicose, 3) Cystic (Saccular).

1- Fusiform Bronchiectasis: There are small dilatations in the bronchial walls due to minimal damage; the number of bronchial branching is within normal limits.

2- Varicose Bronchiectasis: Damage in the bronchi is more and terminal airways decrease due to damage; varicose-like, bud-shaped dilatations develop in the bronchial wall.

3- Cystic (Saccular) Bronchiectasis: Damage develops in the bronchial walls, including the muscle and cartilage tissues.

The number of branches towards the distal in the bronchial structures is severely decreased. The bronchi become vesicles filled with secretions. Reid attributed the decrease in bronchi branching in bronchiectasis to the absence of bronchi filled with pus and narrowed by
mucosal edema on bronchography. However, in severe bronchiectasis, total obliteration develops due to fibrosis in the distal airways. Three theories have been presented in the mechanism of bronchiectasis development. Dilatation theory is the dilatation caused by increased intraluminal pressure due to mucopurulent secretion distal to the obstruction. Traction theory is the retraction of bronchioles with fibrosis caused by parenchymal damage after infection. The third theory is atelectasis theory. This theory causes atelectasis in the collapsed area and enlargement of the bronchi with viscous material aspiration in the peripheral airways.

As is more common in atypical pneumonia, post-infection bronchial dilatation and enlargement may occur. These dilatations, called pseudobronchiectasis or prebronchiectasis, are temporary and can be reversed entirely with the disease's treatment. Bronchiectasis is usually seen in the lower lobes, especially in the posterobasal segments. The lower lobe involvement involves the lingular segments 60-80% on the left and the middle lobe 45-60% on the right. The bilateral incidence of bronchiectasis is 30-40%. Studies have reported that bronchiectasis is most common in the left lower lobe, which is attributed to the anatomical structure of the left main bronchus. The left lower lobe is more susceptible to the development of bronchiectasis due to the long left main bronchus and a more angled separation from the trachea, and the difficulty in drainage due to the compression of the mediastinal vascular and lymphatic structures on the left main bronchus.

**CLINICAL FINDINGS**

The most common symptom in bronchiectasis patients is recurrent lower respiratory tract infections. Bronchiectasis should be suspected in cough with sputum that usually lasts longer than six weeks. The cause of the malodorous, sputum-mucopurulent cough, especially in the morning hours, is the secretions accumulated in the tracheobronchial system during the night. They also complain of frequent respiratory infections, and the infection is usually accompanied by fever. Although the complaint of hemoptysis is encountered in advanced disease, massive hemoptysis requiring selective angiography and embolization is a rare finding. Shortness of breath, chest pain, clubbing, and wheezing are also rare symptoms. Effort dyspnea may be an indicator of diffuse bronchiectasis. In physical examination, submaturity may be taken in percussion in localized disease, respiratory sounds may be decreased in auscultation, and rough rales may be heard displaced by cough. The possibility of complications decreases with increasing antibiotic use in patients with bronchiectasis. Complications that can be seen are recurrent pneumonia caused by local spread, lung abscess, bronchopleural fistula, empyema, massive hemoptysis, mediastinitis, brain abscess, sepsis, and amyloidosis.
DIAGNOSIS

Laboratory and radiological examinations should be performed first in cases with suspected bronchiectasis due to the anamnesis taken from the patient. Laboratory tests in the diagnosis of bronchiectasis are nonspecific, and an increase in white blood cell and CRP, anemia, and an increase in sedimentation can be seen. S. pneumonia, H. influenza, M. Katarralis, and P. Auroginosa may be found in sputum cultures taken from patients. P. Aeruginosa is frequent in patients with bronchiectasis developing based on cystic fibrosis.

The first radiological examination to be used in the diagnosis of bronchiectasis is posteroanterior chest radiography. Posteroanterior chest radiography is usually expected in mild cases. However, in advanced cases, the normal narrowing of the lung parenchyma's airways may not be visible towards the periphery, and parallel lines with air columns between them are called "train rail or tramway." The train track appearance is not specific to bronchiectasis, as it can be seen in many diseases such as chronic bronchitis. In more advanced cases, cystic bronchiectasis areas can be observed as "bread crumb or honeycomb" appearance on direct graphs. In the past, when computed tomography was not available, the gold standard for the diagnosis of bronchiectasis was bronchography. Bronchography has gradually been replaced by computed tomography, which is a non-invasive examination. In recent years, high resolution computed tomography (HRCT), which shows the lung parenchyma and the extent of the disease better, has been used more frequently in diagnosing bronchiectasis. The reliability of HRCT in the diagnosis of bronchiectasis is between 94-100% depending on the severity of the bronchiectasis. In computed tomography, thick-walled dilated bronchi extending to the periphery (tramway), bud-like appearances in the bronchi, cystic structures showing air-fluid leveling in dilated bronchi, and "stony ring"-like appearances can be observed with larger bronchial diameters adjacent to the artery.

TREATMENT

Bronchiectasis is an irreversible disease. The main purpose of treatment is to prevent recurrent infections, stop the progression of irreversible damage, and increase life quality. Medical and surgical treatment of bronchiectasis is divided into two parts.

Medical Treatment

Medical treatment aims to reduce airway obstruction and to eliminate infective bacteria in the lower respiratory tract. Therefore, antibiotics, mucolytics, expectorants, anti-inflammatory agents, and bronchodilators can be used. Secretions in the respiratory tract can be removed by chest percussion, postural drainage, respiratory physiotherapy methods. Antibiotics are used to treat acute attacks and to prevent bacterial colonization. Patients who do not respond to oral antibiotics and whose
clinical condition is not good should be hospitalized and given intravenous treatment. Prophylactic antibiotic treatment can be applied in recurrent infections. Another antibiotic application method is aerosolization. Although aerosol antibiotics have the advantage of providing a higher concentration in the lung, they also have disadvantages such as the risk of bronchospasm, high cost, and inadequate distribution to the lower airways.

**SURGICAL TREATMENT**

Surgical treatment in bronchiectasis gives definite results in selected and appropriate cases. Notably, patients with localized bronchiectasis who are resistant to medical treatment and whose symptoms persist, patients who receive frequent treatment for recurrent infections, and patients with bronchiectasis accompanied by complications such as massive hemoptysis are the group that benefits from surgery. Patients who are scheduled for surgery should evaluate the localization and extent of the disease with preoperative computed tomography, foreign bodies or endobronchial anomalies, and lesions investigated by bronchoscopy, chest physiotherapy should be performed to remove secretions, prophylactic antibiotic treatment should be initiated, and if smokers quit. Surgery aims to remove all affected segments and maintain maximum function. For this, the lung tissue that has lost its function is removed, and the spread of localized bronchiectasis areas to neighboring areas is eliminated. Therefore, patients' pulmonary reserves should be evaluated carefully. Resection types such as segmentectomy, lobectomy, and pneumonectomy can be applied in surgery. The most suitable cases for surgery are patients with unilateral and localized bronchiectasis.

Pneumonectomy can be performed in unilateral diffuse bronchiectasis where one lung is normal. However, when there is a risk of developing chest deformity after pneumonectomy, an operation is recommended after 18. Surgery has a more limited place in diffuse bronchiectasis, and its results are not very effective. In bilateral bronchiectasis, resection can be performed until a maximum of six regular segments remain. Surgery has no place in bilateral diffuse bronchiectasis. Lung transplantation can be applied in selected cases. Surgery is an effective treatment method in the treatment of bronchiectasis. The surgical indication should be established by evaluating the severity and extent of the disease.
REFERENCES

CHAPTER II

DIAGNOSIS AND TREATMENT IN PEDIATRIC IRON DEFICIENCY ANEMIA

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INTRODUCTION

Iron deficiency (ID) is the most prevalent nutritional deficiency in the world and is the most common cause of pediatric anemia. It is an important public health issue that impacts mother and child morbidity and mortality, affects mental and motor development, particularly in developing countries. Anemia is an indirect indicator of ID and pre-school children (0-5 years) and pregnant women in developing countries are under risk (1). According to World Health Organization data, ID prevalence in children is 40-50%, iron deficiency anemia (IDA) prevalence is 36% in developing countries. While IDA prevalence in developed countries is 8%. Furthermore, 30% of children in 0-4 age group in developing countries. And 48% of children in 5-14 age group are anemic (2, 3, 4).

Anemia is defined as reduced erythrocyte count or hemoglobin (Hb) level below age-based normal levels in healthy individuals. The fact that the ranges defining anemia vary according to age groups and genders must be considered when evaluating a patient. Since anemia is the most important indicator of iron deficiency, ID and IDA are usually interchangeable terms. However, ID may develop without anemia and affect tissues. Iron deficiency is a body iron deficiency that doesn’t prevent hemoglobin (Hb) production. Iron deficiency anemia (IDA) is the reduction in Hb amount due to iron deficiency. When the body receives less iron than its iron requirements, the first thing that occurs is a reduction in the body’s iron stores. Hemoglobin levels may continue within the normal range for a while after the stored iron is consumed. In this period, iron deficiency may be present without accompanying anemia. Only plasma ferritin and transferrin levels are reduced in this period. After the iron stores are depleted, the continued negative iron balance reveals itself through reduced hemoglobin counts. Pediatric IDA is most prevalent in nursing infants and menstruating teenagers; however, all children with increased growth rate and inadequately met requirements need iron supplements because they are under IDA risk.
This article is written after reviewing the literature on current approaches to early diagnosis and treatment of ID and IDA due to their prevalence in children and their permanent negative effects on children’s mental and motor development.

ETIOLOGY

Rapid growth and insufficient iron intake is the most common cause of pediatric IDA. The only source of iron in the intrauterine period is the iron passing through the placenta. The total iron amount in the fetus is 75 mg/kg during the last trimester of pregnancy. The iron stores of a healthy newborn is adequate to ensure erythropoiesis for the first six months after birth. Iron in infants with perinatal blood loss or low birth weights is depleted earlier, since their stores are insufficient. Delaying cutting the umbilical cord may improve the iron situation and reduce the risk of iron deficiency (5). The amount of iron in mother’s milk is at the maximum level in the first month after birth, this level gradually drops in later lactation (6). Although mother’s milk seems deficient in iron when compared to cow’s milk, the fact that at least half of its iron contents are adsorbed (its bioavailability is high) makes it an incomparable source of iron for term babies born with adequate iron stores in the first 6 months of their lives. It is known that feeding infants foods other than mother’s milk in the first six months disrupts iron absorption from mother’s milk. Although the absorption rate of iron from mother’s milk is high, infants also use the iron in the stores for the first six months because iron from exclusive breastfeeding is insufficient for normal growth (7, 8). As the infant’s increasing iron requirement cannot be met beyond 6th month, ID/IDA may easily appear in exclusively breastfed infants.

According to World Health Organization data, 6-23 months old infants should take 98% of their iron requirements from supplemental foods (9, 10). Supplemental foods fed after the sixth month have to be particularly rich from iron, zinc, phosphorous, magnesium, calcium and vitamin B6. Early and excessive cow’s milk consumption in infants may cause chronic blood loss from the intestines caused by heat-sensitive proteins inside cow’s milk. Furthermore, iron absorption from cow’s milk is much less than mother’s milk, and calcium and caseinophosphopeptides may disrupt iron absorption.

Chronic IDA accompanied by concealed hemorrhage is relatively rare in children. Blood loss should be considered if the infant develops iron deficiency despite adequate iron intake or doesn’t adequately respond to oral iron treatment. Digestive system issues such as peptic ulcers, Meckel diverticulum, polyps, hemangiomas or inflammatory bowel disease may lead to IDA. Rarely, IDA may develop due to hemorrhages such as celiac disease, chronic diarrhea or pulmonary hemosiderosis. Iron deficiency
anemia is observed in 2% of girls in puberty due to growth attacks and menstrual blood loss (11). A detailed menstruation history should be obtained from girls in puberty and underlying hemorrhage disorders such as von-Willebrand disease should be considered in girls with heavier menstrual bleeding than expected. Furthermore, it must be noted that parasitosis may contribute to iron deficiency in developing countries. Malnutrition, overconsumption of cow’s milk, low socio-economic status and previous infections play an important role in the emergence of common DEA in the period of rapid growth. Iron deficiency anemia risk factors in children are presented in table 1 (12).

Table 1: Infants at high risk for iron deficiency

<table>
<thead>
<tr>
<th>Increased iron needs:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Low birth weight</td>
</tr>
<tr>
<td>- Prematurity</td>
</tr>
<tr>
<td>- Multiple gestation</td>
</tr>
<tr>
<td>- High growth rate</td>
</tr>
<tr>
<td>- Chronic hypoxia- high altitude, cyanotik hart disease</td>
</tr>
<tr>
<td>- Low hemoglobin at birth</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood loss:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Perinatal bleeding</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dietary factors:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Early cow’s milk intake</td>
</tr>
<tr>
<td>- Early solid food intake</td>
</tr>
<tr>
<td>- Rate of weight gain greater than average</td>
</tr>
<tr>
<td>- Low-iron formula</td>
</tr>
<tr>
<td>- Frequent tea intake</td>
</tr>
<tr>
<td>- Low vitamin C intake</td>
</tr>
<tr>
<td>- Low meat intake</td>
</tr>
<tr>
<td>- Breast-feeding &gt;6 months without iron suplements</td>
</tr>
<tr>
<td>- Low socioeconomic status (frequent infections)</td>
</tr>
</tbody>
</table>

**PATOPHYSIOLOGY**

Iron is an essential element and is required for erythropoiesis, oxidative metabolism and cellular immunity. Most of the iron in the body (65%) is contained within haemoglobins and 10% is located inside muscle fibers (myoglobins) and other tissues (such as enzymes and cytochromes). The remainder is stored in the liver, in the reticuloendothelial system macrophages and bone marrow. Since there is no active pathways for iron excretion from the body, the regulation of iron absorption from the duodenum plays a critical role in iron homeostasis. Since excessive iron loading causes cell death and toxicity through the generation of free
radicals and lipid peroxidation, iron homeostasis requires tight regulation (12, 13).

