

Original article

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A Critique of Systemic Steroids in the Management of Caustic Esophageal Burns in Children

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Summary

Five hundred and nineteen NaOH ingestion cases were admitted to our department between 1975 and 1994, and examined via esophagoscopy in the first 48 hours. Two hundred and forty-six patients in this series were diagnosed as severe burns endoscopically. This group of 246 patients were evaluated in a retrospective study to determine whether systemic steroid treatment had any place in preventing stricture formation following severe esophageal burns. Seventy-nine patients in this group were divided into three subgroups and they received methyl prednisolone

parenterally in three different regimens. The control group consisted of 167 patients admitted between the years 1986 and 1994 who did not receive any form of steroid treatment. There were no statistically significant differences between the healing rates of the subgroups and the control group ($p > 0.01$). The authors concluded that, systemic steroid treatment has no beneficial effect on esophageal wound healing following caustic esophageal burns.

Key words: Esophagus – Caustic injuries – Steroids

Résumé

519 cas d'ingestion de soude ont été hospitalisés dans notre département entre 1975 et 1994. Ces cas ont tous été examinés par oesophagoscopie dans les premières 48 heures. 246 patients de cette série ont été diagnostiqués par endoscopie comme brûlure sévère. Ce groupe de 246 patients a été étudié dans une étude rétrospective pour préciser si le traitement corticoïde avait sa place pour prévenir les rétrécissements cicatriciels secondaires à des brûlures oesophagiennes sévères. 79 patients dans ce groupe ont été divisés en 3 sous-groupes qui ont reçu de la méthyle prednisolone en intramusculaire de 3 façons différentes. Le groupe contrôle a comporté 167 patients admis entre les années 1986 et 1994 et qui n'ont reçu aucune espèce de traitement stéroïdien. Il n'y a pas eu de différence statistiquement significative entre le pourcentage de guérison des sous-groupes et le groupe de contrôle ($p > 0,01$). Les auteurs ont conclu que le traitement stéroïdien n'a pas d'effet bénéfique sur la cicatrisation de l'oesophage dans les suites d'une brûlure caustique de cet organe.

Mots-clés: Oesophage – Aggression caustique – Corticoïde

Zusammenfassung

519 Patienten mit einer NaOH-Verätzung wurden im Zeitraum von 1975 bis 1994 in der Kinderchirurgischen Abteilung der Ege Universität Izmir/Türkei behandelt.

Innerhalb der ersten 48 Stunden wurden eine Ösophaguskopie durchgeführt. Dabei wurden bei 246 Patienten schwerste Verätzungen gefunden. Diese 246 Kinder wurden retrospektiv analysiert, um zu prüfen, ob eine systemische Steroidgabe die Entwicklung von Narben und Strikturen verhindern kann.

79 Patienten, die so behandelt wurden, wurden entsprechend der Therapie in 3 Untergruppen gegliedert. Eine Kontrollgruppe bestand aus 167 Patienten, die keinerlei Steroidbehandlung erfahren hatten. Sowohl zwischen den einzelnen Subgruppen der systemisch mit Prednisolon behandelten Patienten wie zwischen den Prednisolon behandelten Patienten und der nicht behandelten Kontrollgruppe ergaben sich keinerlei statistische Unterschiede ($p > 0,01$). Die Autoren schließen hieraus, daß eine systemische Steroidgabe die Bildung von Narben und Strikturen am Ösophagus nicht verhindern kann.

Schlüsselwörter: Ösophagus – Ösophagusverätzung – Steroidgabe

Introduction

Stricture formation following caustic esophageal burns is one of the detrimental effects of normal wound healing process. Steroids have been subjected to experimental or clinical research in an attempt to prevent stricture formation in the esophagus (1, 6, 7, 8, 11, 14). There are many reports in the literature using different methods particularly regarding time, dose, and the course of steroid treatment in caustic esophageal burns. Lack of uniformity between study groups, and insufficient patient numbers resulted in conflicting assumptions. Most of the investigators suggested steroid usage in the early management of caustic esophageal burns, although there is not any direct evidence that steroids prevent esophageal stricture formation in the long-term. Formerly steroids were a part of treatment protocol in this department, followed by the present one without steroids. The long-term follow-up results of these different patient groups set up the basis of this comparative retrospective study.

