ORIGINAL PAPER

Influence of Age on the Survival and Mortality Rate in Acute Caustic Poisonings

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ABSTRACT

Objective: Acute poisonings with caustic substances can cause severe chemical injuries to the upper gastrointestinal tract, which can be localized from the mouth to the small intestines. They are seen very often among young people in their most productive years. The aim of this study is to examine the influence of patient's age on the mortality rate and survival of patients with acute caustic poisonings, and also to analyze their correlation. **Material and Methods:** We studied medical records from 415 patients, aged between 14 and 90 years, who were hospitalized and treated at the University Clinic for toxicology and urgent internal medicine, Skopje, Republic of Macedonia, in the period between 2007 and 2011. **Results:** In the survey we included 415 patients with acute corrosive poisonings, from which 295 (71.08%) were females and 120 (28.92%) were males. 388 (93.49%) from the total number of patients ingested the corrosive agent with suicidal attempt and 27 (6.5%) ingested it accidentally. **Conclusion:** Unregulated production, import, packing and labeling of various caustic agents, due to inappropriate legislative, made them one of the most often abused substances in everyday life, especially in developing countries where the number of caustic poisonings rises.
Key words: caustic substances, age of patients, mortality, survival rate, intensive care

1. INTRODUCTION

Acute poisonings with caustic substances can cause severe chemical injuries to the upper gastrointestinal tract, which can be localized from the mouth to the small intestines. They are a result of a sudden or intentional ingestion of caustic substances and can be seen in patients of different ages. These kind of poisonings often end up with post corrosive complications, such as stenosis, but they can also have a fatal ending due to the perforation of the gastrointestinal lumen or tracheal necrosis (1-3). Severity of the post corrosive chemical injuries of the upper gastrointestinal tract depends on nature of the caustic substance, its quantity and concentration, time of exposure, act of swallowing and many other factors(4). Unlikely in children, where caustic poisonings are most often accidental, in adult patients these poisonings are intentional, with suicidal attempts (>90%)(5).

In many countries there are educational programs and activities, organized among population with lower health culture, all with an aim to explain the danger of abuse of caustic chemicals and consequences of ingestion. Regardless, the number of caustic poisonings is very high, they have severe clinical expression, clinical diagnostic investigations are hard to perform, and outcome is often uncertain (6). The annual report of the American poison control center from 2011 reports that from the total number of registered poisonings 202056 are intoxications due to abuse of cleaning agents, which are in the group of chemical agents with mainly corrosive characteristics. A five year study conducted in Turkey stated that 2.5% of the total numbers of poisonings are caustic poisonings. A similar study performed in England and Wales showed that a third of the total number of poisonings are due to the abuse of agents used for maintaining of the hygiene in the households, and these poisonings are more often among the adults, alike as among children (7-9).

Many authors consider that findings from the urgent esophagogastroduodenoscopy can be used as a basis for treatment of caustic poisonings. They are many endoscopic classifications of the post corrosive injuries, but we use the one suggested by Kikendal. Treatment of these poisonings is conservative in milder and uncomplicated cases. The treatment is strictly surgical in patients with severe and life-threatening complications (10-11). Through literature there are many reports that show the mortality rate in acute caustic poisonings and all the effort that should be made to reduce it.

The aim of this study is to examine the influence of patient's age on the mortality rate and survival of patients with acute caustic poisonings, and also to analyze their correlation.

2. MATERIAL AND METHODS

We studied medical records from 415 patients, aged between 14 and 90 years, who were hospitalized and treated, in the period between 2007 and 2011. After admission to hospital all patients were immediately situated at the Intensive care unit (ICU) and in the first 12-24 hours all of them went under urgent esophagogastroduodenoscopy. It was performed using an endoscope for upper endoscopy, type Olympus (Japan) with a

diameter of 9.2 mm. Control esophagogastroduodenoscopy was carried out after 15 to 25 days after caustic ingestion. For a better accomplishment of the procedure we prepared the patients with pre-medication with Xylocaine gel, as a local anesthetic. Methods as insufflations and retro-visualization were performed very carefully because of the great risk from causing additional iatrogenic injuries. Post-caustic injuries are classified according to the Kikendal's classification (Table 1).

