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Therapeutic And Clinical Traits Of Ludwig's Angina: A 10-year Retrospective Study Of 24 Patients

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ABSTRACT

Introduction: Ludwig's angina is a life-threatening infection that affects the floor of mouth and originates from odontogenic infections in more than 90% of cases.

Materials and Methods: In this retrospective study, medical records of hospitalized patients in the Oral and Maxillofacial Department, Tehran Taleghani Hospital between 2006-2016 with deep neck infections and Ludwig's angina diagnosis were checked. Then patients were compared in terms of demographic, anatomical, risk factors, clinical course and treatment characteristics. Data were analyzed with SPSS software version 18.

Results: The results showed that of 325 studied patients, 24 patients (7.38%) had Ludwig's angina which of these, 3 patients (12.5%) died ultimately. There was a statistically significant relationship between the occurrence of dyspnea, involved anatomical areas and days of hospitalization in ICU and death; however, there was no significant relationship between gender, age, socioeconomic status, fever, maximum and minimum blood pressure, heart rate, white blood cells count, odynophagia, origin of infection, received antibiotics, hospitalized days and systemic diseases with death.

Conclusion: Ludwig's angina is a fatal infection and requires immediate intervention and results showed involved about 8% of Deep Infections of Head and Neck Area, and the mortality rate of these patients is approximately 12.5%. Therefore, diagnosis and treatment of this disease is important in emergencies.

Keywords: Ludwig's angina; Deep head and neck infections; Mortality; Odontogenic infection.

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Introduction

Ludwig's angina is a progressing cellulitis infection involving the bilateral submandibular, sublingual, and submental spaces and elevation of the floor of the mouth [1]. Most cases of Ludwig's angina infection occur in people without underlying disease. However, people with diabetes mellitus, immune system deficiency, malnutrition, and alcoholism have an increased risk of developing the disease. Also, a direct relationship between smoking and poor oral hygiene and the occurrence of Ludwig's angina has been reported [2,3]. The occurrence of Ludwig's angina symptoms depends on the patient and the degree of infection. The occurrence of general symptoms such as fever, weakness, and fatigue depends on the immune response related to the bacterial infection. The inflammatory response leads to edema of the neck and the tissues of the submandibular, sublingual, and submaxillary spaces. Significant edema of these areas can lead to trismus and inability to swallow saliva. Pain, especially during tongue movements, is a common finding in Ludwig's angina. The symptoms of the progressive form of the disease include airway obstruction, respiratory distress, shortness of breath, and speech disorder.

As with other bacterial infections, sepsis can occur. Without immediate treatment, the submandibular infection may quickly spread to the mediastinal and pharyngomaxillary space or eventually to the bone and cause osteomyelitis [3,4]. The treatment of these patients includes antibiotic administration, airway control, drainage and surgery if necessary [5]. Tracheostomy with local anesthesia is recommended as the gold standard for airway management of these patients, but sometimes this is not possible in patients with a complicated condition [6,7]. The mortality rate of Ludwig's angina in studies depends on the clinical characteristics of the studied population and varies from 4 to 60%. The most common cause of death is upper airway obstruction. Of course, some researchers believe that this difference in mortality is due to the late diagnosis of the disease [2,7]. The purpose of this study was to recognize the clinical and therapeutic traits and risk factors in patients with Ludwig's angina (LA).

Materials and Methods

Ethics approval of the study

In this retrospective study, the files from all patients with head and neck deep infections who were admitted to Taleghani Hospital in Tehran, Iran from 2006-2016 were collected. The study was approved by the ethics committee of the Kermanshah University of Medical Science with the ethical code IR.KUMS.REC.1395.491.

Participants, study design, and setting

Assessed data included gender, age, socioeconomic status (uneducated, Lower than high school diploma, Higher than high school diploma), Temperature, systole blood pressure, diastole blood pressure, pulse rate, WBC count, odynophagia, dysphasia, dyspnea, previous treatment, involving spaces number, Airway management method, antibiotic treatment number, ICU admission days, hospital stay days, systemic condition, and source of infection.