Materials and methods

Five-hundred and nineteen patients admitted to the Pediatric Surgery Department of Ege University Hospital in the first 24 hours following accidental sodium hydroxide (NaOH) ingestion between 1975 and 1994 were reviewed. The age at admission was

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3.0 ± 1.9 years (mean ± standard deviation). The clinical symptom observed almost uniformly in all patients with or without esophageal burn was hesitance to swallow in the first 24–48 hours. Real swallowing difficulty, mainly for solid food, developed in all injured patients within 2–4 weeks postburn, and guided for esophagoscopy control and dilatation requirement during follow-up.

Esophagoscopy performed routinely in the first 48 hours revealed 246 patients (mean age 2.9 ± 2.0 years) having severe esophageal burns which constituted the main study group. Esophagoscopy assessment was performed by the same single investigator (O.M.) in the first 16 years of the study period, and confirmation of the burn injury whenever observed was made by the same investigator later on. Patients having mucosal edema and/or hyperemia alone, patients without any evidence of burn, the ones healed without dilatation, patients who could not complete the steroid management protocol for any reason, and patients lost to follow-up were not included in the study. Grading of the severity of the burn injury was abandoned in this institution in 1986. All patients in this study were started on a standard antibiotic prophylaxis composed of cefazoline and gentamycine (followed by ceftriaxone and amikacine in the last 7 years of the study period) upon admittance, and continued for ten days after esophagoscopy confirmation of the burn injury.

Systemic steroid treatment was instituted in 79 patients between the years 1975 and 1986 which constituted the first group in this study (Group I). Methyl prednisolone was applied parenterally in different regimens to three separate patient subgroups (Group IA, IB, IC) following documentation of burn injury (Table 1). The three different regimens for steroid treatment were simply derived from three consecutive trials, starting with Group IA in 1975, followed by Group IB in 1981, and ended with Group IC. Because these subgroups were not in a study design originally, the number of patients in the study groups varied according to withdrawal of the old and start of a new management protocol for acutely injured patients. The failure of a protocol, after some time, led to establishment of a new one.

Table 1 Patient groups according to different steroid treatment schedules, and controls (Group 0).

	Patients (n)	Steroid Regimen	
		Methylprednisolone	Duration of treatment
Group IA	21	2 mg/kg/day	21 days
Group IB	20	6 mg/kg/day (7 days)	28 days (total)
		4 mg/kg/day (7 days)	
		2 mg/kg/day (7 days)	
Group IC	38	1 mg/kg/day (7 days)	48 hr
		30 mg/kg/6 hr	
Group 0	167	0	-

The control group (Group 0) consisted of 167 esophageal burn patients admitted between the years 1986 and 1994 who did not receive any form of steroid treatment.

The patients in each study group were comparable regarding age. The mean ages for the groups IA, IB, IC, and 0 were; 2.7 ± 1.3 years, 2.8 ± 1.4 years, 2.6 ± 1.0 years, and 3.0 ± 2.2 years respectively.

All patients were followed-up by periodical esophagoscopies and dilatations performed every 21 days. The follow-up was terminated after one year (average) from the last dilatation, provided that esophageal patency was achieved, and the passage confirmed by an esophagogram.

The number and frequency of patients with documented esophageal healing were noted for each study group. To assess treatment results and to quantify the act of esophageal healing for statistical comparisons between the study groups, the ratio of patients whose esophagus healed following only a single dilatation were also calculated. The healing frequencies of the three study groups separately, and as a total were compared to the healing frequency of the control group. The ratio of patients who had only one dilatation in each group, which possibly represented the ratio of rapidly healing, or slightly injured patients, were compared. The results were analysed using chi-square test and t-test as appropriate. P values of less than 0.01 were considered to be statistically significant.

Results

There was no statistically significant difference between the ages of the study groups compared to each other (p > 0.05). The ages of the patients with and without esophageal burn were comparable as well (p > 0.05). This suggested an even age distribution in the total group of patients admitted.