Patients, according to their age, were divided in three groups:
- Group of patients aged between 14 and 35 years
- Group of patients aged between 35 and 55 years and
- Group of patients older than 55 years.

They were also divided according to their gender, purpose of intoxication, type of abused corrosive substance and severity of post-corrosive injuries.

We analyzed the influence of age on several parameters: need of intensive care, duration of stay in the Intensive care unit, duration of hospitalization, severity of post-corrosive lesions on the upper GIT, mortality and survival rates.

3. RESULTS

In the survey we included 415 patients with acute corrosive poisonings, from which 295 (71.08%) were females and 120 (28.92%) were males. 388 (93.49%) from the total number of patients ingested the corrosive agent with suicidal attempt and 27 (6.5%) ingested it accidentally.

The age of patients varieties in the interval 41.38±18.06 years, ±Cl: 39, 64-43, 13; where the minimal age is 14 years, and maximal 90 years. Distribution of patients' age in different ages groups showed that the majority of patients 181 (43.61%) belong in the first group, subjects aged between 14 and 35 years, 144 (34.70%) were patients aged between 35 and 55 years, and only 90 (21.69%) were patients older than 55 years. Greater number of patients, 388 (93, 49%), ingested the corrosive agent on purpose and the majority of them abused hydrochloric acid.

Clinical characteristics of patients	
Total number	415
Woman (%)	295 (71.08)
Man (%)	120 (28.92)
Age	17-88 (51.43± 17.82)
Age groups	
14-35	181 (43.61)
35-55	144 (34.70)
> 55	90 (21.69)
Motive for intoxication	
Suicidal	388 (93.49)
Accidental	27 (6.5)
Type of corrosive agent (%)	
HCl	205 (49.39)
NaOH	107 (25.78)
CH3COOH	37 (8.91)
H2SO4	2 (0.48)
NaClO4	63 (15.18)
H2O2	1 (0.24)
Grades of post-corrosive injuries (%)	
I	48 (11.56)
II A	149 (35.90)
II B	101 (24.33)
III	93 (22.40)
IV	24 (5.78)

Table 1. Clinical characteristics of patients

Degree of injuries	N (%)	Mortality (%)
Grade I	48	0
Grade II A	149	0
Grade II B	101	1
Grade III	93	6
Grade IV	24	23
Person Chi-square: 316.49; df=4; p=0.000 ***		

Table2. Degree of post-corrosive damages and mortality rates

Years	Median	Mean	Std. Dv.	No. uncsd	N. censrd	Total N
14-35	180.00	176.09	26.10	4	177	181
>35-55	180.00	170.09	41.00	8	136	144
>55	180.00	144.94	70.56	18	72	90
Total	180.00	167.25	45.74	30	385	415
Chi=28.86; df =2; p=0.000***						

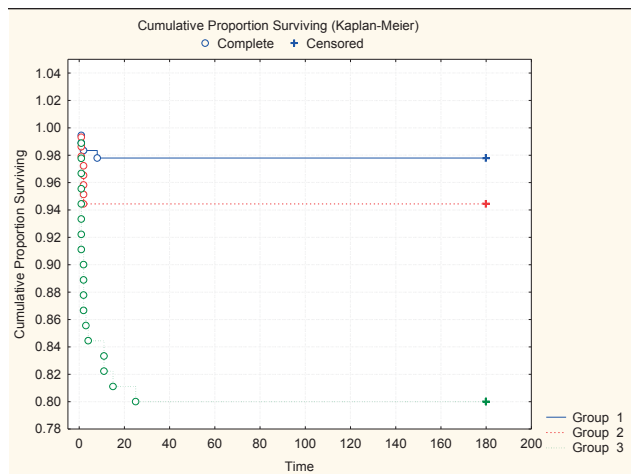Table 3. Descriptive analysis for age groups

Figure 1. Cumulative proportion surviving

According to the classification of Kikendal the greater number of patients had post-corrosive lesions of grade II A (Table 2).

Results regarding on differences in duration of stay in ICU, also considering the distributions of patients in different ages groups, showed that F=22.86 and p<0.001 (p=0.000) and there is a significant difference in the duration of stay along different ages groups in patients with corrosive poisonings. On graph 1 we show the relation between age of patient and stay in the ICU. For r=0.32 (p<0.05) there is mild, but still significant correlation. In fact with greater age of patients the duration of stay in ICU becomes longer and that is why the correlation between patients' age and hospitalization in ICU is significant.

