Intralesional steroids in refractory caustic esophageal stricture

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ABSTRACT

Objective. To analyze the efficacy of intralesional steroid treatment in refractory caustic esophageal stricture.

Materials and methods. An analytical, retrospective study of patients receiving intralesional steroid treatment with triamcinolone acetonide as a result of refractory caustic esophageal stricture was carried out. Demographic variables, stricture characteristics, number of dilations, steroid injections, and dilation score (no. of dilations/follow-up period in months) pre- and post-treatment were collected. Stricture characteristics (diameter and length) and dilation score pre- and post-treatment were compared using the T-Test or Wilcoxon test.

Results. N= 5. Median age: 5 years (17 months-7 years). Follow-up: 6.60 ± 2.70 years. Swallowed products included NaOH, KOH, and ClH. Zargar classification at follow-up initiation was IIb (n= 2), IIIa (n= 1), and two chronic strictures. 6.6 ± 9.23 esophageal dilations were carried out before steroid treatment initiation. The mean number of intralesional therapy sessions was 11.20 ± 6.14. Stricture length decreased by 3.60 ± 2.63 cm (t= 3.06; p= 0.019). No differences were found in terms of diameter increase: −1.60 ± 3.58 mm (t= −1.00; p= 0.187). The dilation score diminished from 1.47 ± 0.86 to 0.47 ± 0.18 dilations per month of follow-up (Z= −2.02; p= 0.043).

Conclusions. Even though there is limited evidence available in the pediatric population, intralesional triamcinolone treatment is seemingly useful in the treatment of refractory caustic esophageal stricture, since it reduces length and dilation score.

KEY WORDS: Esophageal stricture; Caustics; Steroids; Intralesional injection.

CORTICOSTEROIDE INTRALESIONAL EN ESTENOSIS ESOFÁGICAS CÁUSTICAS REFRACTARIAS

RESUMEN

Objetivo. Analizar la eficacia del tratamiento intralesional con corticosteroide en estenosis esofágicas cáusticas refractarias.

Material y métodos. Estudio analítico y retrospectivo de pacientes tratados con corticosteroide intralesional (triamcinolona acetónido) por estenosis esofágicas cáusticas refractarias. Se recogieron variables demográficas, características de la estenosis, número de dilataciones, inyecciones de corticosteroide e índice de dilatación (nº dilataciones/periodo de seguimiento en meses) pre y post tratamiento. Se compararon las características de la estenosis (diámetro y longitud) e índice de dilatación pre y post tratamiento con T-Test o Test de Wilcoxon.

Resultados. N= 5. Edad mediana 5 años (17 meses-7años) y seguimiento de 6,60 ± 2,70 años. Los productos ingeridos fueron NaOH, KOH y ClH. La clasificación de Zargar al inicio del seguimiento fue IIb (n= 2), IIIa (n= 1) y dos estenosis crónicas. Se realizaron 6,6 ± 9,23 dilataciones esofágicas previas al tratamiento con corticosteroide. El número de sesiones de terapia intralesional promedio fue 11,20 ± 6,14. La longitud de la estenosis mostró una reducción de 3,60 ± 2,63 cm (t= 3,06 ; p= 0,019). No encontramos diferencias en el incremento del diámetro: −1,60 ± 3,58 mm (t= −1,00 ; p= 0,187). El índice de dilatación se redujo de 1,47 ± 0,86 a 0,47 ± 0,18 dilataciones por mes de seguimiento (Z= -2.02 ; p= 0.043).

Conclusiones. Aunque la evidencia disponible en población pediátrica es limitada, la terapia con triamcinolona intralesional parece ser útil en el tratamiento de estenosis esofágicas cáusticas refractarias, al reducir su longitud y el índice de dilatación.

PALABRAS CLAVE: Estenosis esofágica; Cáusticos; Corticosteroide; Inyección intralesional.

INTRODUCTION

Endoscopic dilation is a safe and effective method for the treatment of esophageal stricture in the pediatric population, with an efficacy of 80-90%[1-3]. However, 10-20% of strictures are refractory or recurrent, with treatment becoming a challenge for pediatric surgeons[2].

