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Acute cyanide poisoning and challenges in the diagnosis

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Abstract

Objective: Cyanide that is known may be cause poisoning for centuries by mankind is a poison that can cause fatal intoxications in minutes, even in very small doses. It was aimed to emphasize the importance of acute cyanide poisoning that may occur by consuming apricot kernels containing amygdalin, a cyanogenic glycoside.

Method: Between September 2016 and October 2018, the data of the patients exposed to cyanide poisoning due to apricot seeds were examined retrospectively.

Results: The mean age of the patients was 39 months (23-65 months). Nine of the patients were female and 12 patients were male. Ten of all patients were native Turkish citizens and 11 of the patients were foreign national. It was learned that the patients ate an average of 15 pieces (10-30) of raw apricots kernel in their anamnesis. The complaints of the cases begin on average 45 minutes (30-90 minutes) after eating apricot seeds.

Conclusion: However acute cyanide poisoning is rare, it has a high potential for mortality when being suspected of cyanide poisoning based on the anamnesis and clinical features of the cases; should be supported immediately and specific treatment should be started.

Keywords: Amygdalin, apricot kernel, cyanide poisoning

INTRODUCTION

Cyanide is called hydrocyanic acid or prussic acid and it has been firstly decomposed from Prussian Blue in 1782, it is one of the strongest and most deadly poisons. In fact, cyanide that is known may be cause poisoning for centuries by mankind is a poison that can cause fatal intoxications in minutes, even in very small doses (1, 2). Diagnosing of cyanide poisonings is difficult due to it has been nonspecific symptoms. Cyanide can be found as free molecules in nature as compounds of hydrogen, sodium, and potassium. Sodium or potassium compound of cyanide that it is called cyanide salts are white color and its solid form (1-4). Cyanide poisoning may occur with oral intake, inhalation, or direct skin transmission (2, 5, 6). Cyanogenic glycosides are found in more than one thousand plants. In the literature it has been reported that, Amygdalin is one of the cyanogenic glycosides also known as vitamin B17are found in almond, apple, apricot, cherry, peach, pear, quince, plum kernels, flaxseed, and legumes. Acute cyanide poisoning can occur in children even if they eat the foods containing cyanide glycosides due to it is released the cyanide result of hydrolysis of this cyanide glycosides (1, 2, 5, 6, 7). In acute cyanide poisoning, the use of oxygen of the cells has deteriorated, so it's seen hypoxia at the tissue level and metabolic acidosis occur. Clinical manifestations of cellular hypoxia due to cyanide poisoning are abdominal pain, general drowsiness, nausea, vomiting, headache, hypothermia, increased salivation, increased sweating, tachypnea, confusion and convulsion. These symptoms can be developed very rapidly within minutes. Even, respiratory failure and death may occur within minutes, if quickly not understood the cause of clinical symptoms (2-4, 7). The diagnosis of acute cyanide poisoning should be kept in mind in children who had the anamnesis of eating cyanogen fruit seed, the smell of bitter almond in the breath, and the gastric irrigation and increased metabolic acidosis in the laboratory test. It should not be forgotten that complete recovery of these patients may occur with early diagnosis and treatment. Management of cyanide poisoning is supportive and specific treatment. Supportive treatments include monitorization,

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oxygen therapy, fluid therapy, and intensive care when necessary. Cyanokit (hydroxocobalamin) and Nithiodote (sodium nitrite and sodium thiosulfate) are specific treatments against cyanide poisoning. In the treatment, despite sodium nitrite and sodium thiosulfate are the most common known antidote agents, due to the hydroxycobalamin and cobalt EDTA have faster and earlier effects, they are recommended use alone or in combination with these agents (1, 2, 8).

In this study, it was aimed to draw attention to acute cyanide poisoning which is may occur with the eating of apricot kernel including amygdalin as cyanogenic glycosides.

