Correct time determination for beginning of the first bougienage in cases with Stomatoe sophagitis corrosiva is probably the most important step for successful outcome of treatment procedures. The aim of this study was to describe patterns of acid burns of the oesophagus in Guinea pigs. We tested 20 animals (mean initial weight of 520 g on average) divided into two groups: Group 1 (subjected to 98% H$_2$SO$_4$) and Group 2 (15% H$_2$SO$_4$). Changes in weight, pathohistological findings (biopsy), time and cause of death (after International Classification of Diseases - 9th revision) were analysed. The results revealed that animals from Group 1 died about the day 6 from ingestion of the acid with mean decrease of weight of 9.83% as the difference with the initial one was statistically significant (p<0.05). Peritonitis (ICD9 Dx:567) was the cause of death with highest frequency. During the study period of 1 month, Peritonitis and Mediastinids acuta (Dx:518) were pathohistological diagnoses with highest frequency. Only 3 animals from Group 2 died during the period of observation while the rest (n=7) survived afterwards. The relative risk of dying up to the day 9 included after ingestion of 98% against 15%H$_2$SO$_4$ was 9 (p<0.05). The histological analysis on the day 10 from ingestion revealed severe necrotic changes of all layers of the oesophagus by concentrated acids. Above results might be found useful in planning larger experimental studies on acid burns of the oesophagus in the future. Acta Medica Medianae 2003; 42 (2): 5-8.

Key words: chemical burns, oesophagus, Guinea pigs, oesophageal stenosis, relative risk (RR)

Department of Otorhinolaryngology
Faculty of Medicine, Stara Zagora (Bulgaria)*
Department of Social Medicine, Faculty of Medicine, Plovdiv (Bulgaria)*

Correspondence to: Valentin K. Stojanov
Department of Otorhinolaryngology, Faculty of Medicine
Stara Zagora, Bulgaria

Introduction

Stomatoesophagitis corrosiva are severe disabling diseases. Affected persons are usually young people which determines medico-social importance of this problem. The type of corrosives (acid or alkali) is also very important in respect to the degree of possible damages and risk of development of subsequent stenoses. In this sense, the key aspect of treatment strategy is the right determination of the initial moment of oesophageal dilatation which, at the end, leads to surmounting of newly appearing strictures.

Since a big deal of subjectivism in determination of periods for bougienage existed, a number of experimental studies during last 40 years were performed aiming at determination of stages of fibrous tissue formation. In most studies, however, caustics used were alkalii and experimental animals - dogs and rabbits (1-8). There were single studies on damages by acids (1). In spite of efforts of different authors, only Peacock Ir (6) had presented a proper hypothesis on the need for early bougienage based on the fact that collagen content in the granular tissue increased during first 8-10 and further remained constant or decreased.

The aim of our preliminary study is to add new data to clarify the relationship between concentration of the caustic ingested, processes of cicatrisation and initial moment for the beginning of oesophageal dilatation. This might also help in planning larger experimental studies on acid burns of the oesophagus in the future.

Material and methods

Experimental animals. The study was carried out in the Department of Otorhinolaryngology in collaboration with the Department of General and Special Pathology from the Faculty of Medicine at the Thracian University, Stara Zagora, Bulgaria. One of the particular purposes of the experiment was to describe changes of the oesophageal wall in Guinea pigs after ingestion of acid. Test pigs (N=20) from the vivarium of the Faculty of Medicine were divided into two groups of 10 animals (N$_1$=10, N$_2$=10). The mean weight of animals at the beginning of the experiment...
was 520 g on average. This parameter was especially important for determination of the adequate dose of caustic per animal to be ingested.

Application of the corrosive. It was calculated from the mean initial weight of animals that 2-3 drops of the corrosive were equal to 25-30 g of the same when ingested by a person with weight of 70 kg. Animals from the first group were given 2-3 drops of concentrated sulphuric acid (98% H₂SO₄, Group 1) while the animals from the second group were given 2-3 drops of diluted sulphuric acid (about 15% H₂SO₄, Group 2). The acid was provided by 'Merck & Co.' (USA). Guinea pigs from both groups were under careful supervision of authorised personnel and treated humanely at all times. Until death, they were provided with water and food ad libitum.

Laboratory methods. The period of observation was 1 month. We followed clinical changes every day and, at regular time intervals under general anaesthesia, biopsies were taken from the wall of the oesophagus and stomach for inspection and histological examination. Probes were prepared according to the routine methods and stained with hemalauneosin. Slices were also stained for collagen after the method of Van Gieson for visualisation of the fibroplastic processes. We used different magnifications (x32, x100, x125, x250 and x400) on a microscope 'Jena Med' from 'Carl Zeiss' (Germany).

Statistical analysis. For purposes of this study were used the following statistical methods: descriptive statistics, nonparametric tests and a method for calculation of the relative risk (RR with Taylor series 95% confidence interval). Different tests were applied assuming 5% significance of the null hypothesis (two-tailed p=0.05): Student's t-test, maximum-likelihood ratio x²-test (x²-LR), Fisher's exact test (FET) and Kendall's nonparametric test for correlation (Kendall's T). The statistical software SPSS 5.0.2 (USA) was used for calculations and chart presentations.

Results

Initial weight. Descriptive statistic analysis indicated that mean initial weights of test animals in both groups were equal (t=0.78, p=0.45): 520.10 g (SD=1.10) for Group 1 and 520.70 g (SD=2.16) for Group 2.