Classical western diet contains 90% non-heme, 10% heme iron and 1-2 mg of these is absorbed daily through the intestines (mostly duodenum). Based on increasing iron requirements (growth, pregnancy, blood loss, etc.) daily iron absorption may increase. Non-heme iron in the diet is in oxidized (Fe$^{+3}$) form, and is reduced to Fe$^{+2}$ by the enzyme ferric reductase, which uses vitamin C as coenzyme, before being transported through the intestinal epithelium. Iron transport into the enterocyte is carried out by divalent metal transporter 1 (DMT1), which also carries other metal ions such as zinc, copper and cobalt. Non-heme iron absorption may be disrupted by the simultaneous use of tetracyclines, proton pump inhibitors and antacid treatments, phytates (high-fiber diet), calcium and phenolic compounds (tea, coffee). Furthermore, gastric atrophy caused by helicobacter pylori infection may lead to both hemorrhage and iron deficiency anemia. When heme enters the enterocyte, hem oxygenase produces Fe$^{+2}$. Some heme molecules pass through transporters in the kidneys, liver and erythroblasts without modification and leave the enterocyte. Heme in plasma is cleared by hemopexin, transported into the liver and metabolized. Most Fe$^{+2}$ is released into the basolateral membrane by ferroportin-1 when it enters the intestinal epithelium cell, converted into Fe$^{+3}$ by hephaestin, and bound to plasma transferrin (Tf) (12-14). Iron in the blood is bound to transferrin and transported to where it will be used and stored. Transferrin constitutes the most dynamic iron pool and uses 30-40% of the iron binding capacity within physiological limits. Iron in transferrin enters the target cell (erythroid cells, immune and hepatic cells) through receptor-dependent endocytosis. The Tf-Tf receptor complex that forms is taken into the cell and create an endosome. pH inside the endosome is lowered through hydrogen (H$^+$) ions taken into the endosome via a proton pump. The acidic effect causes Tf to separate from iron, and iron is reduced from its ferric (Fe$^{+3}$) to its ferrous (Fe$^{+2}$) form. Iron passes from the endosomal membrane to the cytoplasm via DMT1. Iron in the cytoplasm is used for heme synthesis in the mitochondria in addition to other metabolic works. Heme transporters transfer the new heme from the mitochondria to the cytosol. Heme binds with globin and forms hemoglobin. Excess heme is removed from erythroid cells via cytosolic heme transporters. Excess iron is stored as ferritin. Although macrophages and the liver are the most important stores, transferrin-bound iron is the most important source in meeting functional demand (12-14).

Most of the iron required to produce erythrocytes is obtained through the iron cycle in macrophages. Since 1-2 mg/day absorption can only replenish the daily iron loss, the internal cycle of iron in the body is very important in meeting the iron demand required for erythropoiesis in
the bone marrow. Macrophages acquire iron from erythrocytes they phagocytose. Iron produced within macrophages is either released into the plasma through macrophage ferroportin, or stored inside the macrophage as ferritin. Ferroportin is the sole iron remover in the cell, as is the case with enterocytes. As iron is released into the plasma from hepatocytes or macrophages, it has to be converted into its ferric (Fe^{3+}) form and oxidized to be able to bind to transferrin. Plasma ceruloplasmin, which acts as a copper-bound ferroxidase, plays a role in this oxidation process (12-14).

Hepcidin is a peptide synthesized in hepatocytes depending on iron increase and inflammation in the body. Hepcidin synthesis is transcriptionally regulated by iron. Depending on stored iron and erythropoiesis requirements, hepcidin controls the expression of ferroportin, which transports iron out of the cell, on the cell surface. Under normal and pathologic conditions, changes in iron absorption and consumption lead to changes in serum transferrin saturation, and holotransferrin reflects these effects into hepatocytes. Hepatocytes are not only cells that make and release hepcidin, which is the iron regulatory hormone, but they are also sensors for the concentration of plasma holotransferrin, which reflects the systemic iron balance. As transferrin saturation increases, actions to reduce iron are initiated. Hepcidin/ferroportin system also contributes to host defenses by blocking pathogens from taking up iron. It was shown that when hepcidin synthesis increases along with Interleukin 6 (IL-6) and other cytokines, the absorption of iron for hemoglobin synthesis and erythropoiesis is blocked and reduced, iron release from macrophages is reduced and anemia may emerge. In addition to its hypoferritinemia-inducing effects, hepcidin also disrupts the proliferation and life cycles of erythrocyte precursor cells and suppresses erythropoiesis. In contrast, hepcidin synthesis is reduced in anemia and hypoxia, and cell surface ferroportin is increased. Consequently, iron absorption and the amount of iron released from macrophages back into circulation increases (12-15).

**CLINICAL FINDING**

Iron is an essential element, needed by all cells in the body. Since most of the iron in the body is used for hemoglobin synthesis, the most important symptom of iron deficiency is anemia. Its deficiency affects all systems and produces many systemic signs and clinical symptoms. Clinical symptoms of iron deficiency in children is different than those in adults and symptoms other than anemia are more prevalent. IDA symptoms are closely related to the development rate of anemia. Adaptation mechanisms that are activated in clinical conditions that develop slowly allow patients to tolerate even very low Hb levels (<7.0 g/dL) with very few overt symptoms. Although decreased Hb levels reduce the blood’s oxygen carrying capacity, this doesn’t cause important physiological changes
unless this level drops below 7-8 g/dL. Below this level, skin and mucosa paleness appears (13, 16). In the early stages of IDA, non-specific symptoms such as fatigue, restlessness and anorexia may be observed. Severe anemia frequently presents with heart murmur (soft, apical and systolic), tachycardia, cardiomegaly, dyspnea, white ridges and fragility in nails, angular stomatitis, taste disorder, difficulty swallowing, polyuria, polydipsia, excessive sleep, attention deficit, lethargy, headaches, dizziness, tinnitus, behavioral disorders, difficulty learning, restlessness, loss of appetite, rapid fatigue, delayed crawling and walking. 30% of chronic IDA patients exhibit blue sclera, atrophy in tongue papillae, koilonychia, and 10-15% of cases may exhibit hepatosplenomegaly (17).

The most critical symptoms of iron deficiency anemia are its effects on the neurocognitive system. Iron deficiency in growing children delays the maturation of the central nervous system and psychomotor development. Studies indicate pediatric iron deficiency may lead to motor and cognitive retardation and emotional disorders in children (18-20). ID that didn't develop into IDA may cause disruptions in mental and motor functions and these effects may be permanent. Some authors associate central nervous system symptoms in patients with decreased MAO enzyme levels (21-23). Some studies suggest that it decreases the expression of dopamine receptors, disrupts myelinization or disrupts the functions of various enzymes in the nerve tissue (24-26). Iron deficiency affects the synthesis of neurotransmitter enzymes such as dopamine, norepinephrine and serotonin (23). This disrupts the intellectual and personality development of children (27-30). Since it causes permanent damage to infant neurologic development, it is essential to diagnose and prevent iron deficiency in the pre-anemic period. Although anemia can be treated through iron supplementation, disruptions in cognitive functions may not be fully repaired. Recent studies indicate that DEA is associated with fever convulsions (31-35). It is known that breath-holding spells are associated with IDA and oral iron treatment prevents the episodes. If not IDA, ID may be present in children experiencing breath-holding spells.

Pica, defined as eating unusual materials such as earth, clay, wall liquids, etc. is frequently observed in children with IDA (17, 37, 38). Since children with ID may also exhibit zinc deficiency, zinc levels of these children should be measured (19, 36). Dr. Memduh Tayanç was the first to report (1942) anemia, retarded development and hepatosplenomegaly in earth-eating children. Later, this syndrome characterized by zinc deficiency, hypogonadism, iron deficiency, pica, hepatosplenomegaly was named Tayanç-Reimann-Prasad syndrome (39).

Clinical studies have shown that ID has important effects on the immunological system (40-42). IDA increases infection tendency. Cellular immunity, response to NBT (Nitro Blue Tetrazolium) test and PPD
(Purified Protein Derivative) are disrupted. Furthermore, it was shown that it may affect the number and function of T-lymphocytes, affect the intracellular bacteria killing functions of neutrophils, and disrupt chemotactic functions. Iron treatment may correct these changes in immunity within 4-7 days.

LABORATORY FINDINGS

Biochemical evidence that indicate reduced iron stores in the body are diagnostic. The classical biochemical markers for DE and IDA are serum iron, transferrin, transferrin saturation and ferritin levels (12, 16, 45-47). The first finding in iron deficiency is a serum iron level below 12 ng/mL. In the second phase, serum iron decreases (<30 µg/dL), serum total iron binding capacity (TIBC) increases (>350 µg/dL) and transferrin saturation percentage (TSP) decreases (<15%). Transferrin saturation is calculated by dividing serum iron level to TIBC (48) (Table 2). While the normal range is between 20-50% it falls below 20% in IDA. When TSP falls to 10-15%, the lack of iron for Hb synthesis leads to an increase in heme precursor free erythrocyte protoporphyrin levels (23). Serum ferritin levels are used to evaluate total body iron stores. This level is between 50 and 200 µg/dL in healthy adults. 12-15 mg/L range defines the boundary values for ferritin in IDA diagnosis. If a chronic disease is present, the limit may be considered <50 mg/L (Table 3). Serum transferrin receptor levels rapidly increase in iron deficiency. Serum transferrin receptor/ferritin ratio may be the best differential indicator to distinguish between iron deficiency and inflammation. While a low value (<2.5) indicates an inflammatory anemia, a high value (>2.5) may indicate iron deficiency anemia. While erythrocytes are morphologically normocytic and normochromic, they become hypochromic and microcytic as anemia develops further. As anemia becomes more severe, poikilocytosis and anisocytosis may develop. Smaller erythrocytes (microcytes) and fewer Hb inside them (hypochromic) are characteristic of IDA. This morphologic change is best reflected in values below normal for mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC). MCV indicates whether anemia is microcytic, macrocytic and normocytic. MCV is <80 fl in IDA, and its evaluation depends on gender and age (49) (Table 4). Normal MCH value is 29±2 picograms (pgr), and it indicates the level of Hb per erythrocyte in grams. MCH levels decrease in IDA. Normal RDW value is 13.4±1.2 and the red cell distribution width is an indicator of anisocytosis. RDW increases in DEA (> 15 fl), and RDW is normal in cases of minor thalassemia, infection and inflammation. RBC (Red Blood Cell) level is usually below 5 million per millimeter cube in IDA. MCHC is the last value to be affected by IDA and indicates the amount of Hb per 100 ml of erythrocyte in grams. Its level falls below 30% in IDA. These
findings become apparent when Hb level drops below 10 g/dL. Number of reticulocytes may be normal or slightly increased. Reticulocyte level may be increased to 3-4% in severe IDA. Although the number of leukocytes is normal in ID, 20% of cases may exhibit mild leukopenia. Thrombocytosis or thrombocytopenia may also be present (2, 43, 50). Bone marrow store iron level is determined through Prussian blue staining of bone marrow aspiration materials. Iron granules are reduced or nonexistent in iron deficiency anemia. Erythrocyte zinc protoporphyrin increases in IDA. This increase may be identified even before anemia appears.

Table 2: Serum iron and saturation percentage according to age (12).

<table>
<thead>
<tr>
<th>Age</th>
<th>Serum iron (µg/dL)</th>
<th>Transferrin of saturasyon(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 month-2 age</td>
<td>68±3.6 (16-120)*</td>
<td>22±1.1 (6-38)</td>
</tr>
<tr>
<td>2-6 age</td>
<td>72±3.4 (20-124)</td>
<td>25±1.2 (7-43)</td>
</tr>
<tr>
<td>6-12 age</td>
<td>73±3.4 (23-123)</td>
<td>25±1.2 (7-43)</td>
</tr>
<tr>
<td>&gt;18 age</td>
<td>92±3.8 (48-136)</td>
<td>30±1.1 (18-46)</td>
</tr>
</tbody>
</table>

* Mean±SD (min-max)

Table 3: Serum ferritin levels according to age (12).

<table>
<thead>
<tr>
<th>Age</th>
<th>Ferritin (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn</td>
<td>25-200</td>
</tr>
<tr>
<td>1 month</td>
<td>200-600</td>
</tr>
<tr>
<td>2-5 month</td>
<td>50-200</td>
</tr>
<tr>
<td>6 month - 15 age</td>
<td>7-140</td>
</tr>
<tr>
<td>&gt;15 age (boy)</td>
<td>15-200</td>
</tr>
<tr>
<td>&gt;15 age (girl)</td>
<td>12-150</td>
</tr>
</tbody>
</table>
Table 4: Normal full blood values according to age and gender (49).