Intralesional steroid (IS) injection as an adjuvant therapy to endoscopic dilation has demonstrated to be effective in preventing stricture recurrence, reducing the number of dilations, and extending the symptom-free period[1,4]. Its action mechanism is based on inhibiting the inflammatory response, thus preventing collagen synthesis and favoring disintegration[1,3-5]. In the pediatric population, evidence regarding this practice is limited. The articles published present heterogeneous results, with sample sizes being small, which means valid conclusions are difficult to draw[5,6]. However, the most recent NASPGHAN recommendations propose this therapy as a second-line treatment in pediatric patients in whom endoscopic dilation has failed[2].

The objective of this study was to assess the impact of intralesional steroid therapy (IST) on symptom resolution and endoscopic dilation frequency in pediatric patients with refractory or recurrent caustic esophageal stricture.

MATERIALS AND METHODS

An observational, analytical, retrospective study of pediatric patients treated with IS as a result of refractory or recurrent caustic esophageal stricture from 2014 to 2023 was carried out. According to the 2023 NASPGHAN guidelines[2], refractory stricture was defined as any stricture where an adequate esophageal diameter according to patient age was not achieved following more than five dilation sessions over five months, or after seven sessions regardless of the time period. Recurrent stricture was defined as the inability to maintain an adequate esophageal diameter according to patient age for more than one week once it had been achieved[2].

Esophageal stricture treatment consisted of endoscopic balloon dilation, whereas IST was used as a second- or third-line therapy in refractory or recurrent strictures. Preoperative antibiotic prophylaxis was administered in all cases, and esophagogastroduodenoscopy (EGD) was conducted under general anesthesia and endotracheal intubation. Olympus GIF-XP160, GIF-180, and GIF 165 gastroscopes were used according to patient age and stricture caliber. The steroid used was triamcinolone acetonide (40 mg/ml) at a 0.3-0.5 cc dose per quadrant, followed by pneumatic balloon dilation. Dilation sessions were scheduled according to symptoms (dysphagia or impaction).

Demographic variables (age and sex), Zargar classification, and stricture characteristics (diameter and length) were collected. Multiple, irregular, and angulated strictures, as well as strictures under 2 mm, were regarded as complex[2,4]. The number of dilation sessions conducted before steroid injection, the total number of dilations, and the use of other adjuvant therapies (esophageal stents) was recorded. The number of intralesional therapy sessions, the dose administered, technique-related complications, and endoscopic and clinical response were also gathered.

In terms of result variables, changes in stricture characteristics –increase in diameter and decrease in length– were calculated. At follow-up initiation, this characterization was performed based on esophagogastric transit with contrast and endoscopic findings. During follow-up, endoscopic findings only were considered. Dilation score (DS) pre- and post- triamcinolone treatment was calculated as the number of dilations per time period in months. Therapeutic failure was defined as the absence of clinical, endoscopic, and DS improvement.

For data analysis purposes, the IBM SPSS Statistics software, version 29.0.2.0, was employed. The Shapiro-Wilk test was used to identify normal distribution variables. Parametric quantitative variables were represented as mean ± standard deviation, whereas non-parametric ones were expressed as median and interquartile range. Student's t-test was applied to coupled samples to assess differences in stricture characteristics, and the Wilcoxon test was employed to compare dilation scores pre- and post-treatment.

RESULTS

A 5-patient (n= 3 male) sample was achieved. Median age at follow-up initiation was 5.08 years (16 months-5.83 years). Swallowed products were NaOH in one case, ClH in one case, KOH in two cases, and unknown in one case. Strictures were classified as Zargar IIa (n= 1), IIb (n= 2) and IIIa (n= 1), and they were all complex. 1 patient had chronic stricture in the first endoscopy conducted in our institution, which means Zargar grade was unknown. Mean stricture length was 7.10 ± 2.79 cm, and stricture diameter was 3.00 ± 0.67 mm –both parameters were calculated by comparing the stricture with the dilation balloon. DS at follow-up initiation was 1.47 ± 0.87 monthly dilations. Demographic characteristics are featured in Table 1.

The number of endoscopic dilations before IST initiation was 6.60 ± 9.23 per patient. IST duration was 34.69 ± 26.68 months, with a mean of 11.20 ± 6.14 sessions per patient. Stricture length decreased by 3.60 ± 2.63 cm (t= 3.06; p= 0.019). No statistically significant differences were noted in terms of diameter increase (–1.60 ± 3.58 mm (t= –1.00; p= 0.187) (Table 2). Out of the 5 sample patients, a significant increase in stricture diameter was observed in 1, whereas no changes were detected in the remaining 4. However, in the latter, a mean 4cm length reduction had occurred. 4/5 patients (80%) were asymptomatic in the latest control, with dysphagia being resolved and no impaction events being recorded. DS decreased from 1.47 ± 0.86 to 0.47 ± 0.18 dilations per month of follow-up (Z= –2.02; p= 0.043) (Table 2).