METHOD

Study Design

In this study, between September 2016 and October 2018 in the Hatay Mustafa Kemal University Faculty of Medicine, Department of Pediatrics, the data of the patients who were hospitalized and treated with a diagnosis of cyanide poisoning due to apricot seed were examined retrospectively. The diagnosis of the patients was made based on the development of clinical findings (fatigue, abdominal pain, sweating, drowsiness, nausea, saliva increase, vomiting, respiratory distress, loss of consciousness, convulsion etc.) approximately 1 hour after eating 15-20 apricot seeds according to their anamnesis. Ethical permission was obtained from the Hatay Mustafa Kemal University, Medical Faculty Clinical Research Ethics Committee for this study with date 2018 and number 06, and Helsinki Declaration rules were followed to conduct this study..

Data collection

Demographic data, clinical findings, the time to onset of symptoms from to eating the apricot seed, first intervention of families, time of admission to the health facility, hospitalization time, intensive care support requirements, blood gas analysis, liver and kidney function tests, coagulation parameters, diagnosis, and treatment algorithm of those patients were obtained from hospital records.

Laboratory analysis

Laboratory analyses including complete blood count (Mindray BC 6800 hematology analyzer), electrolyte values, liver, kidney function tests (Abbott, architect c 8000, USA); coagulation parameters, and also electrocardiography and echocardiography were evaluated.

Treatment

It was suspected from diagnosis cyanide poisoning with the careful anamnesis of patients, their clinical findings, and especially the smell of bitter almond in their breaths. Then, it was applied supportive treatment without losing time. During this time, blood gas analysis was evaluated. Due to there was no enough laboratory equipment, the serum cyanide levels of patients could not be measured. All patients were treated based on evidence-based medicine guidelines. After the first evaluations in the pediatric emergency department, the all of patients were done quickly monitoring, gastric lavage, oxygen therapy with the mask, and intravenous fluid therapy. Gastric lavage was applied to all of the patients especially patients with the smell of bitter almond in the breath. The parts of the apricot kernels were removed from their gastrointestinal tract with the repeated gastric lavage.

Patients with high liver and kidney function tests were treatment with N-acetylcysteine.

Patients with hypotension were treatment with positive inotropic agents (Dopamine, dobutamine).

Cases with prolonged coagulation parameters were given vitamin K and fresh frozen plasma. And also patients with respiratory failure were treatment mechanical ventilators (Figure 1).

Statistical analysis:

Data were analyzed using SPSS for Windows 18.0 version. (SPSS Inc., Chicago, IL, USA). The differences between the groups were examined by the student's t-test. Categorical variables were evaluated by the ki kare test. $P < 0.05$ was considered significant.

RESULTS

The mean age of the patients was 39 months (23-65 months). 12 of the patients were male and 9 were female. 10 of all patients were native Turkish citizens and 11 of the patients were Syrian refugees. In the anamnesis of the patients, it was learned that they ate an average of 15 pieces (10-30) of raw apricots kernel. It was learned that the complaints of cases started at an average of 45 minutes (30-90 minutes) after eating the apricot kernel. The first intervention of their families was drinking buttermilk, vomiting, washing their hands, and their mouth. The mean duration of admission to the health facility was 90 min (60-120 min). Clinical signs were fatigue (n=21, 100%), abdominal pain (n=21, 100%), pallor (n=21,100%) , sweating (n=21, 100%), drowsiness (n= 21, 100%), nausea (n=20, 95.23%), saliva increase (n=19, 90.47%), vomiting (n=17, 80.95%), respiratory distress (n= 17, 80.95%), loss of consciousness (n: 5, 23.80%) and convulsion (n: 2, 9.52%) (Table 1).

As a matter of fact, in this study, one of the patients was referred to our department with mimicking of encephalitis clinic because of suddenly developing respiratory failure.

In this study, it was found that patients had the smell of bitter almond in the breath of 17 patients and gastric lavage of all patients.