<table>
<thead>
<tr>
<th>Age</th>
<th>Hb (g/dl)</th>
<th>Hct (%)</th>
<th>MCV (fl)</th>
<th>MCH (pg)</th>
<th>MCHC (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>-2SD</td>
<td>M</td>
<td>-2SD</td>
<td>M</td>
</tr>
<tr>
<td>Cord blood</td>
<td>16.5</td>
<td>13.5</td>
<td>51</td>
<td>42</td>
<td>108</td>
</tr>
<tr>
<td>1-3 day</td>
<td>18.5</td>
<td>14.5</td>
<td>56</td>
<td>45</td>
<td>108</td>
</tr>
<tr>
<td>1 week</td>
<td>17.5</td>
<td>13.5</td>
<td>54</td>
<td>42</td>
<td>107</td>
</tr>
<tr>
<td>2 week</td>
<td>16.6</td>
<td>13.4</td>
<td>53</td>
<td>41</td>
<td>105</td>
</tr>
<tr>
<td>1 month</td>
<td>14.9</td>
<td>10.7</td>
<td>44</td>
<td>33</td>
<td>101</td>
</tr>
<tr>
<td>2 month</td>
<td>11.2</td>
<td>9.4</td>
<td>35</td>
<td>28</td>
<td>95</td>
</tr>
<tr>
<td>6 month</td>
<td>12.6</td>
<td>11.1</td>
<td>36</td>
<td>31</td>
<td>76</td>
</tr>
<tr>
<td>6 mo-2 age</td>
<td>12</td>
<td>10.5</td>
<td>36</td>
<td>31</td>
<td>78</td>
</tr>
<tr>
<td>2-6 age</td>
<td>12.5</td>
<td>11.5</td>
<td>37</td>
<td>34</td>
<td>81</td>
</tr>
<tr>
<td>6-12 age</td>
<td>13.5</td>
<td>11.5</td>
<td>40</td>
<td>35</td>
<td>86</td>
</tr>
<tr>
<td>12-18 age (girl)</td>
<td>14</td>
<td>12</td>
<td>41</td>
<td>37</td>
<td>90</td>
</tr>
<tr>
<td>12-18 age (boy)</td>
<td>14.5</td>
<td>13</td>
<td>43</td>
<td>36</td>
<td>88</td>
</tr>
</tbody>
</table>

Hb: Hemoglobin, Hct: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, M: Mean
DIFFERENTIAL DIAGNOSIS

Hb, MCV, ferritin and serum iron are reduced and TIBC is increased in IDA. Reticulocyte crisis appearing 7 days after beginning iron treatment is an important finding supporting IDA diagnosis. Diseases causing microcytic anemia such as hypochromic microcytic anemia-inducing thalassemia, sideroblastic anemia, anemia of chronic disease (ACD) (collagen tissue diseases, chronic kidney failure, malignity, etc.), lead intoxication, copper deficiency and zinc poisoning must be evaluated in the differential diagnosis of IDA. While serum iron levels are normal or increased in thalassemia, they are decreased in IDA and ACD. TIBC increases in IDA but decreases in ACD. Hemoglobin electrophoresis is required for the differential diagnosis of thalassemia. Anemia of chronic disease is caused by inflammation. Although this anemia is usually called anemia of chronic disease, it may also develop in acute inflammatory cases such as pneumonia and cellulitis. In inflammatory anemia, both iron absorption and its transfer from reticuloendothelial cells to erythroid precursors are disrupted as part of the inflammatory process. While anemia is mild (>10 g/dL) in acute inflammation, it is more severe in chronic inflammation. Inflammatory anemia may be differentiated from IDA through patient history and clinical findings, low serum iron with reduced total iron binding capacity, normal or increased ferritin, and a serum transferrin receptor/ferritin level ratio of <2.5 (Table 5).

If the patient exhibits iron deficiency along with ACD, diagnosis becomes more difficult solely based on parameters used to diagnose iron deficiency. In such complex cases, bone marrow aspiration and evaluation of iron conditions inside the bone marrow through staining may be necessary. sTfR is a parameter used to differentiate IDA from ACD since it is not an acute phase reactant (22, 51-53). Another disease that must be considered in the differential diagnosis of IDA is beta thalassemia. Beta thalassemia may be differentiated from IDA by normal RDW, increased Hb A2 levels in Hb electrophoresis (>3.5%) and increased RBC levels. Table 5 compares the use of laboratory studies in the diagnosis of the most common microcytic anemias.
Table 5: Laboratory studies differentiating the most common microcytic anemias

<table>
<thead>
<tr>
<th>Study</th>
<th>Iron Deficiency Anemia</th>
<th>α or β Thalassemia</th>
<th>Anemia of Chronic Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>RBC</td>
<td>↓</td>
<td>N-↑</td>
<td>N</td>
</tr>
<tr>
<td>RDW</td>
<td>↑</td>
<td>N</td>
<td>N-↑</td>
</tr>
<tr>
<td>MCV</td>
<td>↓</td>
<td>↓</td>
<td>N-↓</td>
</tr>
<tr>
<td>Serum Fe</td>
<td>↓</td>
<td>N</td>
<td>↓</td>
</tr>
<tr>
<td>TIBC</td>
<td>↑</td>
<td>N</td>
<td>↓</td>
</tr>
<tr>
<td>TS</td>
<td>↓</td>
<td>N</td>
<td>N-↓</td>
</tr>
<tr>
<td>sF</td>
<td>↓</td>
<td>N</td>
<td>↑</td>
</tr>
<tr>
<td>TR</td>
<td>↑</td>
<td>N</td>
<td>↑</td>
</tr>
<tr>
<td>BM Fe</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>FEP</td>
<td>↑</td>
<td>N</td>
<td>↑</td>
</tr>
<tr>
<td>RHC</td>
<td>↓</td>
<td>N</td>
<td>N-↓</td>
</tr>
</tbody>
</table>


**TREATMENT**

Basic treatment principles should be eliminating the cause, replenishing the deficiency (oral treatment, parenteral treatment, erythrocyte transfusion), diet and nutrition arrangements, informing and educating the family. To ensure the effectiveness and benefits of the iron treatment, the condition that causes iron deficiency should be investigated and eliminated.

The diet contains two forms of iron (heme iron and non-heme iron). Non-heme iron comes from non-meat food sources, while heme-iron comes from meat products. Heme iron is absorbed much more than non-heme iron but only 10% of the iron in the diet is heme iron. While the absorption of heme iron is only slightly affected by environmental factors, non-heme iron is affected by other nutrients and ambient pH. Therefore, an increased amount of meat and meat products is crucial in preventing and treating iron deficiency. Other iron rich products include egg, well-cooked dry legumes, green and dried vegetables. Oral treatment is preferred in iron treatment because it is cheaper and has few side effects. Iron preparations may be ferrous (+2) or ferric (+3). Fe$^{+2}$ (ferrous) iron is absorbed better than Fe$^{+3}$ (ferric) iron (17, 38, 43, 46, 47). The ferric type must first be converted to ferrous type for absorption. Therefore, the biologically important iron is ferrous iron with a valence of +2. Divalent ferrous preparations used in oral treatment are ferrous sulphate, ferrous gluconate,
ferrous fumarate and ferrous succinate. Ferrous sulphate is the most common, cheapest and effective preparation. Ferrous sulphate has high absorption and high bioavailability but it may cause digestive system side effects such as irritation, constipation, nausea and epigastric pain.

Oral preparations should be administered between meals and on empty stomach for 6-12 weeks in doses of 4-6 mg/kg/day as elemental iron (18, 56). Administering iron along with lemonade or orange juice that contains vitamin C increases its absorption through the intestines, while its administration along with milk reduces it. When the patient’s hemoglobin level becomes normal for the patient’s age, half doses of iron preparation should be continued for 4-8 weeks to fill the iron stores. Teeth may temporarily be stained black when oral iron is being administered (particularly in drop or syrup form). Side effects of iron treatment in infants under one year may be reduced by administering a daily dose 30 minutes before breakfast. The family should be informed that the color and smell of the stool may change, that the stool may be darker in color.

Parenteral treatment may be considered for patients who can't tolerate oral treatment, in cases where anemia must be rapidly treated, in cases of GIS absorption disruption and acute diarrhea. Parenteral iron requirement can be calculated using the formula (Normal Hb-Patient Hb/100) x Blood Volume (mL) x 3.4 x1.5 = Total Parenteral Iron dose (mg). The result gives the iron deficiency in mg. This amount is divided into 6 equal doses (daily maximum dose 100 mg) and is administered via deep IM injection (17, 37, 38, 50, 51).

Blood transfusion is not necessary in IDA without complications. However, in emergencies such as sudden blood loss, decompensated heart failure in which Hb levels have to be rapidly increased, angina, severe pulmonary disease and cerebral ischemia, an erythrocyte suspension of 5-10 mg/kg may be administered in 3-4 hours, monitoring the vital signs (17).

Response to treatment; findings such as restlessness, loss of appetite, etc. rapidly disappear within 24-48 hours after treatment and the patient begins gaining weight (56). In severe IDA, response to oral iron treatment begins on day 2-3 along with bone marrow response, erythroid hyperplasia and reticulocyte response and reaches its peak in days 7-8. Reticulocyte response may not be apparent in mild and medium anemias. Effective iron treatment results in increased Hb levels in 4-30 days (0.25-0.4 g/dL/day). Iron stores fill within 1-3 months. Microcytosis is eliminated in approximately 3-4 months.

While the patient is being treated for anemia, anemia-inducing nutrition mistakes should be fixed, and the patient and his/her family should be informed about the disease and ways of preventing it. To avoid
iron overloading in the body, oral iron treatment must not exceed five months (17, 38, 43, 52, 54) (Table 6).

Table 6: Responses to iron therapy in iron-deficiency anemia

<table>
<thead>
<tr>
<th>Time after iron administration</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-24 hr</td>
<td>Replacement of intracellular iron enzymes; subjective improvement; decreased irritability; increased appetite</td>
</tr>
<tr>
<td>36-48 hr</td>
<td>Initial bone marrow response; erythroid hyperplasia</td>
</tr>
<tr>
<td>48-72 hr</td>
<td>Reticulocytosis, peaking at 5-7 bdays</td>
</tr>
<tr>
<td>4-30 days</td>
<td>Increase in hemoglobin level</td>
</tr>
<tr>
<td>1-3 mo</td>
<td>Repletion of stores</td>
</tr>
</tbody>
</table>

PROTECTION

Iron supplement programs in developing countries have been largely effective in the mitigation of the problem. Although mother’s milk doesn’t contain much iron, its bioavailability is very high and therefore the importance of mother’s milk should be emphasized, mothers should be encouraged and supported (37, 43). Feeding infants a mother's milk-only diet for the first 6 months, continuing breastfeeding up to age two, supported by appropriate iron-rich foods after the sixth month, increasing the consumption of iron-rich traditional foods and educating parents on nutrition will be effective in the prevention of anemia. Mild iron deficiency anemia doesn't affect the fetus in pregnancy, but mothers with medium or severe anemia should receive iron supplementation during pregnancy since their babies may develop IDA. If mother’s milk is not accessible, baby formulas containing 6-12 mg iron per liter should be preferred. Cow’s milk should not be recommended in the infant’s first year because it is poor in iron. Furthermore, consumption of more than 500 ml of cow’s milk should be prevented after age 1 (50). The diet should include red meat, fish and foods that contain vitamin C, which facilitates iron absorption; the consumption of tea, phytates and phosphates that disrupt iron absorption (37, 38). To prevent pediatric IDA, iron prophylaxis of 1 mg/kg/day after the 4th month for term infants and 2 mg/kg/day after the 2nd month for premature infants (Table 7) (56). It was shown that these measures decrease the prevalence of iron deficiency in nursing children.
Table 7: Daily iron requirements according to age groups and genders (56).

<table>
<thead>
<tr>
<th>Age group</th>
<th>Iron requirement (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premature</td>
<td>2</td>
</tr>
<tr>
<td>Infant ve child</td>
<td>1</td>
</tr>
<tr>
<td>Adolescent</td>
<td>2-3</td>
</tr>
<tr>
<td>Boy</td>
<td>1</td>
</tr>
<tr>
<td>Girl</td>
<td>2-3</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>3-4</td>
</tr>
</tbody>
</table>
REFERENCE


47. Holmberg L. Soluble transferrin receptor in the diagnosis of anaemia and iron deficiency in childhood. Acta Paediatr 2000; 89(10); 1152-1153.


EFFECTS OF A TRAINING PROGRAMME ON THE AWARENESS OF INADVERTENT PERIOPERATIVE HYPOTHERMIA AMONG SURGICAL NURSES

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INTRODUCTION

Research reports that inadvertent perioperative hypothermia is estimated to affect 70% of the surgical patients and is associated with adverse clinical outcomes longer hospitalizations and increased costs (1). It is crucial but often an underestimated problem frequently seen during the perioperative period, leading to severe complications (1-3). The core temperature of the body is regulated through behavioral and physiological responses, by generating heat if the temperature is too low and by lowering it if, on the other hand, is too high. Unconscious people and individuals under anesthesia cannot adopt proper behavioral responses, as a consequence of which the risk of hypothermia increases (4.5). IPH sets in as a result of the suppression of the thermoregulation mechanisms managed by the hypothalamus due to anesthesia and exposure of wide skin surfaces to cold temperatures for a long time during the intraoperative period (3.6). Hypothermia occurs when the body core temperature is lower than 36°C (7). Apart from the cases in which patients should undergo induced hypothermia during cardiac surgery hypothermia develops in most surgical patients (8-10). Patients are at high risk of hypothermia during the pre-, intra- and postoperative phases. The thermal balance of a hypothermic patient is restored in 2-5 hours; hypothermia must therefore be prevented before it sets in. It is a common consequence of anaesthesia, which increases morbidity and potentially increases mortality (11). Prevention of perioperative hypothermia and having a clear understanding of its signs and symptoms including its complications, and using effective active and passive heating methods are among the principal responsibilities of the nurses (12). The present study performed in a descriptive research design aimed to assess the IPH awareness of nurses working in the surgical units of a university hospital before, during and after a training programme. This study sought to address the following
question: **Q1.** Do the nurses working in the surgical units have a higher awareness level concerning inadvertent perioperative hypothermia immediately and three months after the IPH training when compared with their awareness before the training? **Q2.** Can be inadvertent perioperative hypothermia prevented by training?