Follow-up was conducted over 6.60 ± 2.70 years. No IST-related complications were observed in this sample. Endoscopic adjuvant therapies included esophageal stents

Table 1. Characteristics of patients with caustic esophageal stricture treated with IST.

Patient	1	2	3	4	5
Sex	Male	Female	Female	Male	Male
Caustic	20% NaOH	Industrial dishwasher	15-30% KOH	ClH	–
Age at dilation (years)	5.5	5.08	1.75	1.33	5.83
Total dilations	26	31	13	16	19
Zargar classification	IIB	IIB	IIA	IIIA	–
Baseline length (cm)	10	8	8	7	2
Baseline diameter (mm)	4	4	2.5	3	3
Age at ITA (years)	7	5.16	2.17	1.42	6
Dilations pre-ITA	23	3	4	1	2
Length pre-ITA (cm)	3	8	6	7	2
Diameter pre-ITA (mm)	2	5	7	6	3
ITA sessions	4	21	10	10	11
Dose	0.5	0.3	0.3	0.3	0.3
Final length (cm)	1	1.5	2	1.5	2
Final diameter (mm)	10	5	7	6	3
Dilation score pre-ITA	1.35	3	1	1	1
Dilation score post-ITA	0	0.36	0.32	0.38	0.77

Table 2. Analysis of changes in stricture characteristics and dilation scores.

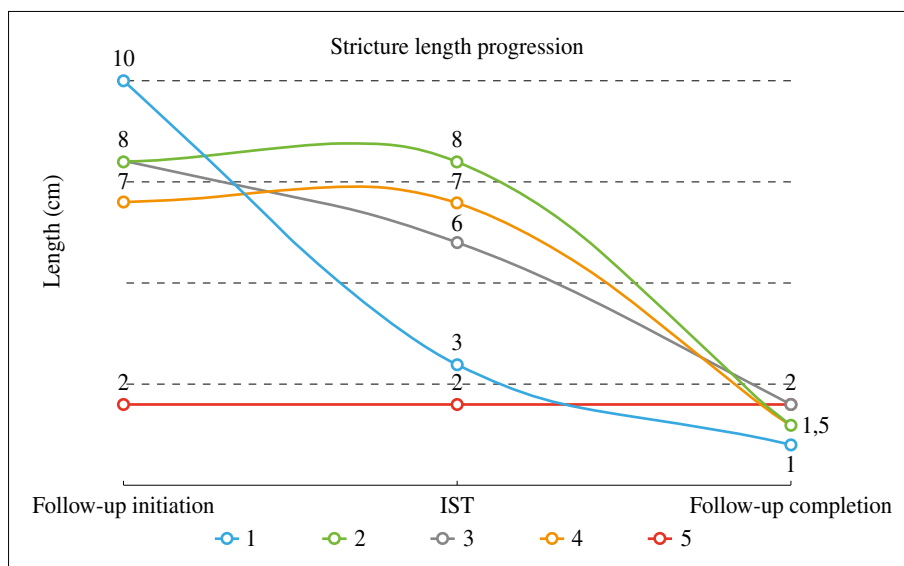| Variables	Mean	Standard deviation	t	p value
Length decrease (cm)	3.6	2.63	3.06	0.019
Diameter increase (mm)	−1.6	3.58	−1	0.187
	Baseline	Final	Z	p value
Dilation score	1.47 ± 0.86	0.47 ± 0.18	−2.02	0.043