Figure 1 illustrates results from the difference in duration of hospitalization, considering distribution of patients in different age groups, which showed that for F=27.32 and p<0.001 (p=0.000) there is a significant difference in days of hospitalization in ICU between the age groups of patient with corrosive poisonings.

Correlation between different ages of patient and duration of hospitalization with r=0.30 (p<0.05) there is mild, but still significant correlation.

Studied correlation between ages of patients and grades of post-corrosive injuries showed strong and significant correlation for R=0.47 (p<0.05). Increasing of age goes with a higher grade of post-corrosive injury. The correlation between ages and grades

of post-corrosive injuries for R=0.43 (p<0.05) showed mild, but significant correlation. The raise of patients' age is followed with higher grades of injuries.

We also analyzed the correlation between grades of post-corrosive lesions and mortality rate. For Chi-square=316.49; df =4 and p=0.000 *** there is a significant correlation between mortality rate as dependent variable and influence of grades of post-corrosive injuries as independent variables (Table 3).

Mortality

Logistic regression analyses for mortality rate in acute corrosive poisonings as dependent variable and influence of age intervals as independent variables showed that for Chi square=25.13 and p<0.001 (p=0.000) there is a significant correlation between mortality and influence of age.

We took the group aged between 14 and 35 years as a referent category.

From OR values we can show that:

- Patients older than 55 years have 11.06 times (OR=11.06/Exp(B)) greater risk of fatal ending of the poisoning correlated to patients aged between 14 and 35 years, in fact the influence of age higher than 55 years is significant (95.0% Cl: 0.3, 62-33, 82/p<0.001(p=0.000)).
- Patients aged between 35 and 55 years have 2.60 times (OR=2.60/ Exp(B)) greater risk for fatal ending of the poisoning correlated to patients aged between 14 and 35 years, but the influence of this age group, 35-55 years, is not significant (95.0% Cl:0, 77-8, 82/ p>0.05(p=0.125)).
- Analyses of survival rates in 415 patients with caustic poisonings was in a follow up period of 180 days. Total 30 (7.23%) patients died from the intoxication and 385 (92.77%) patients (censored patients) were alive until the end of our study.
- Patients aged between 14 and 35 years consisted of 177 (42.65%) patients and time of survival varied in the interval 176.09±26.10 days.
- Patients aged between 35 and 55 years consisted of 136 (32.77%) patients and the time of survival varied in the interval 170.09±41.00 days.
- 72 (16.87%) patients were older than 55 years and their survival time varied in the interval 144.94±70.56 days.
- In the total number of patients (415) the survival time varied in the interval 167.25±45.75 days (Table 4).
- We can see that the majority of deaths were recorded in the first 10 days of follow-up.
- Differences in survival between different age groups
- For Chi=28.86 and p<0.001(p=0.000) there is a significant difference in the survival rates between different age groups.
- Patients aged between 35 and 55 years have a shorter survival period compared to patients aged between 14 and 35 years, but the difference for Log-Rank Test=1.58 and p>0.05 (p=0.11) is not significant. (Log-Rank Test/14-35 years and 35-55 years/Test statistic=-1.58; p=0.11).
- Patients older than 55 years have shorter survival period compared to patients aged between 14 and 35 years and the difference in survival for Log-Rank Test=-5.03 and p<0.001 (p=0.000) is significant. (Log-Rank Test/14-35 years and >55 years./ Test statistic=-5.03; p=0.000).
- Patients older than 55 years have shorter period of survival compared to patients aged between 35 and 55 years and