The number and frequency of patients with documented esophageal healing are shown in Table 2 and Figure 1. The comparison of the healing rates of the total steroid receiving patients (Group I) to that of non-steroid receivers (control group) did not reveal statistical significance (p > 0.01). There were no significant differences between the healing rates of the different steroid groups (IA, IB, IC) either (p < 0.01). The healing rates of steroid groups IA and IB when compared to healing rate of the control group separately, were not significantly different also (p < 0.01). The application of chi-square test to Group IC and 0, reveals a p value of 0.043, which still loses significance on a

Table 2 The comparison of the outcome in different treatment groups to the outcome in controls did not reveal any significance (p > 0.05).

	Total	Patients (n)	
		Healed	Not-healed
Group IA	21	13 (62%)	8
Group IB	20	12 (60%)	8
Group IC	38	29 (76%)	9
Group 0	167	95 (57%)	72

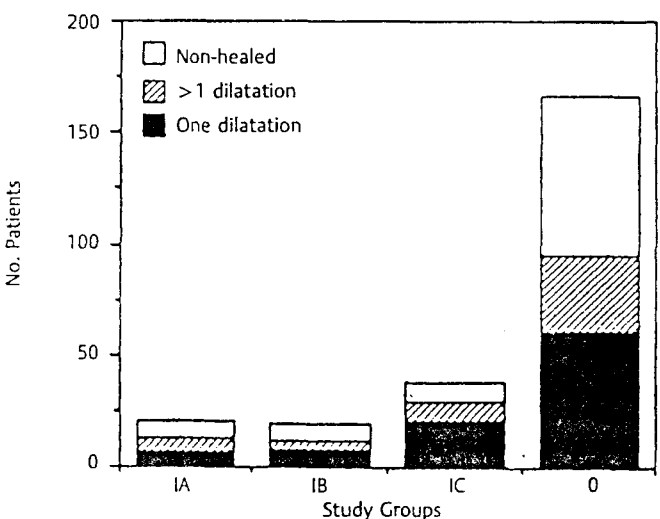


Fig. 1 The healing rates of the study (IA, IB, IC) and control (0) groups.

Table 3 The number and ratio of patients healed after only one dilatation were comparable between the study groups ($p > 0.05$) (dil: esophageal dilatation, n: the number of patients).

	One dil (n)	More than one dil (n)	Total (n)
Group IA	7 (54%)	6	13
Group IB	8 (67%)	4	12
Group IC	21 (72%)	8	29
group 0	60 (63%)	35	95

99% confidence limit ($p < 0.01$). The ratio of patients whose esophagus healed following a single dilatation in each study group was not significantly different (Table 3 and Fig. 1). No specific complication related to the steroid treatment was noted.

Discussion

Steroids have two distinct effects on wound healing. One is to reduce the collagen content of the tissue by way of both decreasing prolyl hydroxylase activity, and amplifying collagenase activity. Besides altering the activities of these two enzymes, which are responsible for the synthesis and degradation of collagen respectively, steroids also inhibit lysyl oxidase, preventing cross-linking of collagen molecules (2). The second important effect of steroids is against inflammation normally taking place in the first three days of wound healing (2). This is accomplished through inhibition of arachidonic acid synthesis in the cell membrane, which in turn results in the prevention of the synthesis of eicosanoids (4).

In order to find out any dose dependent appearance of anti-collagen and antiinflammatory effects of steroids on esophageal healing, three different doses, in various schedules were applied to different patient groups. Although the highest healing rate (%) was observed in the patient group who received the steroid in the highest dose (Group IC), even that could not attain statistical significance.

The reason for the abandonment of grading was the impression gained that there was no correlation between the acute esophagoscopic findings and the final outcome in terms of stricture formation, given that superficial injuries (former grade I) are excluded. No single patient having stricture following grade I injury was noted in our series. The depth of injury is more likely to determine the intensity of the stricture formation than mucosal changes alone.

The grading of the injury was not used in this study, so, one can argue that a possible beneficial effect of steroids on superficial burns might be obscured. However, the authors believe that most superficial injuries (all former grade I injuries) heal without any consequence. And for higher grades, there is no clue to predict stricture incidence, which is sufficiently reliable to indicate whether to treat or not to treat.