Statistical Analysis

The data were analyzed in two parts, i.e., via descriptive analysis and Inferential Statistics. The descriptive statistics are presented as the mean standard±deviation. As for the inferential statistics, Kolmogorov-Smirnov, Fisher's Exact Test, Monte Carlo Chi-Square Test, and Pearson Correlation were used. To analyze the length of hospital stay and factors affecting it used Multiple Linear Regression and Stepwise. Statistical analyses were applied with SPSS software 18.0 (Inc., Chicago, IL, USA).

Results

In this retrospective study, the files of 325 patients with deep neck infections were examined. Of these patients, 24 cases (7.38%) were hospitalized with the diagnosis of Ludwig's angina infection. In the search of the patients' files, it was found that 3 cases died due to the disease, and 21 cases were discharged from the hospital. Among them, 16 (66.7%) were men and 8 (33.3%) were women. Their age ranged from 18 years to 62 years with a mean of 35.04±10.49 years. The patient demographic data and characteristics are summarized in Table 1. The average age of the deceased was 36.67 years and those of the discharged was 34.81 years. There was no statistically significant difference between the ages of the deceased and discharged cases. Two of the deceased patients were over 36 years old, and one case was under 35 years old. There was no statistically significant relationship between categorized age and death) p-value=0.526 Fisher's Exact Test). All three deaths occurred among cases with Ludwig's angina in the low socioeconomic status group. There was no statistically significant relationship between socioeconomic status and death (p-value=0.505، Mann-Whitney U). Twenty-two patients with Ludwig's

angina had dysphagia, and all three cases of death occurred among patients with dysphasia. Eight of the patients with Ludwig's angina had dyspnea, and all three died among the patients with dyspnea. There was a statistically significant relationship between dyspnea and death (p-value=0. 028 ، Fisher's Exact Test). Among the deceased, two cases had not received previous treatment, and one person had received previous treatment. There was no statistically significant relationship between previous treatment (no treatment) and death (p-value=1 Monte Carlo Chi-Square Test). Among the deceased patients, two patients had received previous treatment (medicine). There was no statistically significant relationship between previous treatment (medicine) and death. The average WBC count of deceased patients was 14.8 and discharged patients was 16.8 and there was no statistically significant relationship between WBC count and mortality. Among the deceased patients, two patients had involvement of eight anatomical spaces, and one person had involvement of six anatomical spaces. There was a statistically significant relationship between the number of anatomic spaces involved and death (p-value=0.017 Monte Carlo Chi-Square Test). All 24 patients with Ludwig's angina showed involvement of the submandibular space, and all three deceased patients showed involvement of the submandibular space. Among the 24 patients, 10 cases showed involvement of the buccal anatomical space. Out of 24 patients, 23 patients showed involvement of the submental anatomical space. Among the 24 patients, 15 patients showed involvement of the sublingual anatomical space. Among the 24 patients, three showed involvement of the lateral pharyngeal anatomical space. The airway of one person was opened through the Nasotracheal intubation method, 18 patients through Fiberoptic intubation, and five patients through Tracheostomy. There was no statistically significant relationship between the method of opening the airway and death (p-value=1 Monte Carlo Chi-Square Test). The average number of days of hospitalization in the ICU for discharged cases was 3.52 days, and for deceased patients, it was nine days. There was a statistically significant difference between the number of days stayed in the ICU of deceased and discharged patients (p-value=0.031، Mann-Whitney U). The average number of days stayed in the hospital for discharged cases was 9.52 days, and for deceased cases, it was 9.33 days. There was no statistically significant difference between the number of days stayed in the hospital of the deceased and those who were discharged (p-value=0.896، Mann-Whitney U). Among the 24 patients, 10 had one systemic disease, five had two diseases, and one had three systemic diseases. Eight patients did not have systemic disease (Table 1). Among the patients, 2 were treated with one antibiotic, 14 with two antibiotics, and 8 with three antibiotics. The most common antibiotic received was cephalosporin and metronidazole in 9 patients. There was no significant statistical association between the type of antibiotic and mortality (Fisher's Exact Test p value=.082). In the multiple linear regression model using the stepwise method, only the lateral pharyngeal space involvement variable was statistically significant. The involvement of this area adds an average of 4.39 days to hospital stay days. There was a direct and significant correlation between hospital stay duration and intensive care unit stay duration (p-value =0.029, ρ=.445). There was also a direct and significant correlation between hospital stay duration and high blood pressure (p-value=.032, ρ=0.438) (Table 3). Among the 24 infected individuals, 24 patients had involvement of the mandibular teeth and one patient had involvement of the maxilla region. The most affected tooth was the mandibular third molar.