**METHODS**

**Research Design and Sample**

This study was conducted descriptively. This study was conducted between February and May 2019 with nurses working in the surgical units of a university hospital to assess their awareness concerning IPH before, during and after a training program. The study population consisted of 260 nurses serving in the surgical units of the involved hospital. Aiming to examine the entire population, the researchers opted to use the technique of total population sampling in this study. However, due to various reasons such as maternity leave, leave for military service, annual leave and refusal to participate in this research project, this study was completed with a final sample that comprised 200 surgical nurses.

**Data Collection**

Demographics Form and an Inadvertent Perioperative Hypothermia Assessment Form were used to collect data in this study. The forms were developed by the researchers in accordance with the relevant literature (1,3,10,13)

**Demographics Form**

This form included four questions aiming to solicit surgical nurses’ personal information (e.g., age, educational background, work unit and length of service).

**Inadvertent Perioperative Hypothermia Assessment Form**

The inadvertent perioperative hypothermia awareness was assessed on the basis of 41 questions, whereby each item of questions 2, 16 and 18 were accepted as a question. Each response with the option false was awarded 0 point, and each response with the option true got 1 point, with 41 being the highest score. The scores obtained were converted into percent in our research. The internal consistency was measured using Cronbach’s alpha test. The Cronbach’s alpha coefficients of the responses, which turned out to be .729, .727 and .754, respectively, before, immediately after and three months, after the training show that the “Inadvertent Perioperative Hypothermia Assessment Form” is a very reliable tool. Nurses were visited by the researcher during their working hours based on their working schedules, and all nurses were informed about this study’s aim and education. Study data were collected using face-
to-face interviews conducted before, immediately after and three months after the 30-minutes interactive IPH training.

**Study Question**

This study sought to address the following question:

**Q1.** Do the nurses working in the surgical units have a higher awareness level concerning inadvertent perioperative hypothermia immediately and three months after the IPH training when compared with their awareness before the training?

**Q2.** Can be inadvertent perioperative hypothermia prevented by training?

**Ethical Considerations**

The ethical clearance required to conduct this study was obtained from the Ethics Board for Non-invasive Clinical Research affiliated to the Dean’s Office of XXX, XXXX No:2018.149.10.14 and also from the Directorate of Health Research and Application Centre also based in the same university. This study is master's thesis. All the surgical nurses who agreed to participate in this study were informed about this research project, and oral consent was obtained from all the participating nurses.

**Statistical Analysis**

NCSS (Number Cruncher Statistical System) 2007 Statistical Software program (NCSS LLC, Kaysville, Utah, USA) was used to analyses the data obtained in this study. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum and maximum values) were used to evaluate the study data. While the Kolmogorov-Smirnov test and Box Plot graphs were used to test the normal distribution of the study data, Kolmogorov-Smirnov test and pot-hoc test were used to assess the variables that showed no normal distribution by groups. For group-intern evaluations, Friedman test and Bonferroni-corrected Wilcoxon Signed Rank test were used. The results were evaluated at a 95% confidence interval and a significance level of p<0.05.

**RESULTS**

The mean age of the nurses who participated in this study was 28.65±5.32 years and their mean length of service was 6.57±5.42 years, and the majority had only 1-5 years of experience. We think this validates the need for this education given that most of the staff is newer (**Table 1**).

While most of the nurses before the training responded the following statement “Perioperative hypothermia is a significant problem for patients” as true, they responded the following statement “Perioperative hypothermia facilitates the development of infections at the
incision area” as false. In the period immediately after the training, while most of the nurses responded the following statement “Perioperative hypothermia is a significant problem for patients” as true, they responded the following statement “Patients who undergo pre-warming in the post-operative recovery unit have a lower risk of hypothermia in the intra- and postoperative period” as false. Three months after the training, while most of the nurses responded the following statement “Perioperative hypothermia is a significant problem for patients” as true, they responded the following “Patients who undergo pre-warming in the post-operative recovery unit have a lower risk of hypothermia in the intra- and postoperative period” as false (Table 2).

The findings indicate that the IPH awareness scores of the nurses varied between 29.27 and 92.68 before the training, and that mean scores recorded immediately after and three months after the training were higher than those recorded before the training. The highest awareness mean scores were those achieved in the phase immediately after the training session (Table 3).

The results reveal, based on the influence of educational background on the awareness scores, that there was no statistically significant difference concerning the phases before, immediately after and three months after the training (p=0.667; p=0.468; p=0.274, respectively). Another result that emerged based on the evaluations carried out using Bonferroni correction is that the difference in the scores achieved by the nurses with high school diploma and under- and postgraduate degrees in the phases immediately after and three months after the training was statistically significant when compared with the scores they had before the training (p<0.001; p=0.001, respectively). This study also showed, on the basis of the abovementioned evaluations, that the difference in the scores of the nurses with a bachelor’s degree recorded in the phases immediately after and three months after the training was statistically significant when compared with their scores recorded before the training, and there was also a statistically significant difference between their scores recorded immediately after the training and scores they achieved three months after it (p<0.001; p<0.001; p<0.001, respectively) (Table 4).

The results broken down by work units indicate a difference concerning the awareness scores recorded before the training (p=0.015). Data evaluated using Bonferroni correction demonstrate that the nurses working in the intensive care unit had IPH awareness scores higher than those of the nurses serving in other wards (p=0.023). Records by other wards did not show any significant difference (p>0.05) (Table 5).
The demographic data about the surgical nurses who participated in our study show that the majority of the nurses were in the age group of 26-35 and had a bachelor’s degree. More than half of the nurses expressed having worked in a surgery department already for a length between one to five years. Cakir & Cilingir reported that the nurses who participated in their study were in the age group of 26-35 years and that the majority had graduate and postgraduate degree with a length of service between 0 and 15 years (14). Mendoza et al. report that most of the participants in their study noted a length of service between one to five years, and half of were in the 20-30 age group (15). Participant demographics in our study, such as age group, work units, educational background and lengths of service, are similar to previous studies performed with a similar sample.

Inadvertent perioperative hypothermia is the condition in which the body core temperature drops below 36°C (10,13). IPH increases the incidence of complications, such as cardiac disorders, incision infections, bleeding, shivering, respiratory disorders and delays in wound healing, consequently disturbing patients’ comfort and leading to longer hospitalisations, higher costs and increased mortality (1,7,16-19). Almost all the nurses were in agreement that “IPH is a significant problem for patients” and chose the response option true for this statement in all the phases of the training. Minimal differences in body temperature may cause changes in the pharmacodynamics and pharmacokinetics of the agents/drugs used in the perioperative period. In case when the body temperature drops by 2°C, the reaction time of neuromuscular blocking agents increases by 100%, a condition that may lead to long-term muscle weakness (12). The majority of the nurses had knowledge, already before they received the IPH training, as to the complication that IPH increases the effects of neuromuscular blocking agents and triggers muscle weakness, and that the patient needs more oxygen if shivering sets in and that it leads to longer hospital stays and increased costs. Research reports that IPH causes shivering, as a result of which oxygen consummation increases, provoking, in turn, hypoxia and acidosis (20-22). An increase in the consumption of oxygen due to shivering was the most expressed complication before the training. In a similar study conducted by Giuliano & Hendricks (2017), the IPH complications reported by the most of nurses were shivering, surgical area infection cardiac events, by the less than half of nurses were bleeding and pressure wounds (1). In the study performed by Cakir & Cilingir, the most of the ward nurses and of the nurses working in the recovery unit expressed having knowledge that the development of shivering provoked an increase in oxygen consummation (14). Hegart et al. reported, on the other hand, that half of the nurses who participated in their research had knowledge as to this complication (23).
The study findings indicate that, even though the nurses were aware of the complications IPH could provoke, they still needed to be further informed in this respect. It may be assumed that shivering can be reduced by precautions taken to prevent the emergence of hypothermia. The results of the present study are consistent with the results revealed in previous studies.

The results show that the scores of the nurses before and after the training they received to raise their IPH awareness varied between 29.27 and 92.68. The highest mean score was that that was recorded immediately after the training. In their study performed to investigate the level of knowledge on hypothermia before and after a training session, Mendoza et al. reported that the participants had mean scores, before and after the training, a result indicating higher awareness scores after the training (15). Results indicating higher scores recorded after the training in our study match those observed in his study. The study concludes that periodical in-service training to be offered every month on a regular basis would be effective in preventing and manage IPH and enhance IPH awareness.

The awareness scores broken down by work units show that before the training, ICU nurses had scores higher than those of ward nurses. The scores by work units also indicate no difference between the scores recorded immediately after the training and three months after it. The more complex structure of the practices in an ICU compared with wards and the necessity of continuous monitoring of the hemodynamics of patients hospitalized in an ICU and the requirement of prompt intervention in such units led us to conclude that nurses working in critical care units are more conscious than others in respect of keeping their knowledge and skills updated.

STRENGTHS AND LIMITATIONS

The strength of this study is that this has been conducted in a sample that included the most common surgical units. The results of this study will contribute to the literature on the current awareness of surgical nurses toward IPH and will keep this issue current. There are some limitations that should be considered in this study. The study data are limited to nurses working in the surgical units of a university hospital within a province of Turkey, which limits the generalization of the results to all nurses. It also would be interesting to follow up this study with a different study to investigate whether surgical nurses' awareness change over time. An interesting follow up may be to evaluate any change in temperature of negative patient outcomes. Ideally, the education would not just impact knowledge but also nursing practice and turn to show up as improved outcomes or changes to clinical variables like temperature.
CONCLUSION

The findings of this study revealed that the nurses had a higher level of IPH awareness in the phases immediately after and three months after the training when compared with their awareness before the training. This study concludes that usage of IPH guides in hospitals, continual updating of the relevant knowledge, organization of monthly in-service training on a regular basis supported with case reports to maintain the available knowledge would be effective in preventing and managing IPH.
REFERENCES

Table 1. Distribution of Demographic Data

<table>
<thead>
<tr>
<th>Age (year)</th>
<th>Min-Max</th>
<th>Min-Max</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>19-46</td>
<td>28.65±5.32</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>X±SD</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>28.65±5.32</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Educational Background; n (%)</th>
<th>High School</th>
<th>Undergraduate degree</th>
<th>Graduate degree</th>
<th>Postgraduate degree</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20(10)</td>
<td>12(6)</td>
<td>148(74)</td>
<td>20(10)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Length of Service (year)</th>
<th>Min-Max</th>
<th>Mean ± ss</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-27</td>
<td>6.57±5.42</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Length of Service (year); n(%)</th>
<th>1-5 years</th>
<th>6-10 years</th>
<th>11-15 years</th>
<th>16-20 years</th>
<th>&gt;20 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>107(53.5)</td>
<td>51(25.5)</td>
<td>30(15)</td>
<td>5(2.5)</td>
<td>7(3.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Unit; n (%)</th>
<th>Operation Theatre</th>
<th>ICU</th>
<th>Ward</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>23(11.5)</td>
<td>65(32.5)</td>
<td>112(56.0)</td>
</tr>
</tbody>
</table>
Table 2. Distributions on Responses to Inadvertend Perioperative Hypothermia

<table>
<thead>
<tr>
<th>Perioperative hypothermia is a significant problem for patients.</th>
<th>Before the Training</th>
<th>During the Training</th>
<th>3 Months after the Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>False</td>
<td>No Idea</td>
<td>True</td>
</tr>
<tr>
<td>192 (96)</td>
<td>2 (1)</td>
<td>6 (3)</td>
<td>200 (100)</td>
</tr>
</tbody>
</table>

Anaesthesia induction should not be started unless body temperature rises to 36 °C.  

<table>
<thead>
<tr>
<th>Anaesthesia induction should not be started unless body temperature rises to 36 °C.</th>
<th>Before the Training</th>
<th>During the Training</th>
<th>3 Months after the Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>False</td>
<td>No Idea</td>
<td>True</td>
</tr>
<tr>
<td>124 (62)</td>
<td>17 (8.5)</td>
<td>59 (29.5)</td>
<td>190 (95)</td>
</tr>
</tbody>
</table>

Perioperative hypothermia increases the effect of neuromuscular blocking agents and leads to long-term muscle weakness.  

<table>
<thead>
<tr>
<th>Perioperative hypothermia increases the effect of neuromuscular blocking agents and leads to long-term muscle weakness.</th>
<th>Before the Training</th>
<th>During the Training</th>
<th>3 Months after the Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>False</td>
<td>No Idea</td>
<td>True</td>
</tr>
<tr>
<td>138 (69)</td>
<td>9 (4.5)</td>
<td>53 (26.5)</td>
<td>181 (90.5)</td>
</tr>
</tbody>
</table>

Patients who undergo pre-warming in the post-operative recovery unit have a lower risk of hypothermia in the intra- and postoperative period.  