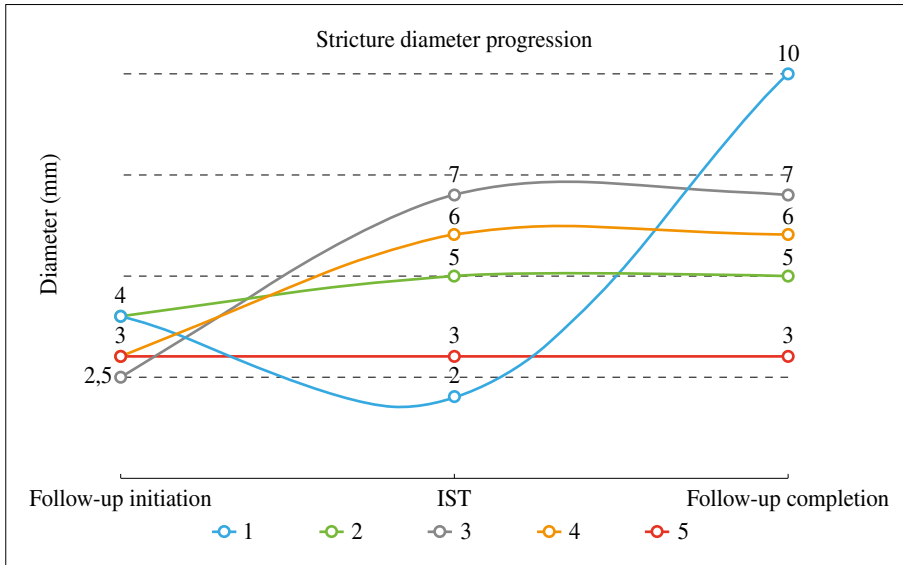**Figure 1.** Stricture length progression at follow-up initiation, pre-, and post-IST.

Figure 2. Stricture diameter progression at follow-up initiation, pre-, and post-IST.
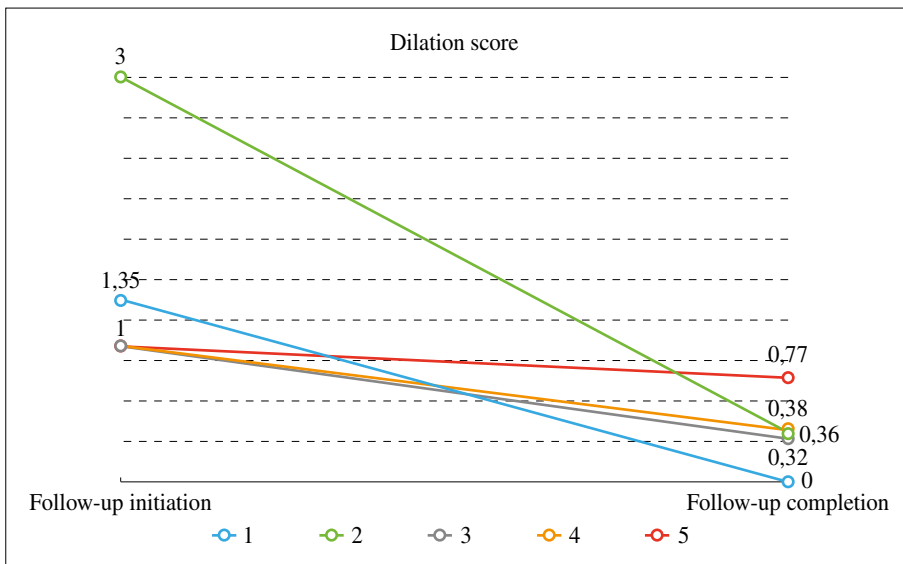

Figure 3. Dilation score (DS) progression at follow-up initiation and post-IST completion.

in 2 patients –applied before and after triamcinolone treatment, respectively. None of the patients was treated with other adjuvant therapies such as mitomycin-C or incisional therapy.

DISCUSSION

7-15% of the patients who swallow caustics develop esophageal stricture. Even though prevalence has decreased in the last decades as a result of primary prevention, it remains the first cause of esophageal stricture in developed countries[1,7,8].

The fact stricture is classified as simple and complex is due to practical reasons. Simple strictures typically resolve after 3-5 endoscopic dilations, whereas complex ones tend to become refractory or recurrent, require multiple dilation sessions, and are associated with long resolution times[1,9]. As a result of this, numerous general anesthesia procedures and hospital admissions are required, which increases healthcare costs[10]. IST was proposed to improve prognosis in refractory and recurrent stricture, since it reduces local inflammatory response, collagen synthesis, fibrosis, and re-stricture following endoscopic dilations[8,10,11]. In strictures refractory to adjuvant therapies, the administration of systemic steroid therapy following IST in order to reduce recurrence rates has been described[12]. All strictures reviewed in this study were complex and refractory, probably because the simple ones had resolved without further therapies required –

apart from balloon dilation–, which means they were not recruited for analysis purposes.