In this study, apricot kernels were detected during gastric lavage in 57.14% (n: 12) of the patients. The patients who it was learned they are healthy before their complaints were diagnosed cyanide poisoning with anamnesis of eating apricot kernel and clinical findings. However, apricot kernels were detected in the gastric lavage of the 4 patients who had a sudden loss of consciousness and respiratory failure but had no that anamnesis of eating apricot kernel, no pathological

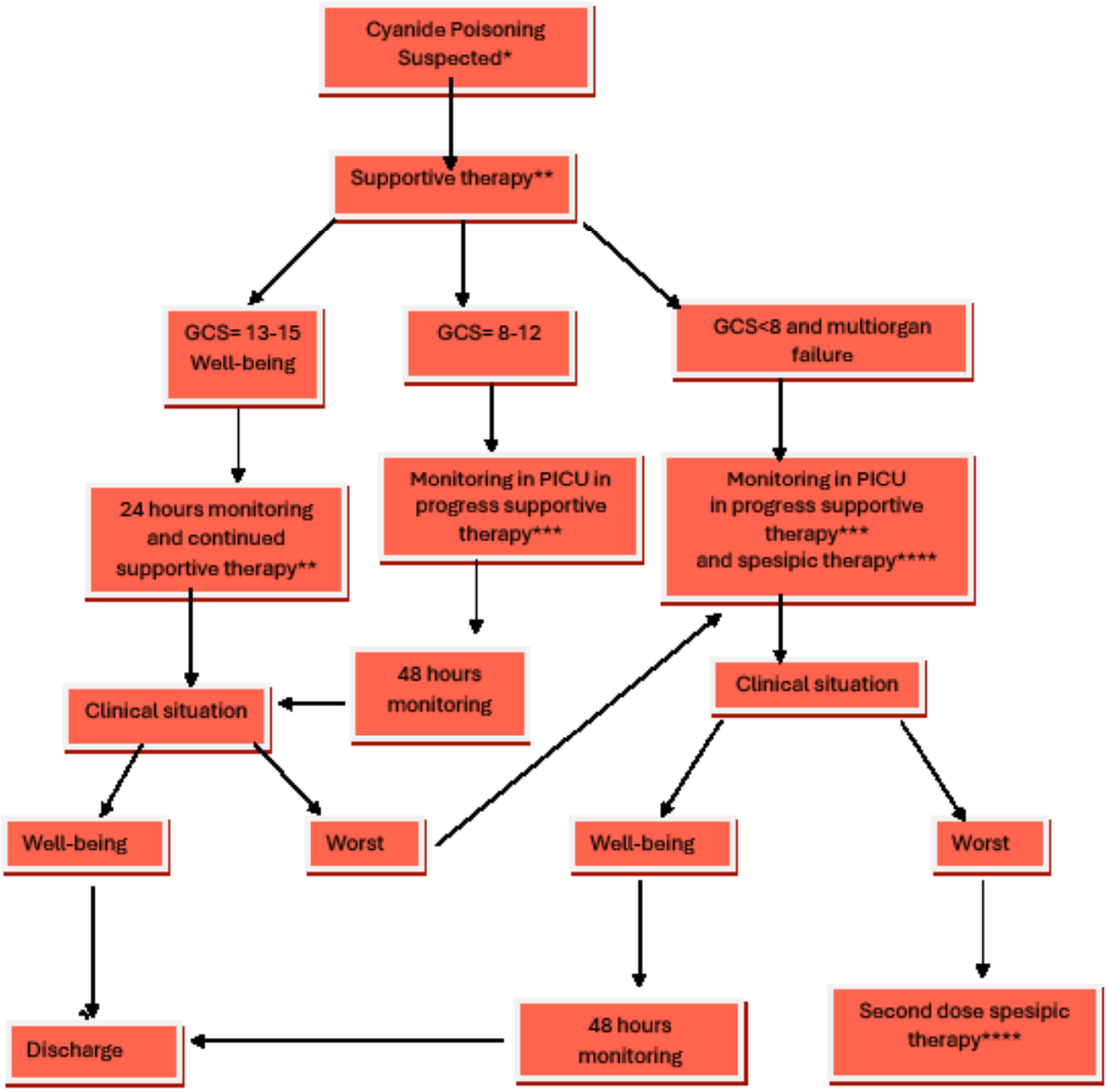

Figure 1: Algorithms in cyanide poisoning management
*It was suspected from diagnosis cyanide poisoning with the careful anamnesis of patients, their clinical findings and especially the smell of bitter almond in their breaths.
**The all of patients were done quickly monitorization, gastric lavage, oxygen therapy with mask and intravenous fluid therapy.
***Patients with high liver and kidney function tests were treatmented N-acetylcysteine and with hypotension was treatmented positive inotropic agents (Dopamin, dobutamin).
****Spesific teratment with hidroksikobalamin(Cyanokit: Pfizer)