Since the evaluation of clinical symptoms may be subjective in children, loss of symptoms during follow-up never played a determining role in the termination of follow-up without radiographic documentation of esophageal healing. Recurrent symptoms observed long after termination of follow-up in a small group of patients were attributed not to the recurrent stricture but gastroesophageal reflux disease developing most probably due to the loss of esophageal length and altered antireflux mechanisms. In a recent study the reflux was also thought to be responsible for strictures resistant to dilatations and stenting for prolonged periods (more than a year) in some cases of caustic esophageal burns (10).

The effects of steroids on collagen are limited to the period that they remain in the circulating blood. Once steroid treatment is ceased, collagen accumulation starts again with cross-binding of collagen fibers. This may even be exaggerated because collagen production has already increased in a previously injured tissue, and the cross-binding process usually lasts up to two years (12). The failure of steroids in preventing stricture formation although used for 3 and 4 weeks in two of the study groups supports these data. The idea of using steroids for two years is not reasonable due to their untoward effects either systemically, or on wound healing (2, 11).

Being unsatisfied with the above steroid protocols, the authors started a high dose steroid regimen in another patient group with the objective of suppressing the initial inflammation which takes place in the early days following injury. This might limit the inflammation to the superficial layers of the wound, which in turn would prevent stricture formation. This presumption was based upon the well-known natural behaviour of superficial injuries that, they heal with minimal, if any, fibrosis (1). However, even this high dose of methyl prednisolone was unavailing to prevent stricture formation. Besides, there is at least one study which might argue that the inflammatory response normally taking place following any injury is indispensable for a satisfactory wound healing (2). One may think out a prospective study using this high dose of steroids just depending on the moderately low probability value ($p = 0.043$) emerging from the comparison between high dose steroid and control groups. Yet the routine use of high doses of steroids in such severely injured children is not currently recommended.

Local injection of steroids in the treatment of patients with esophageal strictures has been suggested previously (3, 5). This series does not include the authors' experience with local steroid treatment. However a recent review of this center's experience regarding local steroid injection treatment in caustic esophageal strictures concluded that, it can be an alternative management and recommended as a first-line treatment in short strictures (13). The conflicting results of systemic steroid treatment with that of local injections may be explained by obtaining a high local steroid concentration in the strictured area by injections, which could not be reached by systemic application within safe dose limits.

This study certainly lacks the advantages and power of a blinded randomized protocol. Yet as a retrospective evaluation, it clearly shows that systemic steroids have no beneficial clinical effect on esophageal wound healing following severe caustic esophageal burns. This is a confirmation of our previous impressions gained from smaller patient populations regarding systemic steroid treatment (9).

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ÇOCUKLARDAKİ KOSTİK ÖZOFAGUS YANIKLARININ TEDAVİSİNDE STEROİDLERİN DEĞERLENDİRİLMESİ

1975-1994 yılları arasında bölümümüze 519 NaOH alımı yatırılarak ilk 48 saat içerisinde özofagoskopi ile incelenmiştir. 246 hasta endoskopik olarak ciddi yanık olarak değerlendirilmiştir. Bu 246 hasta retrospektif olarak değerlendirilmiş ve sistemik steroid uygulamasının ağır özofagus yanıklarında striktürü önlemede yerinin olup olmadığı araştırılmıştır. Bu gruptaki 79 hasta 3 subgruba ayrılmış ve 3 değişik rejim halinde parenteral metil prednosolon uygulanmıştır. Kontrol grubu 1986-1994 yılları arasında tedavi edilen ve steroid kullanmayan 167 hastadan oluşmaktadır. Subgrupların ve kontrol grubunun iyileşme oranlarında istatistiksel olarak anlamlı bir fark bulunamamıştır ($p>0,01$). Sonuç olarak kostik özofagus yanıklarının iyileşmesinde sistemik steroid uygulamasının herhangi bir yararının olmadığı gözlenmiştir.

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Dear Doctor Mutaf,

Cologne, 8th of February 1997

Thank you very much for your interesting manuscript entitled:

A critique of systemic steroids in the management of caustic esophageal burns in children.

We are glad to be able to confirm that your manuscript has been accepted by the editorial board and our advisers for publication in the European Journal of Pediatric Surgery. We have sent your paper to the publishers and thank you very much again for having let us see your paper.

With kind regards
Yours sincerely



(Prof. Dr. A. M. Holschneider.)