<table>
<thead>
<tr>
<th>Patients who undergo pre-warming in the post-operative recovery unit have a lower risk of hypothermia in the intra- and postoperative period.</th>
<th>Before the Training</th>
<th>During the Training</th>
<th>3 Months after the Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>False</td>
<td>No Idea</td>
<td>True</td>
</tr>
<tr>
<td>129 (64.5)</td>
<td>37 (18.5)</td>
<td>34 (17)</td>
<td>162 (81)</td>
</tr>
</tbody>
</table>

Perioperative hypothermia disturbs the drug metabolism.  

<table>
<thead>
<tr>
<th>Perioperative hypothermia disturbs the drug metabolism.</th>
<th>Before the Training</th>
<th>During the Training</th>
<th>3 Months after the Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>False</td>
<td>No Idea</td>
<td>True</td>
</tr>
<tr>
<td>109 (54.5)</td>
<td>27 (13.5)</td>
<td>64 (32)</td>
<td>172 (86)</td>
</tr>
</tbody>
</table>

Oxygen consumption of patients increases when shivering sets in due to perioperative hypothermia.  

<table>
<thead>
<tr>
<th>Oxygen consumption of patients increases when shivering sets in due to perioperative hypothermia.</th>
<th>Before the Training</th>
<th>During the Training</th>
<th>3 Months after the Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>False</td>
<td>No Idea</td>
<td>True</td>
</tr>
<tr>
<td>162 (81)</td>
<td>20 (10)</td>
<td>18 (9)</td>
<td>189 (94.5)</td>
</tr>
</tbody>
</table>

Perioperative hypothermia increases the incidence of nausea-vomiting.  

<table>
<thead>
<tr>
<th>Perioperative hypothermia increases the incidence of nausea-vomiting.</th>
<th>Before the Training</th>
<th>During the Training</th>
<th>3 Months after the Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>False</td>
<td>No Idea</td>
<td>True</td>
</tr>
<tr>
<td>116 (58)</td>
<td>24 (12)</td>
<td>60 (30)</td>
<td>174 (87)</td>
</tr>
</tbody>
</table>

Perioperative hypothermia causes longer hospitalisations and higher costs.  

<table>
<thead>
<tr>
<th>Perioperative hypothermia causes longer hospitalisations and higher costs.</th>
<th>Before the Training</th>
<th>During the Training</th>
<th>3 Months after the Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>False</td>
<td>No Idea</td>
<td>True</td>
</tr>
<tr>
<td>152 (76)</td>
<td>19 (9.5)</td>
<td>29 (14.5)</td>
<td>194 (97)</td>
</tr>
</tbody>
</table>

Perioperative hypothermia facilitates the development of infections at the incision area.  

<table>
<thead>
<tr>
<th>Perioperative hypothermia facilitates the development of infections at the incision area.</th>
<th>Before the Training</th>
<th>During the Training</th>
<th>3 Months after the Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>False</td>
<td>No Idea</td>
<td>True</td>
</tr>
<tr>
<td>114 (57)</td>
<td>46 (23)</td>
<td>40 (20)</td>
<td>178 (89)</td>
</tr>
</tbody>
</table>

Major surgery increases the risk of hypothermia.  

<table>
<thead>
<tr>
<th>Major surgery increases the risk of hypothermia.</th>
<th>Before the Training</th>
<th>During the Training</th>
<th>3 Months after the Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>True</td>
<td>False</td>
<td>No Idea</td>
<td>True</td>
</tr>
<tr>
<td>170 (85)</td>
<td>5 (2.5)</td>
<td>25 (12.5)</td>
<td>196 (98)</td>
</tr>
</tbody>
</table>
Table 3. Findings emerging from Inadvertent Perioperative Hypothermia Awareness Scores

<table>
<thead>
<tr>
<th>Awareness Scores</th>
<th>Minimum</th>
<th>Maximum</th>
<th>X±SD</th>
<th>Cronbach’s alpha</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before the Training (BT)</td>
<td>27.27</td>
<td>92.68</td>
<td>61.77±13.33</td>
<td>0.729</td>
</tr>
<tr>
<td>Immediately after the Training (IAT)</td>
<td>43.90</td>
<td>100</td>
<td>82.76±10.16</td>
<td>0.727</td>
</tr>
<tr>
<td>3 Months after the Training (3M AT)</td>
<td>39.02</td>
<td>97.56</td>
<td>77.56±11.78</td>
<td>0.754</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Difference</th>
<th>X±SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAT – BT</td>
<td>21.00±14.67</td>
<td>0.001**</td>
</tr>
<tr>
<td>3M AT – BT</td>
<td>15.79±14.84</td>
<td>0.001**</td>
</tr>
<tr>
<td>3M AT – IAT</td>
<td>-5.21±13.25</td>
<td>0.001**</td>
</tr>
</tbody>
</table>

**p<0.01 Before the Training (BT). Immediately after the Training (IAT). 3 Months after the Training (3MAT)
Table 4. Evaluation of Inadvertent Perioperative Hypothermia Awareness Scores According to Educational Background

<table>
<thead>
<tr>
<th>Awareness Scores</th>
<th>Educational Background</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>High school</td>
<td>Undergraduate degree</td>
<td>Graduate degree</td>
<td>Postgraduate degree</td>
<td></td>
</tr>
<tr>
<td></td>
<td>X±SD</td>
<td>X±SD</td>
<td>X±SD</td>
<td>X±SD</td>
<td></td>
</tr>
<tr>
<td>BT</td>
<td>59.76±12.45</td>
<td>59.15±14.07</td>
<td>61.93±13.73</td>
<td>64.15±10.91</td>
<td>0.667</td>
</tr>
<tr>
<td>IAT</td>
<td>80.00±10.00</td>
<td>85.37±10.3</td>
<td>83.06±10.33</td>
<td>81.83±9.04</td>
<td>0.468</td>
</tr>
<tr>
<td>3MAT</td>
<td>77.07±14.03</td>
<td>73.37±14.69</td>
<td>77.42±11.34</td>
<td>81.59±10.51</td>
<td>0.274</td>
</tr>
<tr>
<td></td>
<td><strong>p&lt;0.01</strong></td>
<td><strong>p=0.001</strong></td>
<td><strong>p=0.001</strong></td>
<td><strong>p=0.001</strong></td>
<td></td>
</tr>
<tr>
<td>Difference</td>
<td><strong>p=0.001</strong></td>
<td><strong>p=0.001</strong></td>
<td><strong>p=0.001</strong></td>
<td><strong>p=0.001</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20.24±13.82</td>
<td>26.22±13.56</td>
<td>21.13±15.19</td>
<td>17.68±11.92</td>
<td>0.460</td>
</tr>
<tr>
<td>3MAT – BT</td>
<td>17.32±16.63</td>
<td>14.23±18.86</td>
<td>15.49±14.85</td>
<td>17.44±10.65</td>
<td>0.886</td>
</tr>
<tr>
<td>3MAT – IAT</td>
<td>-2.93±14.3</td>
<td>-11.9±18.56</td>
<td>5.64±12.79</td>
<td>0.24±10.5</td>
<td>0.999</td>
</tr>
</tbody>
</table>

**p<0.01  Before the Training (BT). Immediately after the Training (IAT). 3 Months after the Training (3M AT)
Table 5. Evaluation of Inadvertent Perioperative Hypothermia Awareness Scores According to the Unit Worked

<table>
<thead>
<tr>
<th>Awareness Scores</th>
<th>UNIT</th>
<th></th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Operation Theatre</td>
<td>Intensive care unit</td>
<td>Ward</td>
</tr>
<tr>
<td></td>
<td>X±SD</td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>BT</td>
<td>64.58±16.57</td>
<td>64.92±14.15</td>
<td>59.36±11.64</td>
</tr>
<tr>
<td>IAT</td>
<td>85.47±9.05</td>
<td>84.02±10.19</td>
<td>81.49±10.26</td>
</tr>
<tr>
<td>3MAT</td>
<td>80.91±10.55</td>
<td>78.35±11.83</td>
<td>76.42±11.93</td>
</tr>
<tr>
<td>Difference</td>
<td>X±SD</td>
<td>X±SD</td>
<td>X±SD</td>
</tr>
<tr>
<td>IAT – BT</td>
<td>20.89±20.1</td>
<td>0.001**</td>
<td>19.1±13.58</td>
</tr>
<tr>
<td>3MAT – BT</td>
<td>16.33±14.02</td>
<td>0.001**</td>
<td>13.43±15.38</td>
</tr>
<tr>
<td>3MAT – IAT</td>
<td>-4.56±14.9</td>
<td>0.469</td>
<td>-5.67±12.13</td>
</tr>
</tbody>
</table>

**p<0.01  Before the Training (BT). Immediately after the Training (IAT). 3 Months after the Training (3M AT)**
CHAPTER IV

MAJOR VIRAL PANDEMICS AND THEIR ORIGIN:
ZOONOSES

Lale Turkmen
(Asst. Prof. Dr.), Gazi University, e-mail: lturkmen@gazi.edu.tr
0000-0003-4856-3809

INTRODUCTION

Zoonoses are described as diseases and infections, which are transmitted naturally between humans and vertebrate animals (6,20,21). Globally, it is estimated that about one billion cases of disease and millions of deaths occur from zoonoses every year. Zoonoses are some 60 per cent of emerging infectious diseases reported globally. Over the last three decades, more than 30 new human pathogens have been detected, 75% of which originated in animals (20). Human pathogens include zoonotic species from all taxa. Approximately that infect humans 95% of helminths, 80% of viruses, 70% of protozoans 50% of bacteria, and 40% of fungi are zoonotic. Most of the reservoirs identified are mammals (roughly 80%) or fewer birds. In addition, humans share some pathogens with invertebrates that are vectors or intermediate hosts (10).

Why are zoonotic infections important: There are several reasons why zoonoses pose a threat to global health: the regular emergence and spread of new pathogens that cause zoonotic diseases (particularly viruses); high epidemic potentials; high mortality and morbidity rates; lack of treatment and vaccines for many; and the devastating economic consequences they are cause in health systems (20,21).

How do Pathogens Spread over from Animals to People? Pathogen spread occurs when a host species-specific pathogen infects a new host species (animal or human) directly or through an intermediate host species. As pathogens exploit new niches and adapt to new hosts, the development of zoonotic diseases can be considered a result of pathogen ecology and evolution (20).
Factors causing the occurrence of zoonoses: In animal and human populations several factors contribute to the transition between species. Many ecological, behavioral and socioeconomic factors contribute to the spread of zoonotic diseases, including the frequent emergence of new pathogens, population growth, poverty, poor health systems, international travel and trade, climate change, deforestation, intensification of agriculture and biodiversity loss. As a result, humans and animals are closer than ever with the diseases they carry (10,16,18,20,21).

An Overview Major Viral Pandemics in Recent History

1. Coronaviruslar: SARS, MERS and COVID-19:
Coronaviruses belong to the Coronavirinae subfamily of the Coronaviridae family and to the order Nidovirales (International Committee on Taxonomy of Viruses). Based on their phylogenetic relationships and genomic structures, this subfamily comprises four genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus. Severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are two highly contagious and pathogenic viruses that emerged in humans at the beginning of the 21st century. Since circulating coronaviruses in humans mostly cause mild infections in people with sufficient immune systems, these diseases were not thought to be highly pathogenic to humans. Both viruses likely originated from bats, and genetically related coronaviruses related to SARS-CoV and MERS-CoV have been discovered in bats worldwide. (2,3,8,15,25). On December 31, 2019, a new type of coronavirus (2019-nCoV) was isolated from pneumonia cases of unknown etiology in Wuhan City, Hubei Province, China. The World Health Organization named this disease COVID-19 disease, and on March 11, 2020, it identified COVID-19 as a pandemic, both because of its alarming levels of spread and its severity. With the rapidly increasing death and disease rates in the world, the devastating effects of the COVID-19 epidemic on health, economy and security continue. (12.22). For the first time in history, there is not enough scientific evidence to reveal the origin of SARS-CoV-2, the causative agent of a pandemic, and the potential role of animals. However, researchers report that bats will act as reservoirs due to their genomic similarity with coronaviruses similar to SARS-CoV(3).
2. Pandemic Influenza: A global epidemic of a new influenza A virus is an influenza pandemic. Three flu pandemics existed in the 20th century: "Spanish Flu" "Asian Flu" and "Hong Kong Flu" (23). Modern virology has revealed pathways for the emergence of pandemic influenzae. Influenza A is a zoonotic virus that is found as a reservoir in wild birds. These avian viruses, in rare circumstances, infiltrate human populations and transform into pandemic viruses. However, the time required for avian viruses to adapt to their new host is unknown (7, 9, 11).

2.1.1. The Spanish Flu (A H1N1): An extraordinarily deadly influenza pandemic caused by the H1N1 influenza A virus was the Spanish flu, also known as the 1918 flu pandemic. This pandemic, which took place in four successive waves between 1918 and 1920, affecting nearly a third of the world population at the time, was one of the deadliest epidemics in human history, with between 17 million and 50 million deaths. Spanish flu arose from an H1N1 virus derived from the avian gene (9, 11, 17).

2.2.2. Asian Flu (A H2N2): The Asian flu pandemic of 1957–1958 was a global influenza A virus subtype H2N2 pandemic that originated in Guizhou, China. The number of deaths caused by the pandemic of 1957-1958 is estimated worldwide to be between 1-4 million (9, 11).

2.2.3. Hong Kong Flu (A H3N2): The Hong Kong flu, also known as the 1968 flu pandemic, was a flu pandemic that killed an estimated 1-4 million people worldwide in 1968 and 1969. Most of the deaths occurred in people aged 65 and over. This virus was described by the WHO as a new subtype and named A3. The mechanism by which this virus occurred was very similar to that of the A H2N2 virus and was attributed to the human and avian virus genetic re classification (9, 11).