For the time being, there are no globally accepted recommendations regarding the management of refractory esophageal stricture in pediatrics, but the use of adjuvant therapies after 3-5 dilation sessions is generally accepted[1,13]. Mean dilations before IST initiation (6.6 dilations/patient) were higher than those recommended in the literature, probably because one patient had received 23 previous dilations. In this specific case, adjuvant treatment initiation was delayed due to lack of experience in our institution, since this was the first individual undergoing this technique, which was used as a third-line therapy following stent therapy failure. In addition, patients from our sample were treated with a mean of 11.2 IST sessions, even if such doses were administered over a long time period –a mean of 3 years. Based on the evidence available today, it is impossible to establish the number of intralesional steroid sessions recommended per patient and the ideal treatment duration. While some articles recommend a maximum of 3-5 sessions per patient[1], other publications report administering up to 13 doses before considering other therapies or surgery[13,14].

According to adult studies, intralesional therapy brings about a reduction in dilation frequency, stricture diameter, and dysphagia[10]. In the pediatric population, the evidence is limited, based on case series and retrospective studies, but results are promising[8,10]. In 1989, Gandhi et al. reported good clinical results with the application of intralesional triamcinolone in 12 pediatric patients with corrosive and anastomotic esophageal stricture refractory to endoscopic dilations[14]. Similarly, Nijhawan et al. described a significant reduction in dysphagia in 11 patients with refractory caustic stricture treated with five endoscopic dilations and IST over one year[15]. Even though the therapeutic strategy in our institution was different and dilations were indicated according to clinical signs, symptoms improved in 80% of our series.

Regarding stricture characteristics, our results show that IST is effective in reducing stricture length, consistent with Bicacki et al., who reported a decrease in stricture length in 10 pediatric patients following IST application[8]. Randomized clinical trials in adult patients have described an increase in mean stricture diameter following IST vs. controls[7,13]. However, in our series, no differences in terms of stricture diameter were found following intralesional therapy.

DS significantly diminished following IST, consistent with Diverci, E. et al., who reported reduced dilation sessions, decreased dilation frequency, and DS improvement in 32 patients with caustic esophageal stricture[10,16]. However, when dividing the sample according to stricture length, no improvement was noted in patients with a long stricture (> 3 cm)[14]. Conversely, in our sample, therapeutic failure was recorded precisely in the only patient with a stricture < 3 cm. In addition, a 2018 meta-analysis concluded that IST significantly improves DS[16].

2 patients were treated with esophageal stents, with results being poor. In one of them, who was previously mentioned, two non-absorbable self-expandable stents were placed following the fourth and eight endoscopic dilation sessions, respectively, and were left in place for 4 weeks. No improvement in terms of stricture characteristics or symptom-free period was observed. IST was administered as a third-line therapy, with stricture resolving after four sessions.

The second case where stent therapy was employed was the patient in whom therapy had failed in terms of clinical, endoscopic, and DS improvement following IST. The follow-up of this patient started late –two years following caustic intake. In the first endoscopy, there were two diverticula at the level of the upper esophageal sphincter and two complex stenoses –a punctiform, 5 cm long one that has not undergone IST so far, and a 2.5 cm long, 3 mm diameter one that showed no caliber or length changes following intralesional therapy. In light of the subsequent therapeutic failure occurred with stents as a third-line treatment, the patient has been scheduled for surgery.

IST is considered to be a safe technique, but it has been associated with adverse effects such as candida esophagitis, iatrogenic Cushing's syndrome, and adrenal suppression caused by exogenous steroids[1,17]. In our sample, no technique-related complications were noted. A 55-article systematic review of local steroid therapy safety in the pediatric population concluded it is a safe technique, with a complication rate of 7.1%. Most adverse effects reported were local (10% vs. 0.7% systemic) and did not require any treatment for resolution purposes[18].

The main limitations of this study are its small sample size and its retrospective nature. In addition, analytical follow-up of adrenal function was not carried out following treatment, which means ionic and/or hormonal disorders cannot be ruled out, despite the fact no cases of suppression were clinically reported. On the other hand, the characterization of strictures during follow-up was performed based on endoscopic techniques, with no radiological studies being conducted to measure stricture length and diameter in a systematic fashion.

In conclusion, even though IST results as an adjuvant therapy to endoscopic dilation are promising, most pediatric studies published are retrospective and provide with little scientific evidence. According to our results, IST could prove useful in reducing stricture length and DS.

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