Table 1. Distribution of the studied cases according to different characteristics.

Variable	*N (%)*
Gender	
Male	*16 (66.7 %)*
Female	*8 (33.3%)*
Age (year)	*35.04±10.49 (y)*
Mean±SD	
Space involved number	*1 (4.2%)*
Three	*3 (12.5%)*
Five	*9 (37.5%)*
Four	*8 (33.3%)*
Six	*1 (4.2%)*

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Variable	N (%)
Seven	2 (8.3%)
Eight	
Outcome	21
Improved	3
Death	
Socioeconomic status	17 (70.8%)
Low (uneducated)	7 (29.2 %)
Moderate (Lower than high school diploma)	0
High (Higher than high school diploma)	
Odynophagia yes	23 (95.8%)
No	1 (4.2%)
Dysphagia yes	22 (91.7%)
No	2 (8.3%)
Dyspnea yes	8 (33.3%)
No	16 (66.7%)
Length of l stay in hospital (days) (Mean±SD)	9.50±2.28
Length of stay in ICU (days)	4.21±2.81
Previous treatment	
Noun	4 (16.7%)
Drug	16 (66.7%)
Surgery	0
Drug & Surgery	4 (16.7%)
Vital sign	
Blood pressure (mm Hg)	119.17/75.83mmHg (mean)
Temperatur e(°C)	37.8333±5088 °C
Pulse rate(Beat per minute)	(mean±sd) 94.29±16.66 (mean±sd)
Systemic disease	
ICU: intensive care unit	8 (33.3%)
	16 (66%)
	5 (20.8%)
Hypothyroidosm	2 (8.3%)
Hepatitis	1 (4.2 %)
Pregnancy & Hepatitis	1 (4.2%)
Tongue SCC & Opium	1 (4.2 %)
Abuse	2 (8.3%)
Drug abuse & Smoking Smoking & Hypertension & Alcoholism	1 (4.2%)

		WBC.count			
		Mean	Standard Deviation	Minimum	Maximum
Death	No	16.8952	4.5317	7.4000	23.0000
	Yes	14.8333	2.3007	12.5000	17.1000
	Total	16.6375	4.3363	7.4000	23.0000

Table 2. Relation between death and different parameters.

	Survived (21)	Death (4)	Test of sig	P
Age (year) Mean±SD	34.81±11.19	36.67±3.06	Mann-Whitney U	.505
Involving spaces number			Monte Carlo Chi-Square Test	
Three	1	0		.017
Four	3	0		
Five	9	0		
Six	7	1		
Seven	1	0		
Eight	0	2		
Dyspnea (8 cases)	5	3	Fisher's Exact Test	.028
ICU stay days (Mean±SD)	3.52± 1.81	9.00± 4.36	Mann-Whitney U	.031

Table 3. Results of multiple regression.