New zoonotic influenza viruses can infect humans and cause a pandemic if the virus changes and spreads quickly and sustainably from person to person (9, 24).

3. Control and Prevention of Zoonotic Diseases

3.1. Challenges in Controlling Zoonotic Diseases: While the largest human infectious diseases are known to be of animal origin, there is no continuous global effort to prevent zoonotic diseases. The lack of successful coordination between the animal and
human health sectors under the "One Health" strategy is the biggest obstacle to the control of these diseases. To summarize the difficulties in controlling zoonotic diseases; insufficient knowledge of zoonotic diseases and their risks, insufficient resources and skilled manpower to control these diseases; weakness or lack of cooperation between the public health, veterinary, agriculture and wildlife sectors; insufficient cooperation in the use of resources for disease prevention and control; lack of collaboration between surveillance, clinical and laboratory services in the health sector; lack of knowledge about high-risk behaviors, including cultural and social factors; lack of evidence on some of the public health control measures (6,16,19,20,21).

CONCLUSION

The viral zoonotic outbreaks of the last century and the current COVID-19 outbreak suggest the strongest probability that the origin of future human pandemics could be zoonotic. The reality is that without appropriate living conditions and social well-being effective zoonose management is unlikely. Another fact is that without veterinary contribution, zoonoses can not be controlled. Veterinary public health may also be regarded in a country as an measure of social well-being (13). In order not to undergo another pandemic, we have to be cautious in combating zoonotic diseases. This means acknowledging the inseparability of human health, animal health and planetary health and making preparations accordingly (18).
REFERENCES


INTENSIVE CARE FOR PATIENTS WITH COVID-19: PRECAUTIONS FOR ORAL CARE

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INTRODUCTION

In the final days of 2019, the World Health Organization (WHO) was notified regarding patients with non-identified pneumonia in China’s Wuhan City. Samples from the patients contained a novel coronavirus. The novel coronavirus was designated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1), and its associated viral pneumonia is called coronavirus disease 2019 (COVID-19). As of March 11, 2020, the disease had already spread worldwide, to the extent that WHO declared a global pandemic.

The respiratory functions of patients with COVID-19 must be followed very closely. In case intubation is recommended, the decision to intubate must be made electively (2). While this pandemic has increased the number of patients in intensive care units (ICUs), patients with COVID-19 require physiological monitoring in the ICU. Airborne isolation reduces the frequency of healthcare provider assessment and nursing frequency (3).

Patients in ICUs may develop nosocomial pneumonia (NP) or ventilator-associated pneumonia (VAP). These infections are caused by microorganisms in the respiratory system and originate from the oral biofilm. Among all infections occurring in ICUs, NP accounts for approximately 25% and VAP accounts for 9%–27% of patients who are intubated (4). NP and VAP increase mortality in ICUs as well as the number of days a patient spends in critical care. NP and VAP infections also increase healthcare costs, cause prolonged hospitalization, increase the need for medication, result in more comorbidities, and increase the use of healthcare resources, including healthcare providers’ time. As healthcare resources and services are very limited during the COVID-19 pandemic, preventing infections of NP and VAP could dramatically offset this limitation.
NP and VAP can be effectively prevented by providing regular oral care to patients in ICUs. Proper oral care removes pathogenic microorganisms from the respiratory system, therefore limiting oropharyngeal infections and reducing the rate of VAP occurrence (5). The challenge exists in how best to provide oral healthcare to ICU patients with COVID-19 under pandemic conditions. We aimed to determine the most efficient standards for providing oral care during the pandemic while ensuring occupational security to prevent nurses and other healthcare professionals from being affected by the spread of SARS-CoV-2.

The exploratory qualitative studies to examin factors affecting oral healthcare protocols to identify significant factors may be useful for ICU caregivers. Also understanding how viral transmission occurs is crucial in preventing nurses from becoming infected with SARS-CoV-2 while providing oral healthcare to intubated COVID-19 patients in ICUs. It has been reported that this virus is transmitted by coughing, inhaling droplets, or sneezing (i.e., direct transmission), whereas contact transmission may occur owing to touching nasal, oral, or eye membranes (6). Saliva may also directly or indirectly be a transmission source for the spread of viruses (7). Nurses must be very careful when providing critical care because viral transmission from contact with asymptomatic COVID-19 patients has also been reported (8).

Studies have suggested that some medical procedures create aerosols, which can lead to the airborne transmission of SARS-CoV-2 (2). It is notable that viral RNA has been detected in specimens of patients with COVID-19 on the 7th day post-transmission (9). However, nasal or oropharyngeal transmission through airborne aerosols is a primary concern for nurses providing oral care to COVID-19 patients in ICUs. It could also be a concern for the public and thus requires confirmation; regardless, maximum care should be taken by ICU staff to avoid possible contamination when providing oral care for patients with COVID-19.

One therapeutic method of maintaining oral hygiene is chlorhexidine rinsing. When used as an oral care method for patients in ICUs, chlorhexidine rinsing has been reported to be effective in preventing NP and VAP (10). While some studies report the effectiveness of chlorhexidine (11, 12), its effectiveness in preventing VAP is controversial in patients with some conditions. The China National Health Commission published the Guidelines for the Diagnosis and Treatment of Novel Coronavirus Pneumonia (5th edition), which stated that chlorhexidine rinsing was not effective in destroying SARS-CoV-2. Instead, the guidelines recommended the use of oral rinses containing other oxidizing agents (e.g., 1% hydrogen peroxide or 0.2% povidone) instead of chlorhexidine to benefit from the oxidation vulnerability of SARS-CoV-2 (13).
Different oral care procedures for ICU patients have been proposed by various researchers from many countries globally. Reports suggest that it is possible to reduce the risk of VAP infection using tested care procedures while at the same time improving oral hygiene and oral health (14). Tooth brushing has been proven to be an effective method in oral healthcare protocols in ICUs; however, it is a time-consuming and difficult procedure for ICU nurses to perform. Additionally, during this procedure, a high risk of contact transmission from secretion fluids, aerosols produced by brushing, and toothbrushes that may have been contaminated is inevitable; this is a potential route for the spreading of the virus (15). Therefore, tooth brushing, whether manual or electric, is not recommended for patients in ICUs during the COVID-19 pandemic, because it creates an occupational safety risk of spreading the virus to ICU staff members and other ICU patients.

The simplest and most secure method of oral care can be provided by nurses using Toothette oral swabs (Toothette is a trademark owned by Sage Products, registered in the USA) or cotton swabs once or twice daily. Yao et al. proposed an effective oral care protocol of first cleaning the oral cavity with a Toothette swab, which also has a suction tube connection. Subsequently, hypopharyngeal suction is performed. This protocol for oral care lessens the risk of direct transmission of SARS-CoV-2 and avoids the creation of aerosols, thus minimizing the risk of airborne transmission as well (12).

**DISCUSSION**

Implementation of these new strategies widely during this pandemic is challenging. Many scientifically accepted oral care protocols pose a risk of the airborne or contact spread of SARS-CoV-2. Tooth brushing has been proven to be an effective method in oral healthcare protocols in ICUs; however, it is a time-consuming and difficult procedure for ICU nurses, and during the procedure, a high risk of contact transmission from secretion fluids, aerosols produced by brushing, and potentially contaminated toothbrushes is inevitable. While there are studies that report the effectiveness of chlorhexidine rinsing in the same setting (11, 12), its effectiveness in preventing VAP is controversial in patients with some conditions. An alternative strategy may be photodynamic therapy (PDT). The combination of a photosensitizer, light, and O2 in PDT may be an effective method of destroying pathogenic microorganisms (16).

The efficacy of PDT as an antimicrobial treatment lies in its not being affected by the resistance of microorganisms; moreover, the spectrum of photosensitizer action has been broadly effective against viruses, fungi, and bacteria (16). This effect may be described as the advantage of PDT over other oral care procedures.

PDT has been described as non-invasive and bio-inert for patients and is associated with no adverse effects; it is also a non-aerosol-creating
medical procedure. Photosensitizers are in direct contact with microorganisms during topical applications (17). However, there is very limited information in the current literature regarding the use of PDT in ICU oral care, with the exception of one study on the topic (18). Thus, more evidence-based information is needed.

High-level protective occupational safety measures are required for nurses working in ICUs with COVID-19 patients, and every effort must be made to reduce the risk of infection. It is necessary for nurses to wear a disposable working cap, a disposable fit-tested respirator N95 (US) or FFP2 (EU), and disposable working clothes such as a surgical gown, face shield for protecting the face and eyes, and disposable gloves for hands (19).

When a patient with COVID-19 requires oral care, critical care nurses cannot avoid close contact; thus, maximum protection with special protective gear is needed. Some centers reported continuous or bi-level positive airway pressure (CPAP/BiPAP) for safe management of COVID-19 patients (20). However, BiPAP may be associated with the risk of SARS-CoV-2 transmission, even for patients at a distance (21).

To support COVID-19 patients with respiratory deficiencies, exhalation filters could be used in CPAP/BiPAP for airborne isolation protection, but the high occurrence of leakage in CPAP/BiPAP masks is a risk factor (4). The use of CPAP/BiPAP may risk deterioration, thereby requiring emergency intubation. Because of a subsequent delay in that case, nurses risk making mistakes when donning their personal protective equipment owing to the stress of resuscitation time, further risking exposure to the virus. CPAP/BiPAP has not been recommended for use while critical care is being provided to COVID-19 patients; if these methods were to be used, proper droplet precautions and airborne isolation would need to be established (2).

CONCLUSIONS

The COVID-19 pandemic has made it increasingly challenging for nurses to perform oral care protocols in the ICU. The findings of this study indicate the importance of preventive measures while providing oral healthcare, which is to be given by secure, minimally-aerosol-creating methods described in relevance to clinical practice. Further research, including clinical trials with COVID-19 patients, will strengthen oral health care recommendations.

RELEVANCE TO CLINICAL PRACTICE

It is difficult to perform oral care protocols for SARS-CoV-2-infected patients in ICUs during the COVID-19 pandemic. There has been a sudden increase in demand for ICU care, and thus appropriate planning is needed. Additional time is necessary not only for oral care procedures but also for an increased number of patients requiring service at the same time. Oral care should be provided for the prevention of NP and VAP, but
healthcare providers must also keep in mind measures for preventing the transmission of the virus, and ICU nurses should take all additional necessary protective measures.

This paper provides information that can inform a simple and secure oral hygiene protocol for nurses caring for SARS-CoV-2-infected patients while also helping to reduce the development of NP and VAP among patients in ICUs during the COVID-19 pandemic.

1. Cleaning of the oral cavity with a Toothette swab that has a suction connection and subsequent completion of the oral care procedure with hypopharyngeal suctioning are recommended.

2. Chlorhexidine rinsing may not be effective in destroying SARS-CoV-2. Using oral rinses with oxidizing agents, namely 1% hydrogen peroxide or 0.2% povidone instead of chlorhexidine, to benefit from oxidation vulnerability of SARS-CoV-2 is recommended.

3. Manual or electric tooth brushing is not recommended. Although tooth brushing provides effective hygiene, it is ineffective in preventing the spread of the virus to ICU staff members and other ICU patients.
REFERENCES


INTRODUCTION

The Coronavirus disease 2019 (COVID-19) outbreak, first reported on 8 December 2019 in Hubei province in China, was then identified as a pandemic by the World Health Organization (WHO) on 11 March 2020. This disease, recognized as an infection with a new betacoronavirus has been spreading exponentially in almost all countries around the World (1). Respiratory droplets and person-to-person contact are the reasons for rapid spread and infectivity (2). When compared to other common viral infections responsible for respiratory tract infections, COVID-19 has a significantly higher mortality. It affects older adults, especially those with co-morbidities such as cardiovascular diseases (CVD) and related risk factors (3). Since most resources in the healthcare system are dedicated to the struggle against COVID-19, the management of patients admitted with cardiovascular conditions may be compromised (4). In this narrative review, our aim is to clarify if CVDs are neglected in coronavirus days and discuss the potential risks of this delay for patients with CVD.

MATERIALS AND METHODS

Composition of this narrative review was performed by entering key words “COVID-19”, “coronavirus”, “cardiovascular diseases” and “myocardial infarction” in scientific database Pubmed® in order to obtain
related articles. Articles with full-texts and explanatory abstracts were included. Those which were written in other languages than English, without explanatory abstracts and contain repetitive information were excluded. After abstracts and full-texts were evaluated, three reviewers independently evaluated the available full texts and explanatory abstracts of the articles extracted from the database according to search criteria. Among almost 100 original researches, case reports and reviews, the most relevant 30 articles were chosen by 3 reviewers. After detailed analyses of the articles, the results of the review was discussed by the reviewers.

**COMMON CARDIOVASCULAR COMPLICATIONS IN COVID-19**

COVID-19 causes not only cardiovascular complications itself but also delays in the management of patients with CVD. When compared to previous outbreaks such as Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS), Coronavirus Disease 19 (COVID-19) is known to be associated with higher incidence of cardiovascular complications (5).