In this study, it was detected that in the blood gas analysis high anion gap, metabolic acidosis, high lactate level, and other laboratory test parameters deteriorated similarly to the literature (Table 1).

Support treatment; in this study, the all of patients were done quickly monitoring, gastric lavage, oxygen therapy with the mask, and intravenous fluid therapy, as the first intervention. The parts of the apricot kernels were removed from their gastrointestinal tract with the repeated applications that gastric wash.

Diagnosis; in this study, it was suspected from diagnosis cyanide poisoning with the careful anamnesis of patients, their clinical findings, and especially the smell of bitter almond in their breaths. Then, it was applied supportive treatment without losing time. During this time, blood gas analyses resulted in metabolic acidosis with a high anion gap and normal PaO2 levels. Due to there was no enough laboratory equipment, the serum cyanide levels of patients could not be measured. In five of all patients who had severe poisoning symptoms (GCS <8, circulatory and respiratory failure) were applied specific treatment with hidroksikobalamin (cyanokit: Pfizer).

Four patients had leukocytosis and 3 patients had thrombocytopenia.

Five patients were detected high in the liver and kidney function tests.

In all patients, the mean base deficit in blood gases was -10.7 (-5.8 to -14.2), the mean pH level 7.14 (7.10-7.29), the mean lactate level 5.5 (4.5-7), and metabolic acidosis was detected (Table 1).

Four of all patients was detected sinus bradycardia.

Five patients who had liver and kidney high function tests were treatment NAC.

Five patients who had hypotension were treatment positive inotropic agents (Dopamine, dobutamine).

Four patients who had prolonged coagulation parameters were given vitamin K and fresh frozen plasma. Five patients who had respiratory failure were treatment mechanical ventilators.

In five of all patients who had severe poisoning symptoms (GCS <8, circulatory and respiratory failure) were applied specific treatment with hidroksikobalamin (cyanokit: Pfizer).

The mean duration of clinical response was 7.4 hours (5-18 hours).

Five patients who had intubation and mechanical ventilator support were extubated at the 13th hour (7-16).

Table 1: Clinical signs of patients

	n (Min-Max)	%
Demographic data		
Mean age of the patients (months)	39	
Gender		
Male	12	52.12
Female	9	47.88
Eating number of apricot kernel	15 (10-30)	
Average complaint start time	45 (30-90)	
Mean duration of admission to health facility (minutes)	90 (60-120)	
Clinical Signs		
Fatigue	21	100
Abdominal pain	21	100
Pallor	21	100
Sweating	21	100
Drowsiness	21	100
Nausea	20	95.23
Saliva increase	19	90.47
Vomiting	17	80.95
Respiratory distress	17	80.95
Loss of consciousness	5	23.80
Convulsion	2	9.52
Detected apricot kernels*	12	57.14
Base deficit(min-max)	-10.7 ((-5.8)-(-14.2))	
Mean pH level (min-max)	7.14 (7.10-7.29)	
Mean lactate level (min-max)	5.5 (4.5-7)	

*Number of patients with detected apricot kernels during gastric lavage

DISCUSSION

The amygdalin, a cyanogenic glycoside, was first isolated from bitter almonds by French biochemists Pierre-Jean Robiquet and Antoine Boutron-Charlard in 1830. After that, it was determined that bitter almond species have more 'amygdalin' content than sweet almond species. When the amygdalin is disintegrated with lysosomal enzymes occur cyanide. Therefore, acute cyanide poisoning may occur within minutes to hours, when the kernel of the apricot is eaten because it is containing amygdalin. As a matter of fact, it has been reported in the literature that it can cause mortality by releasing large amounts of cyanide, especially, when the apricot kernels were eaten. Although it is assumed that the deadly dose of cyanide in humans is normally 1.5

mg/kg, a case with lethal concentrations as low as 0.56 mg/kg has been reported (1, 2, 9). In the literature, it is stated that the cyanide content of the apricot kernel varies between 0.122 and 4.09 mg / g (1, 2).