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	9.105	.395		23.059	.000	8.279	9.932
Involving.spaces.lat. pharyngeal	4.395	1.280	.619	3.435	.003	1.717	7.073

R=.619

R Square=.383

Adjusted R Square=.351

Discussion

Ludwig's angina included about 7.38% of deep head and neck infections in our study. The results of this study showed that 12.5% of infected patients eventually die. The mortality rate was relatively high in Iran, the mortality rate in Wang and colleagues' study was 1%, which was inconsistent with the results of our study [8]. This may be because the medical referral system in Iran has not been fully implemented. The more involvement of men has been identified in our study and other studies. Maybe the reason is their poor oral hygiene and immune system compared to women [7,8,9,10]. The highest occurrence of Ludwig's angina was in patients under 35 years old (59%). The third molar tooth was the most common cause of Ludwig's angina. Maybe the reason is the close anatomical connection of it with the submandibular spaces. As is known, the number of dental abscesses increases with age to 35 years, which can be caused by the growth of wisdom teeth and the lack of health care for these teeth, and shows that attention should be paid to dental diseases and periodontal tissue, especially wisdom teeth. The average age of those who died was 36.67 years, and those who were discharged were 34.81 years. Although all 3 cases of death of patients happened in male patients, there was no statistically significant relationship between gender and death of patients. There were significant differences between dyspnea, involving space number and ICU admission days in the cases of discharged and died. In this study, diabetes was the most common systemic disease (20%) of Ludwig's angina-diseased patients. In Ovassapian's study et al, [11] 40% of patients with Ludwig's angina also had systemic problems. Chou and his colleagues [12] stated in their study that one-third of patients with Ludwig's angina have systemic diseases. Ridder and his colleagues reported that diabetes was the most common systemic disease in patients, which was present in almost 9% of studied patients, which was consistent with the results of our study [13]. The reason for this may be the immune system dysfunction in dia-

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betic patients and the subsequent increase in infection prevalence [14]. The average length of hospital stay was 5-14 days, which is longer than previous studies [15]. In a study by Ridder and colleagues [13] in 2005, the average number of WBC 14.7 cell per mm^3 was reported in subjects with deep cervical infections, which supports our results. Infection of the retropharyngeal space and acute inflammation of the mediastinum and inflammation of the pericardium were not seen in this study. The results of our study showed that the most involved spaces are the submandibular spaces (100%), submental (95.8%), pterygomandibular (75%), sublingual (5.62%), and buccal 41.7%. In other studies, the involvement of submandibular space is mentioned as the main anatomical space involved in disease [16,17]. In our study, the antibiotic group that was prescribed to patients included Cefazolin and Metronidazole (37 percent). In Srirompotong's study and colleagues [18], the most used antibiotics for patients were penicillin and a combination of penicillin and metronidazole, which does not match the results of our study.

Those who died were hospitalized for an average of 9 days, and those who were discharged were hospitalized for 3.5 days. In Rowe's study and his colleagues [15], the average length of stay in hospital and ICU Patients with Ludwig's angina were reported for 2 and 5 days, respectively. In their study was also suggested that surgical intervention can reduce the duration of hospitalization. However, the length of stay hospital of patients with Ludwig's angina in Greenberg study et al. [19] in 2007, 10.5 days was reported to be similar or Chou and his colleagues [12]. Among the airway opening methods, the most used technique is Fiberoptic intubation (75%). Ovassapian's study and his colleagues [11] also stated that most cases of opening the airway through Fiberoptic method intubation have been. In this study, it is also stated that tissue edema and abundant secretions are common obstacles to successful performance of this procedure. Greenberg et al, [19] investigated 29 patients with Ludwig's angina and reported that the average age of the patients was 52 years, and the majority of them were male. Also, in their study, the source of disease in 95% of examined patients was primary dental infection.

Conclusion

Ludwig's angina is a deadly infection that requires immediate intervention. Therefore, immediate diagnosis of this disease in emergencies is very important. Physicians and especially maxillofacial surgeons should be familiar with manifestations of Ludwig's angina because early diagnosis rapid initiation of antibiotic treatment and possible surgical treatment can prevent mortality. The results of our study showed that 12.5% of infected patients eventually die. Therefore, considering that deep head and neck infections in developing countries such as Iran still involve the health system and include some deaths of patients referred to departments involved in the treatment of head and neck diseases, knowing more about this disease will help to improve treatment and prepare medical centers for proper management these patients.

Conflict of Interest

There is no conflict of interest to declare.

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