When the literature is reviewed, it is observed that cardiovascular complications commonly accompanies in COVID-19 patients. The most common cardiovascular complication is acute cardiac injury, such as arrhythmia and heart failure. The reason why risk of cardiac stunning/injury, acute myocardial infarction (MI) or coronary vasospasm is increased is thought to be heightened systemic inflammatory response and procoagulant activity with COVID-19 (6,7). Other factors contribute to CVD observed in COVID-19 are inflammatory infiltrates, microvessel thromboembolism, hypoxia and turbulent hemodynamics (8). In patients with CVD resulting from COVID-19, risk of poor outcomes are increased due to immune system deterioration, metabolic demand increase, and increase in procoagulant activity. In the cardiovascular system, various complications including myocardial injury, acute myocardial infarction, myocarditis, dysrhythmias, heart failure, and venous thromboembolic events may be determined (9,10). Explanation for cardiovascular complications observed in COVID-19 may be hypercoagulation state caused by pneumonia which is associated with platelet and clotting activation (11).

In a study by He et al., when patients with COVID-19 are considered, in-hospital mortality was significantly higher in patients with myocardial injury than in patients without myocardial injury. Another important finding in their study was that the prevalence of myocardial injury is high among severe or critically ill COVID-19 patients (12). Accordingly in another study by Manish et al., acute cardiac injury with elevated troponin levels, was the most common cardiovascular disorder in
COVID-19. In approximately 8-12% of all patients cardiac injury was determined. The possible mechanisms were hypothesized as direct myocardial injury due to viral involvement of cardiomyocytes and the effect of systemic inflammation (13,14). Coronaviruses bind to the transmembrane angiotensin-converting enzyme 2 (ACE2) to enter type 2 pneumocytes, perivascular pericytes, macrophages, and cardiomyocytes. This may lead to myocardial dysfunction and damage, endothelial dysfunction, microvascular dysfunction, plaque instability, and myocardial infarction (MI) (1). In elderly patients, particularly in the presence of underlying coronary atherosclerosis, hypoxemia and stress related to respiratory disease precipitates myocardial injury (15).

**DELAYS IN MANAGEMENT OF PATIENTS WITH CVD DUE TO COVID-19 PANDEMICS**

It is reported that ST elevated MI rates have declined during the pandemic. This may be a consequence of patients reluctant to access the emergency departments (EDs) in order to reduce risk of coronavirus transmission and exposure. In EDs, there is a need for additional screening for COVID-19. The period spent for these tests results in prolonged length of stay in the ED. Transfer from the emergency department to the catheterization laboratory is complicated by risks of additional staff exposure and delays in preparation associated with personal protective equipment. Since the interventions for reperfusion delays, risk for a larger myocardial infarct size, increased risk for heart failure and shock is increased. Additionally, the delay eliminates the advantage of catheterization compared with fibrinolytic therapy (16).

Another challenging issue causing delay is the necessity of protective clothing during transport and treatment of MI patients. In the transport and treatment of AMI patients, the physicians should strictly observe the indications for patient transport with appropriate protective measurements of the medical staff (17).

In a study, large delays in in patients with STEMI seeking medical help after institution of these infection control measures were reported. For example, catheterization laboratories generally have positive pressure ventilation so COVID-19 infection inside these rooms can theoretically cause widespread contamination of the surrounding environment. Measures such as detailed travel and contact history, symptomatology, and chest X-ray, therefore, are taken before transferring patients to the catheterization laboratory at our hospital (18). In management of patients with CVD, Lauren et al. proposes fibrinolysis, though controversial since catheterization laboratories put multiple healthcare workers at risk for (19).
For instance in France, a dramatic drop in the number of admissions to ICCUs after the establishment of containment against COVID-19 was determined. According to Huet et al., self-censorship, because of fear of possible in-hospital contamination or a lengthy wait before consultation in an overcrowded emergency room are possible reasons for this reduction. Patients may also have refrained from consulting cardiologists, delaying detection of heart failure or worsening of coronary artery disease, and subsequent referral to an ICCU (4).

In a report from Hong Kong, a delay in STEMI patients who underwent PCI during the outbreak period was determined. The median time from symptom onset to first medical contact time was 318 minutes before the outbreak and 82.5 minutes during the same time period in the previous year (18).

During pandemics, people hesitate to visit hospitals in order to reduce coronavirus exposure, the reservation of the providers to send their patients to the health care facilities, and the limitation of the resources seem to be the main barriers for evaluation of patients with CVD. Even in the case of the patients who are already admitted to the hospital, when COVID-19 is suspected, it can affect the medical care either by distracting from other diagnoses or delaying the procedures to avoid the exposure. When physicians focus on COVID-19, STEMI may be missed. (20). Another factor that causes prolongation in management of patients with CVD is unfamiliarity of cardiologists to medications used in COVID-19 including remdesivir, hydroxychloroquine and chloroquine, and interleukin (IL)-6 inhibitors (3).

In high-risk areas and economically fragile environments, elderly individuals are isolated for uncertain durations and integration between territory and hospital may not be adequate (21).

SOLUTION FOR THE PROBLEM

Solution for social, economic, environmental and clinical problems, can be achieved by means the contribution of telemedicine and telecardiology (4,21). The public must be informed that facilities minimize exposure to coronavirus in case they present with cardiac symptoms. In cardiac catheterization laboratory facilities, appropriate masking of patients and the use of personal protection equipment (PPE) must be encouraged. After PCI is performed, regardless of the patient’s COVID-19 status, prior to the admission of a new patient, complete disinfection procedures should be performed in the Cath lab. When a need for a resuscitation emerges, it must be performed outside the Cath lab. Radial artery must be the dominant route for intervention. To avoid virus transmission, the benefit/risk ratio must be weighed carefully in selection of treatment method. When a STEMI patient with low hemorrhage risk,
shorter ischemic time, relative less or less important myocardium involved, a third generation of fibrinolytic agent should be preferred as the fibrinolytic therapy (22,23,24).

CONCLUSION

A number of cardiovascular complications accompany COVID-19, including myocardial injury and myocarditis, AMI, heart failure and dysrhythmias (9). During coronavirus days, the cardiologists, should be fully aware of the indications and contraindications of thrombolysis and also protective measurements (17).

Management of heart diseases in COVID-19 pandemics is a challenging issue. COVID-19 makes stress on myocardium and causes cardiac problems. Besides, delays in diagnosis and treatment of patients without COVID-19 but cardiac problems is another challenging issue for healthcare providers.
REFERENCES


CHAPTER VII

PERIODONTAL THERAPIES DURING COVID-19 PANDEMIC

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INTRODUCTION

After December 2019, the world met a new epidemic. Covid-19, which is an epidemic that first affects the Wuhan region of China, then has turned into a pandemic by affecting the whole world(1). According to the World Health Organization data, the number of cases detected was 57.8 million according to the situation report dated November 22, and the number of people who died due to the pandemic reached 1.3 million(2).

The year 2020 has passed under the influence of the Covid-19 pandemic, and there have been measures and restrictions affecting social life in many countries. Health services, one of the non-postponable services, have focused on canceling or delaying many non-urgent treatment of many elective treatments to give priority to individuals affected by the epidemic (3). Oral and dental health treatments have an important place among health services (4). The necessity of providing uninterrupted emergency services to patients in dental treatments is a reality accepted by everyone. In this context, primarily all non-urgent dental treatments were postponed, but as a result of the prolongation of the epidemic process, dental problems that are not very urgent, but that are likely to cause permanent damage in case of delay, have to be treated. In this context, when dental treatments are examined, the most urgent interventional treatments are; tooth fractures, pulpal originated pain and infections, periodontal abscesses, malfunctions and fractures of prosthetic restorations, teeth that need urgent removal (5). However, another treatment focus that should also be noted is periodontal treatments. Because it is known that they cause permanent irreversible damage to periodontal tissues when they are not treated. In these days when the 2nd Wave is experienced globally in the pandemic, it is also mentioned that the 3rd Wave will also be experienced in the coming months. Although promising statements about the Covid-19 vaccine have created a positive perception, it is an undeniable fact that the world will remain under the influence of an epidemic until mass immunity is gained. For this reason,
during the epidemic period, treatments should be carried out in an environment where periodontal treatments can be used with the necessary protective and preventive materials and dentists protect themselves by using personal protective equipment and protect their patients from contamination by taking pandemic measures (6,7).

Periodontal disease, which is an inflammatory disease, affects the gingival and hard tissues surrounding the teeth (8,9). The majority of tooth losses are due to periodontal diseases. The prevalence of periodontal diseases can go up to 90% in population (10). Early diagnosis of periodontal diseases is very important in successful treatment. Evidence based treatment modalities are well known when disease is taken under control before excessive resorption occurs. Prevention from periodontal diseases also brings additional benefits such as protecting the teeth, providing more comfortable chewing and better digestion. Periodontal diseases begin with the first stage; as gingivitis. The first and reversible stage of periodontal disease so called gingivitis can be controlled very quickly and successfully (8). The symptoms are gingival bleeding, red colour of gingiva instead of pink colour and enlarged volume of gingiva. Gingivitis may not be realised by patients in early phases since its not causing much discomfort. In cases when gingivitis is not treated, it can progress to the next stage and turn into periodontitis. Periodontitis is the progress of disease to alveolar bone and cause irreversible damage to the bone structure (11). Irreversible damage occurs to the alveolar bone along with other tissues that support teeth. A pathological periodontal pocket is formed between the tooth and the gingiva surrounding the teeth (12). The existence of a periodontal pocket creates a difficult environment to be cleaned by oral hygiene procedures and enables the location gingival plaque which will lead to an infection and cause the gradual progression of the periodontal disease (11). When the treatment is delayed, the progression of periodontitis can not be taken under control. The supporting periodontal of the teeth become weaker and the teeth begin to shake, their mobility increases, and even in the later stages, the teeth may need to be extracted.

There are many symptoms of periodontal disease, and the findings increase in direct proportion to the severity of the periodontal pathology. Known symptoms such as bleeding of gingival tissues during brushing; colour of gingiva turning to red, swollen and sensitive gums; gums that can be easily separated from teeth, moving away from teeth; mobility as gradually moving away of teeth; changing occlusal relationship between tooth and can create halitosis (13).

Since the main reason for disease is bacterial plaque so the treatment involves the removal of the agent causing inflammation in the gums, namely the bacterial plaque and tartar on the teeth, and providing
polished surface on root to prevent colonisation on surface(9,14). These non surgical procedures, so called initial treatments, are sufficient for the gingiva to adapt to the tooth again or the gingiva to shrink and eliminate the pocket (15). First stage of treatment as initial treatment, has to be followed by patients to be able to control the oral hygiene. The success of the treatment is achieved with acceptance and participation of the patient himself. In more advanced cases, periodontal surgery may be required to eliminate deep periodontal pockets surrounding the teeth, to be able clean deep structures effectively and to ensure a smooth root surface (16). Patients whose treatment processes are completed with initial treatment and / or periodontal surgery should be regularly be followed by periodontist, maintenance visits should be obligatory to control palque and dental calculus. Re-occurrence of periodontal infections and destructive effects on dental support tissues is inevitable in patients who are not kept under regular control (17).

During this long Covid-19 pandemic period, which has almost a year and is not yet clear for how long it will affect the world, patients with periodontal disease or who were treated before because a previous periodontal disease are now required to be in a regular follow-up process. Dental staff carefully following pandemic precautions with necessary personal protective equipments should continue periodontal treatments for patients to be continued to whom unless left untreated, periodontal tissues may develop irreversible defects(6,7).

METHODS OF TREATMENT

Research has shown that viruses with a high potential of transmission such as coronavirus (SARS-CoV) can travel more than 180 centimeters by aerosols (18). For this reason, aerosol release should always be considered in periodontal treatments during the Covid-19 outbreak. While determining the treatment protocol, priority should be given to the treatment methods that cause less aerosol release, or the decision should be made by considering the benefit-harm relationship.

Periodontal diseases can be prevented and controlled to a great extent depending on good oral hygiene, correct and early diagnosis and correct treatment approaches. Therefore, active participation of both the patient and the physician in the treatment is required with correct timing without any delays which may lead to an increase in the severity of periodontal diseases.

The most important step in periodontal treatment is the elimination of infection and also the patient's learning to maintain oral health by effectively and regularly cleaning the gums, teeth and langue. Elimination of infection is possible by the physician to clean the root surface of the microbial dental plaque, tartar and dental calculus that cause the disease
and the patient to protect this condition. This process is called "initial treatment", it is an indispensable step in the treatment of any type of periodontal disease. For removing bacterial plaque and tartar a wide variety of hand tools of various diameters and shapes as well as sonic and ultrasonic instruments are available (19). Again, many tools related to these processes (air-flow, soft tissue laser, water pick etc.) have been developed. These sonic and ultrasonic devices during the operation remove comparatively few root structure and soft tissue trauma is diminished (20). These devices can be preferred because they require less processing time. However, it has been suggested that they cause a rougher root surface (21). In contrast, smoother tooth surfaces can be obtained manually with the use of hand tools and more tartar deposits can be removed (22).

**DISCUSSION**

Clinical results reflect appropriate clinical results in non-surgical periodontal treatments with mechanized instruments similar to hand tools. Obeid et al. based on their work, they could not claim that one method is superior to another; They concluded that mechanized root planning is as effective as general procedures with hand tools and is a suitable alternative method (23).

It is recommended to use a high vacuum volume evacuation device during the periodontal procedure. Although it has been shown that the use of such a high vacuum device during periodontal procedures can reduce aerosol contamination less, methods for minimizing aerosol formation are not clearly justified (24). Eventhough contamination risk may be reduced with some additional procedures, it is recommended to direct the spray at the tip of the tool in a focused way or to design the tip so that it does not emit aerosol (25). However, studies show that aerosol contamination amount generated by the traditional ultrasonic tip and the newly designed insert with focused coolant water is similar (26).