In this study, the mean age of the patients was 39 months (23-65 months). Twelve of the patients were male and 9 were female. In the anamnesis of all of the patients, it was learned that they ate an average of 15 pieces (10-30) of raw apricots kernel. Ten of the patients were native Turkish citizens and 11 of the patients were Syrian refugees.

Clinical manifestations of oral cyanide poisoning occur in 2 to 4 hours after ingestion of apricot kernels in most poisoned cases (1, 2, 10, 11). Although it may be caused only induced salivary and tear secretion depending on irritation, as well as, it may be caused headache, dizziness, tinnitus, vomiting, confusion, dyspnea, tachycardia, non-cardiogenic pulmonary edema, mydriasis, change of consciousness, and even coma (2, 8, 12). Unfortunately, since the onset of clinical symptoms is non-specific general findings, the diagnosis of this poisoning is very difficult. The fact is that the main findings in acute cyanide poisoning are abdominal pain, general lethargy, nausea, vomiting, headache, and tachypnea as related to the lack of oxygen of cells. Especially, It should not be forgotten that symptoms can develop very quickly and death may occur with respiratory failure in 20 minutes or less (1, 2, 7).

In this study, it was learned that the complaints of cases started at an average of 45 minutes (30-90 minutes) after eating the apricot kernel. The most common complaints of patients who are healthy before poisoning were suddenly developing drowsiness, abdominal pain, and sweating (Table 1). And also, it was learned that the first intervention of their families was to drink ayran, vomit, washing their hands and their mouth. The mean duration of admission to the health facility was 90 min (60-120 min). In our study, the absence of mortal complications can be attributed to early admission.

Since the symptoms of cyanide poisoning are nonspecific may be confused with encephalitis or other intoxications, if not kept in mind (2). As a matter of fact, in this study, one of the patients was referred to our clinic with a misdiagnosis of encephalitis because of suddenly developing respiratory failure.

Remarkably, cyanide that it prevents generating energy from the oxygen of the cells thus it causes high-anion-gap metabolic acidosis and hypoxia without cyanosis. Because of there is not often enough time to wait for results of the blood cyanide level or other laboratory tests, in the diagnosis of cyanide poisoning, careful anamnesis and rapid evaluation of clinical findings are very important. For example, the bitter almond smell in the breath is an important finding that supports the diagnosis of cyanide poisoning. Therefore, cyanide poisoning should be kept in mind in patients who had suddenly mental status changes, especially metabolic acidosis with a high anion gap and normal PaO2 levels (1, 2, 7).

In acute cyanide poisoning, due to the deterioration of the using oxygen of the cells, occur hypoxia at all tissues and organs level. Therefore, it may be detected that deteriorated the parameters of blood gas analysis, hemogram analysis, coagulation, liver, and renal function tests. Therefore, cyanide poisoning should be kept in mind in patients who had suddenly mental status changes, especially the high anion gap metabolic acidosis and normal PaO2 levels (1,2).

In this study, it was determined that in the blood gas analysis high anion gap, metabolic acidosis, high lactate level, and other laboratory test parameters deteriorated similarly to the literature (Table-1).