Lethal outcome. Almost all Guinea pigs from Group 1 (98% H₂SO₄) died during first few days from ingestion of the caustic -9 animals up to day 7 incl. and 1 animal later (on day 21). The mean time period for the lethal outcome to occur in this group was between days 2 and 9, that is, on day 6 (5.2±3.7, N=10). The mean final weight (at death registration) of animals was 469.00 g (SD=43.83). The difference of 51.10 g with the initial one was statistically significant (t=3.70, p=0.005), that is, a mean decrease or 9.83% (SD=8.41). Peritonitis was with highest frequency (n=6) as a cause of death (Peritonitis diffusa purulentia or Peritonitis necroticans, ICD9 Dx:567) followed by Mediatinitis acuta (Dx:518) (n=2) and Fistula bronchoesophagealis (Dx:530) (n=2), that is, 60%, 20% and 20% respectively.

Most of animals from Group 2 (15% H₂SO₄) survived after 1 month (n=7), one died on day 3 and two died after the day 21 from ingestion of the acid. Very high differences between the initial and final weights in the latter two pigs should be noted - 111 g and 120 g, that is, a decrease with 21.31% and 23.08% respectively. Mediatinitis acuta was the cause of death of the first pig while the latter two died from Fistula bronchoesophagealis (Dx:537).

Time of death. Time of the death (in days) from the beginning of the experiment was divided into two intervals: up to the day 9 incl. and after the day 9 (see above). The difference in time of the death as depending on the type of acid (98% or 15% H₂SO₄) was statistically significant (x²-LR = 14.72, p=0.00012; FET - p=0.00109). The inverse linear association between time of the death and the type of acid was significant (x = -0.8, p<0.05) as was also the relative risk of 9 (RR = 9.95% CI 1.39-58.4) (Fig.1).

Up to day 9 (incl) Day 9 +

Pathology and pathohistological findings. Causes of death for animals from Group 1 were associated with pathological changes that were carefully described and summarised in two groups. The first group consisted of local alterations of the oesophageal wall, that is, a total necrosis of mucosa and submucosa as well as of the whole thickness of muscularis mucosae. Similar alterations were also found in the stomach region but, probably because of greater thickness of the muscle layer, a perforation was observed in one single case only. Above changes led to severe complications in animals (N=10) as, according to biopsies examination, with highest frequency were Peritonitis (n=6) and Mediastinitis acuta (n=5) followed by Fistula bronchoesophagealis (n=2), that is, 60%, 50% and 20% respectively (Fig. 2). The total exceeded 100% because some of animals were pathohistologially diagnosed with 2 items. The second group of pathological changes consisted of general intoxication with subsequent renal failure. The single pig from Group 1 (reg. No. 11) that survived up to the day 21 was with a decrease of weight of 150 g (29%) at the end. Pathohistological findings on the day 5 from ingestion of the concentrated corrosive revealed that the oesophageal lumen was filled up with necrotic masses (detritus). Surface layers of the epithelium were with well manifested necrotic changes. On the day 10, the finding in pig No. 11 was similar to already well noticed ballon dystrophy of epithelial cells.
The animals from the Group 2 (N=10) were with much better survival rate. On the day 10 from ingestion of the diluted corrosive, pathohistological finding revealed very well manifested necrotic changes, totally penetrating the oesophageal wall from mucosa to muscularis mucosae. Some of the epithelial cells were with well expressed basophilic dystrophy. Histological examination on the day 17 described certain differentiation, that is, superficial necrosis of the epithelium with visible desquamation.

Discussion

Most authors (1-8) recently working on the problems of chemical burns of the oesophagus consider only alkalii to be important in practice as corrosive agents. Our experimental study revealed, however, that ingestion of acids, even diluted ones, could also provoke significant changes in the normal structure of the oesophagus and thus lead also to irreversible alterations and even death. Similar results have also been reported by other authors (15, 17).

Our results, when discussed in respect to the treatment strategy, do not agree with those by Brailski (18) who has found the formation of granular tissue to occur between day 3 and 5 from ingestion. We have not been able to describe collagen fibres, which have been reported by Sotirov (16) to appear on days 7-10 and considered indicators that virtually this is the most appropriate time for beginning of the active treatment, that is, dilatation of the oesophagus.

Subjectivism in endoscopic determination of the degree and volume of corrosive oesophagitis varies considerably with qualification of the team and the type of equipment used. Above circumstances additionally complicate the a priori difficult decision to be taken by physicians in respect to the initial moment for first bouginage. For instance, Rappert (19) recommends days 5-7 as most appropriate for first bouginage while Kabakchiev (15) suggests days 12-15. On the other hand, Tzolov (20) and Ricci (21) represent those authors supporting very late beginning of dilatation of the oesophagus - 3-4 weeks after ingestion.

Our experimental study in Guinea pigs provided evidence to state that determination of the initial moment for dilatation is strictly individual and always must compel with the kind and concentration of the corrosive as well as with the general status of organism before and after the accident. Although differences that exist, we support the idea to refrain from early bouginage in cases with massive alteration of large areas of the oesophageal wall by concentrated caustics and, possible early bouginage on the day 8-10 in lighter clinical forms. This is not a compromise, moreover, it is a need evidenced by our pathohistological findings whereby we have established that granular tissue and subsequent narrowing of the oesophageal lumen are formed after the day 17.

In conclusion, we should note that results from this pilot study might be used in planning larger experimental studies on acid burns of the oesophagus.

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References


PILOTSKO ISTRAŽIVANJE KISELNISKIH OPEKOTINA JEDNJAKA KOD ZAMORČIĆA

Valentin K. Stojanov i Borislav D. Dimitrov


Ključne reči: hemijske opekotine, jednjak, zamorčić, jednjačka stenoza, relativan rizik (RR)