Although comparative research results on the use of hand tools and mechanized devices in the non-surgical initial treatment are still being published in the periodontology literature; considering the conditions specific to the Covid-19 epidemic process, it is more appropriate to use hand tools to clean calculus and root surface smoothening. During the operation of sonic and ultrasonic devices, a great amount of aerosol is emitted into the clinical environment, and scattering caused by pressurized water and vibration inside the mouth poses a risk to both the dentist and the auxiliary staff.

If periodontal condition that cannot be fully treated with the initial periodontal treatment phase is detected periodontal surgical procedures will be recommended. After the initial periodontal treatment, the remaining pocket depths, gum growth and recession, the presence and shape of bone
resorption, and the amount of gums affect the decision to be taken. Gingivectomy is the cutting and removal of a small amount of gum to remove the gum pocket and gum growth (27,28). Flap operation and bone surgery procedures are procedures that concern both the gums and the underlying support tissues and root surfaces. With this technique, the gingiva is removed properly and the underlying tissues are reached and treated.

Through cleaning of root surfaces and pocket depth reduction is the main goal. During the flap operation, the underlying bone tissue is also intervened (29-31). These procedures are called bone surgery procedures (32). After the gums are removed during the flap operation, the dead soft tissues, root surfaces, and also the inside of the pockets formed in the bone are cleaned. Thus, the existing bone shape during surgery is evaluated (8,11). Then, either the bone shape is corrected with resective techniques and the original shape is tried to be resembled, or it is tried to be brought to the original bone level by performing bone repair with regenerative methods and filling in-bone pockets (33). In this technique, various materials such as natural or artificial bone powders, membranes covering them, and protein-based substances are used. In most cases, resective and regenerative techniques are used together (8-11). Mucogingival surgery is applied in the presence of insufficient adherent gum height, gingival recession, high muscle connections (34-36). Thus, it is aimed to provide the natural environment where the patient can provide oral care and to provide sufficient amount of gums to support prosthetic teeth, and to eliminate aesthetic and sensitivity problems.

As described many alternative surgical periodontal treatment options are available for different periodontal diseases. But as compared to non-surgical treatments considering the aerosol distribution, surgical treatments have less potential for coronavirus (SARS-CoV) transmission due to low spread during operations. Of course this is valid surgical operations when sonic or ultrasonic devices are not used.

Another device to be taken into care is airflow and air-powder abrasion. These devices are used as an effective technique for the decontamination. As a new technique, low abrasive air removal of the biofilm layer from the tooth surface and polishing of the root surface, while becoming popular, suggests that it allows periodontal health to be maintained as effective as the relevant conventional debridement modes (37). Although it can be used as a routine treatment mode on flat surfaces, traditional treatment modes should be used in furcations. In addition, considering the Covid-19 epidemic process, it should be noted that these devices produce very high aerosol scatter.
CONCLUSION

Aerosol release should always be considered in periodontal treatments during the Covid-19 outbreak. While determining the treatment protocol, priority should be given to the treatment methods that cause less aerosol release, or the decision should be made by considering the benefit-harm relationship. As described many alternative surgical periodontal treatment options are available for different periodontal diseases. But as compared to non-surgical treatments considering the aerosol distribution, surgical treatments have less potential for coronavirus (SARS-CoV) transmission due to low spread during operations. Of course this is valid surgical operations when sonic or ultrasonic devices are not used.

Considering the conditions specific to the Covid-19 pandemic, it is more appropriate to use hand tools to clean calculus and root surface smoothening. During the operation of sonic or ultrasonic devices or powered air abrasives, a great amount of aerosol is emitted into the clinical environment, and scattering caused by pressurized water and vibration inside the mouth poses a risk to both the dentist and the auxiliary staff.
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CHAPTER VIII

MEASURES TO BE TAKEN IN ENDODONTIC TREATMENT IN THE COVID-19 OUTBREAK

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ENDODONTICS

Endodontics; It is a science that is multidisciplinary, including determination, irrigation, shaping and filling of root canals in three dimensions. Nowadays, developments in aesthetic dentistry is highligting the importance of keeping the tooth in the mouth and therefore endodontic treatment.

Accurate diagnosis, complete cleaning of the pulp cavity, biomechanical enlargement, hermetic filling of the prepared pulp cavity are factors that determine the success in endodontic treatment (photo 1).

Photo 1 case Dr. Emre Eti

At the same time, endodontic surgery is an important part of endodontic treatment. Understanding the causes of failure in endodontic treatments has increased the importance of endodontic surgery. Technological advances have provided us with new materials, and this has been beneficial in the development of endodontic surgery with a variety of
techniques in surgical operations and an increase in successful cases (photo2). Today, endodontic surgery has become an indispensable part of treatment planning for endodontists.

Photo 2 case Dr. Arman Orguneser

COVID-19

Coronavirus infection 19 (COVID-19) started to emerge and has spread in Wuhan, China in 2019. Although initially thought to be low in transmission capacity, it was found to be an influenza-like virus and more contagious. COVID-19 is a derivative of a single-stranded RNA SARS-CoV-2. The genome sequence is very similar to SARS-CoV and MERS-CoV. The spread of SARS-CoV-2 has caused millions of cases and hundreds of thousands of deaths, and this process continues despite all efforts. Given the presence in the saliva of the affected patients, the cases with positive COVID-19 tests and the asymptomatic course of many cases, the risk of infection is high unless all healthcare professionals, including endodontists, take appropriate precautions(1,2,6,13,16).

COVID-19 PREVENTION APPROACHES in ENDODONTIC TREATMENT

Aerosols are particles smaller than 50 micrometers in diameter and can stay in the air for a certain period of time. Coughing, sneezing, and aerosol work of dentists cause the virus to enter the respiratory system. Aerosol (0.5 to 10 μm in diameter) has the potential to diffuse and hold in the lung bronchi, so it is thought to be the biggest factor in Covid-19 transmission (3,4,13,15)

Endodontists or other dentists should work very diligently and take precautions in the treatment of their patients to avoid this deadly virus(14). Air motors are always used in endodontic treatment principles, which will
cause particles to remain suspended in the air. Airotors handpieces, ultrasonic scalers, endodontic motors produce aerosols, which increase the potential for infection as they are dispersed into the environment at high pressure. The use of these instruments should be avoided as much as possible, and the stages of clinical practice should be decided by the endodontist only after taking the necessary precautions to relieve the patient’s pain in emergency situations (2,5,6,7).

Using aerosol-free operation, micromotor without water spray, personal protection equipment, double masks, double gloves and goggles or face shield for treatment will eliminate the risk of contamination from the operation area. It is stated that the use of mouthwash is also beneficial. Both a rubber dam and a high pressure saliva ejector (surgical aspirator) should be used whenever possible in order to minimize contact with saliva and reduce the spread of contaminated aerosol. In addition, in endodontic treatment, it is recommended to disinfect the tooth treated with these solutions after inserting a rubber dam and opening the entrance cavity. Especially during this pandemic period, patients should be informed to maintain oral hygiene (3,4,7,8,9).

In this pandemic period, endodontists and other dentists should pay great attention to their appointment hours. Sufficient time should be allowed to disinfect the environment during the breaks between appointments. Regardless of the fact that disinfection should be done as if aerosol has been studied and patients are considered to be Covid-19 positive. The environment should be disinfected by fogging method using hypochlorous acid with ULV devices (photo 3), then the windows should be opened and the clinic should be ventilated. Patients should not be in the same environment, the other patient should be taken to the clinic at least half an hour after the treatment of one patient. Loop and microscope (photo 4) use has become difficult due to the fact that face shields reduce vision in endodontic treatment and because of the low eye distance with face shield. Designing face shields that will allow the use of loop and microscope is very important in this period. The use of
manual canal files should also be preferred in this period. If possible, disposable materials should be used (10,11,12).

Photo 4
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CHAPTER IX

TREND TOPICS IN POPULAR AND PRESTIGIOUS CARDIOVASCULAR MEDICAL JOURNALS DURING CORONAVIRUS PANDEMIC PROCESS

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As of 2020, the coronavirus disease 2019 (COVID-19) that has swept into at least 213 countries with more than 70,000,000 confirmed cases and caused deaths of more than 1,500,000 people and is announced a pandemic by the World Health Organization. As of October 2020, when you search for “Coronavirus-COVID-19” in PubMed; more than 40,000 results have already found their place in literature.

This new clinical threat (COVID-19) has a much longer contagion period than other outbreaks and we has to face it without sufficient experience of clinical course. Although it usually belongs to the respiratory system, cardiovascular characteristics of the disease were also taken into account after a significant number of patients had signs of cardiac damage (1).

When we examine the data shared since the beginning of the epidemic, we see that the highest mortality rate is seen in the elderly with known cardiovascular diseases. In particular, the presence of risk factors such as coronary artery disease, hypertension, and diabetes mellitus makes the patient more susceptible to coronavirus infection, and if the disease develops, it causes more frequent complications and death rates in this particular patient group (2).

Since over 2000 years, physicians and researchers continue to find solutions for eradicating diseases and improving community health. Every year medical researchers in all areas conduct new clinical studies for this purpose. At this stage medical journals keep a critical role for reflecting on how clinical trials have evolved while researchers manage to overcome many challenges. But what did recent clinical studies in medical field show us in 2020? What were trend topics in medical journals? Where do we go? If we should answer the question, there is no doubt that 2020 will be the year of coronavirus for medical publications. But how relevant are the
popular and prestigious medical journals in cardiovascular medicine on this topic?

The European Heart Journal is an international, peer-reviewed medical journal about cardiovascular disorders. It aims to publish the highest quality clinical and scientific issues, on all perspectives of cardiovascular medicine. In a recent article by Vrachatis et al.; the authors concluded that the balance of the risk and benefits associated with the thrombolysis-first approach should not be recommended in ST-elevation myocardial infarction and, they reported that coronary angiography should remain the most important the diagnostic strategy of ST elevation myocardial infarction patients even in the context of coronavirus disease (3).

Circulation publishes original research articles, review articles, and other issues related to cardiovascular disorders, including observational and clinical studies, epidemiological trials as well as health services and outcomes studies, and progression in basic and interpretation research. As being one of the prestigious medical journals, it can not be expected for the journal to remain indifferent to COVID-19. For instance, almost all of the most read articles of last month were about COVID-19. In a review by Clerkin et al., the authors reported that myocardial involvement is present in >25% of severe cases and presents in 2 models: acute myocardial damage and dysfunction on presentation and myocardial damage that develops as illness severity increases (4). In another article in the journal, it has been also reported that myocardial involvement is common in hospitalized patients with COVID-19 and not exclusive to those with acute coronary syndromes or pulmonary emboli (5). This clearly shows that more serial studies will clarify this and evaluate the long-term clinical implications of these findings.

Journal of the American College of Cardiology; is the one of the leading journals in cardiovascular medicine. The journal remains at the forefront of exciting developments in this area. When the latest issues in the journal are reviewed, articles related to COVID-19 stand out. The article published by Amat-Santos et al., contribute to our understanding of potential risk factor in patients treated with renin-angiotensin-aldosterone system inhibitors placed in the context of an evolving pandemic COVID-19. It has been demonstrated that randomization of high-risk older patients with known cardiovascular disorders, to ramipril group had no impact on the incidence or severity of COVID-19 (6).

European Journal of Heart Failure is a world leading medical journal in heart failure. The journal is the international journal of the European Society of Cardiology focused on the advancement of knowledge in the area of heart failure. One of the latest articles published online ahead of
print in the journal is about pathogenesis and management of myocardial damage in coronavirus disease 2019 (7).

Nature Reviews Cardiology is an international medical journal publishing the important peer-reviewed research articles in all fields of cardiology. Befitting a prestigious scientific journal, the journal has tried to fulfill its duty on studies on COVID-19 disease and its treatment. The latest two articles of the journal are about COVID-19 and cardiovascular disorders: from basic pathophysiological mechanisms to clinical viewpoints and COVID-19 thromboinflammation (8,9).

The studies mentioned above also show that the effect of the virus on the heart has become more common as clinicians act in real time to somehow help people with heart disease and those at high risk of developing coronavirus disease. A growing number of studies show that most patients recovering from COVID-19 disease experience some form of heart injury even if they did not have an underlying heart disease and were not seriously ill enough to be hospitalized.

Two recent studies suggest heart involvement among those patients infected may be more prevalent. In JAMA Cardiology, the authors analysed autopsies of 39 COVID-19 patients and viral existence within the myocardial tissue was documented. Future studies must focus on evaluating the long-term outcomes of this myocardial involvement. (10).

Another JAMA Cardiology study investigated cardiac MRI results of 100 patients who had recovered from COVID-19 within the past two to three months. Authors demonstrated myocardial abnormalities in 78% recovered patients and myocardial inflammation in 60%. The same study showed increased troponin levels, an indicator of cardiomyocyte injury, in 76% of patients tested, although it was observed that left and right ventricular systolic function was preserved globally. Most patients in the study had no indication for hospitalization. (11).

As a last word, every researcher who produces any information in an acute public health situation is obliged to share his/her preliminary conclusions, provided that adequate quality control is carried out. However, it should not be forgotten that ethical rules should not be violated here, and should be published after adequate data quality control. The recent explosion of publications against COVID-19 has increased concerns of ethical violations.

In conclusion, it is not possible to determine when global crises and pandemics such as COVID-19 will occur. COVID-19 will neither be the first nor the last pandemic in human history. While researchers manage to overcome many challenges against this global health emergency, we are going to follow the results of the studies closely.
References