The treatment of the patients with cyanide poisoning varies according to the taken cyanide dose and the severity of the patient's clinic. Unfortunately, due to insufficient anamnesis and laboratory equipment, cyanide dose may not always be determined. Although, Oxygen therapy and supportive treatment are sufficient in clinically mild cases further treatment require in clinically severe cases. In fact, the literature reported that a few cases where cyanide poisoning can be treated with only supportive treatment. However, it should be kept in mind that clinical findings may deteriorate rapidly, and these patients should be followed up in intensive care. Appropriate treatment with an early and accurate diagnosis is essential for the recovery of these patients. The basis of the treatment is a gastric wash, 100% oxygen therapy, cardiopulmonary support, fluid resuscitation, and specific antidote therapy, and, if necessary, mechanical ventilation support. 100% O2 therapy should be continued even if PaO2 pressure is normal (7). The other support treatments include the application of activated charcoal and hyperbaric oxygen therapy (8).

What if it is suspected that the cyanide poisoning, it must never lose time for to treatment by waiting for laboratory results and specific antidote therapy should be initiated as soon as possible. The literature reported that Sodium nitrite and sodium thiosulfate are the most common known as antidotes. Besides, hydroxocobalamin and cobalt EDTA, which have more rapid effects, are recommended for use alone or in combination with these antidotes in the literature (1, 2, 8, 11).

In this study, it was suspected from diagnosis cyanide poisoning with the careful anamnesis of patients, their clinical findings, and especially the smell of bitter almond in their breaths. Then, it was applied supportive treatment without losing time. During this time, blood gas analyses were resulted as metabolic acidosis with a high anion gap and normal PaO2 levels. Due to there was no enough laboratory equipment, the serum cyanide levels of patients could not be measured. In 5 of all patients who had severe poisoning symptoms (GCS <8, circulatory and respiratory failure) were applied specific treatment with hidroksikobalamin (cyanokit: Pfizer).4 patients had leukocytosis and 3 patients had thrombocytopenia. These patients who had hypotension and high liver and kidney function tests were treatment positive inotropic agents (Dopamine, dobutamine) and NAC. 4 of these patients was detected sinus bradycardia. 4 of these patients who had prolonged coagulation parameters were given vitamin K and fresh frozen plasma. Five patients who had respiratory failure were treatment mechanical ventilators. In 5 of all patients who had severe poisoning symptoms (GCS <8, circulatory and respiratory failure) were applied specific treatment with hidroksikobalamin (cyanokit: Pfizer). The mean duration of clinical response was 7.4 hours (5-18 hours). 5 patients who had intubation and mechanical ventilator support were extubated at the 13th hour (7-9).

In this study, in patients with cyanide poisoning who have high mortality potential was no mortality. This situation may be linked to which the timely diagnosis of patients and that were provided treatment of support and specific, without delay.

Limitations of the study

A limitation of this study is that although it would be ideal at diagnosing of cyanide poisining have laboratory confirmation of cyanide exposure, this was not possible due to there was no enough laboratory equipment. However, our study reflects worldwide clinical practice because cyanide levels are not currently used to guide clinical decisions.

CONCLUSION

It should be kept in mind that, acute cyanide poisoning is uncommon but it has a high potential for mortality, it may develop after eating foods included amygdalin. In addition, because of there is not enough time to waiting for results of the cyanide level or other laboratory parameters; when be suspected cyanide poisoning based on the anamnesis and clinical features in the cases; immediately supportly and specific treatment should be started. We think that, where consumption of apricot kernels is common, families should be warned that children should not consume apricot kernels, and family medicine centers and emergency units should be informed about this poisoning. This way, we believe that early diagnosis and treatment can be provided and mortality can be prevented.

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Peer-Review

Both externally and internally peer reviewed.

Conflict of Interest

The authors declare that they have no conflict of interests regarding content of this article.

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Previously presented

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Ethical Declaration

Ethical permission was obtained from the Hatay Mustafa Kemal University, Medical Faculty Clinical Research Ethics Committee for this study with date 2018 and number 06, and Helsinki Declaration rules were followed to conduct this study.

Athorship Contributions

Concept: ÇE, Design: ÇE, Supervising: MEÇ, Financing and equipment: ÇE, Data collection and entry: MEÇ, Analysis and interpretation: MEÇ, Literature search: ÇE, Writing: MEÇ, ÇE, Critical review: MEÇ, ÇE.

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