the difference in survival for Log-Rank Test=-3.41 and p<0.01 (p=0.001) is significant. (Log-Rank Test/35-55 years and >55years./Test statistic=-3.41;p=0.001).
- Predictive role of different age groups
- Results from Cox's regression, the method used for calculating the predictive role of age groups on survival of patients with caustic poisonings, are shown on table 2.
- The patients aged between 14 and 35 years were taken as a referent category.
- Patients aged between 35 and 55 years for HR=2.55; (95% Cl for HR=0.77-8.45; p>0.05) have 2.55 times shorter survival time compared to referent group (14-35 years). The influence of age interval, 35-55 years, is not significant.
- Patients older than 55 years for HR=9.65 (95%Cl for HR=3.26-28.51;p<0.001) have 9.65 times shorter survival period than referent group (14-35 years). The influence of this age interval (>55 years) is significant.
- Statistical analysis of all provided date was made by using the statistical program STATISTICA 7.1 and SPSS 13.0.
- In series with attributive characteristics we calculated structural percentages (%);
- Differences in analyzed parameters in the series with attributive characteristics (gender, corrosive agents, age groups and systemic complications) were tested with Pearson Chi-square (x^2).
- We also provided results from descriptive statistics (Mean ± Std. Dev ± 95.00 Cl. Minimal value, maximal value).

In analyses of survival period we used Kaplan-Meier method, while differences in survival between two age groups were tested with Log-rank Test. Predictive value of influence of different age groups on survival period was calculated with Cox regression method (HR with 95% Cl).

Statistical significance was shown for p<0.05.

In series with numerical characteristics we calculated the following:

- Differences between certain analyzed parameters (intensive care; hospitalization) in different age groups was tested using Analysis of Variance (F)/ Scheffe Test;
- Influence of age groups on duration of hospitalization in intensive care unit and duration of hospitalization in general, tested with Multiple Regression (R);
- Prognostic value of age groups as independent variables on mortality rate, acute and late post-corrosive complications, tested with Logistic regression (Chi square, Wald, Exp(B));
- Relation between age/age groups and grade of post-corrosive injuries, tested with Spearman Rank Order Correlations (R);
- Relation between age of patients and stay in the intensive care unit, duration of hospitalization, tested with Pearson coefficient for correlation (R).

4. DISCUSSION

Unregulated production, import, packing and labeling of various caustic agents, due to inappropriate legislative, made them one of the most often abused substances in everyday life, especially in developing countries where the number of caustic poisonings rises (12). Data for Republic of Macedonia state that caustic poisonings take 15-18% of the total number of poison-

ings, they are responsible for 14-27% of the complications and they have mortality rate of 4-6 % (13). Intoxications with caustic substances cause severe post-corrosive complications in the upper part of the gastrointestinal tract, which can be influenced by age of the patients, gender, amount of ingested agent, duration of exposure and the time frame between initiation of treatment and completion of urgent esophagogastroduodenscopy (14).

Caustic substances cause tissue destruction due to coagulation or colliquative necrosis with high percentage of late post-corrosive complication of 15-85%. The mortality rate is still high despite the intensive hospital care, sophisticated diagnostic and therapeutically approaches. Among literature different mortality rates were shown, from 2 to 10 % (15).

The role of therapy in acute caustic poisonings is to prevent perforation of the gastrointestinal wall and to avoid the processes as progressive fibrosis and stenosis of the esophagus and stomach. Perforation of esophagus or stomach can be treated only surgically. Studies state that elasticity of both esophageal and gastric walls, after caustic poisoning, is decreased due to the low collagen amount, which production is compromised. After progressive fibrosis many cases end up with narrowing of the gastrointestinal lumen, especially in the esophagus and stomach (16). Early and late post-corrosive complications in acute caustic poisonings are related with the severity of the post-caustic injuries, seen with upper endoscopy. They are also related with age of patients and time frame between intoxication and admission to hospital. These factors influence the mortality and survival of patients. Unwanted outcomes can be expected several hours or even several months or years after the poisoning (18).

Age of patients, gender, time frame between ingestion and start of reanimation, consciousness, positive peritoneal signs, shock index, pH value and concentration of bicarbonates in the arterial blood can be used as prognostic factors for mortality in patients with acute caustic poisonings.

Remarkable higher mortality rate is seen among patients who are ≥ 50 years, have positive peritoneal signs, shock index higher than 1, pH value of 7.2 or lower and bicarbonates concentration in arterial blood sample lower than 16 mEq/ L (19-20).\

In our study we confirmed that mortality rate and time of survival are significantly correlated with patients' age. Another study also stated that number of older patients hospitalized at the intensive care unit is decreased and their cumulative survival rate was also lower compared to younger patients. However, despite the greater percentage of systematic complications, and also higher mortality rate in older patients (older than 65 years), seriousness of the post-corrosive injuries of the upper gastrointestinal tract didn't have great influence or didn't have any influence at all on the survival period. This fact is also shown in groups of younger patients (younger than 65 years) who had severe post-corrosive damages (grade III B) (21).

Acute caustic poisonings have great risk of fatal outcome especially during the acute phase (in the first 96 hours) and this is why we should pay special attention on quick transportation of the patients to specialized hospitals and their admission to the intensive care unit, where they should receive prompt therapy and also artificial ventilation if needed. Artificial nutrition should be administrated in the chronic phase of the poisoning, which can last up to few months (22-23).

Estimation of cost/benefit in different therapeutically protocols and also duration of hospitalization are very complex and questionable topics. Doctors for a long time thought that cost of the treatment should not influence the decision making process related to the charge of the entire treatment and duration of hospitalization. Length of hospital stay and treatment in patients with acute caustic poisonings are of a great importance for the final outcome and also for the economical effect and reduction of the hospital costs. Many control studies conducted on large group of patients stated that hospitalization of these patients start in the intensive care units (ICU), usually lasts 10 to 15 days, and can be postponed to 25 or 30 days depending on severity of the post-corrosive injuries of the upper gastrointestinal tract and occurrence of eventual late complications (24-25). Treatment of acute caustic poisonings should be accomplished in the intensive care unit (ICU) due to the severe clinical condition of the majority of patients and also the need for intensive monitoring. This period usually lasts 10 to 20 days, actually until the processes of intensive granulation and healing of the caustic injuries are over. At the same time the patients require different types of artificial nutrition, which depends on the grade of the post-corrosive injuries. Hospital stay in these patients is significantly shorter after standardization of sophisticated ways of artificial nutrition (home enteral nutrition) (26-27).

Post-corrosive complications may cause hemorrhages in the upper part of the gastrointestinal tract, even in the early acute phase, due to the damages of the esophageal and gastric walls, tracheal necrosis and esophageal or gastric perforation, which complications may cause serious and urgent state or even end up fatally. In this kind of cases the only treatment of choice is surgical, where the outcomes are always very unpredictable. Ingestion of greater amount of caustic substance with suicidal attempts usually causes injuries of the esophageal and gastric walls and they go through the muscular layer where the vascular net is very rich and its damage may cause serious and intensive bleeding or rupture of the wall and leakage of the gastrointestinal content in the mediastinal or peritoneal cavity. This can end up with mediatinitis or peritonitis, very urgent and dangerous complications which ask for urgent surgical interventions and are related to high mortality rates (28-30).

Morbidity and mortality rates in acute caustic poisonings are still high and depend on the severity of the post-corrosive injuries of the upper gastrointestinal tracts, approved with urgent esophagogastroduodenscopy. Often these poisonings have unwanted outcomes even before the patient was administered to specialized hospital, where the treatment is very professional and sophisticated. Survival of these patients is still an imperative and it can be prolonged with prompt diagnosis, prevention of perforation and quick treatment with intensive hyper alimentation during the acute phase (first 15 days) and control of fatal infections. During the chronic phase we should pay special attention to surgical treatment and appropriate decision for treating late chronic complications surgically (stenosis of esophagus and stomach) (31).

5. CONCLUSION

Mortality rates in acute caustic poisonings are still very high and are a serious problem during the treatment. Percentage of fatal outcomes is higher during the acute phase of treatment (first 96 hours), usually a result of gastrointestinal complications (perforation), while during the chronic phase number of deaths is lower (21 days after poisoning). Chronic phase of acute

caustic poisonings is related to systemic complications and late post-corrosive complications (esophageal and gastric stenosis).

Mortality and survival rates are higher in patients with more severe grades of post-corrosive injuries in the upper gastrointestinal tract, seen with upper endoscopy (grades II B and III). Admission of patients to the intensive care unit (ICU) and their hospitalization in specialized hospitals are of a great importance for the final outcome. Our study showed that in patients with more severe post-corrosive damages in the upper gastrointestinal tract the mortality rate is higher and survival period is shorter. Duration of hospital stay and stay in the intensive care unit are positively correlated to the age of patients.

CONFLICT OF INTEREST: NONE DECLARED.

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