Efficacy of intralesional triamcinolone injections for benign refractory oesophageal strictures at Counties Manukau Health, New Zealand

Yeri Ahn, Christin Coomarasamy, Ravinder Ogra

Abstract

BACKGROUND AND AIMS: Refractory benign strictures of the oesophagus can present a significant clinical challenge and may require repeated attempts at dilatation. Intralesional triamcinolone injections have been used in a limited number of studies to aid in the dilatation of benign, refractory oesophageal strictures. It is hypothesised that intralesional steroid injection inhibits the scar formation, thereby reducing the need for dilatations. The purpose of this study was to assess if steroid injection reduces the need for serial endoscopic dilatations and aids in maintaining oesophageal patency.

METHOD: We report a case series of 25 patients with refractory oesophageal strictures. The mean age was 75 years and range between 41–95 years. The etiology of strictures consisted of peptic (68%), anastomotic (4%), radiation induced (16%) and eosinophilic oesophagitis (12%). Majority (75%) were distal in location. Triamcinolone (40-80 mg) was injected via 25-gauge sclerotherapy catheter in a four quadrantic manner in aliquots of 0.5 ml each into the proximal end of the stricture and also into the stricture itself after dilatation. Dilatation was carried out with over the guidewire Savary-Gilliard or through the scope (CRE) Balloon dilators depending upon the preference of the endoscopist. Dilatations were continued every 4–6 weeks until asymptomatic and/or endoscopic resolution of stricture. Periodic Dilatation Index (PDI) was calculated by the number of dilatations required over the duration of time in months.

RESULTS: The number of dilatations reduced from mean of 3.12 to 1.41 in the peptic strictures but there was no decrease in the other groups. However, the triamcinolone injection resulted in reducing the periodic dilatation index in all groups except the eosinophilic oesophagitis. The rate ratio of PDI before and after intralesional triamcinolone injection use being 0.45 with 95% confidence interval [0.30 -0.68] (p=0.0005). Furthermore triamcinolone injections showed a trend to increase the maximal achieved diameter of the strictures.

CONCLUSION: This study demonstrates the efficacy of triamcinolone intralesional steroids in reducing the requirement for repeated dilatations in refractory peptic strictures of oesophagus. Strictures related to eosinophilic oesophagitis failed to demonstrate similar efficacy.

Introduction

Since Ashcraft and Holder first demonstrated the effectiveness of intralesional corticosteroid injections in benign esophageal strictures using animal models in 1969,1 steroid injections have been utilised as adjunctive aids to endoscopic dilatation in gastrointestinal stricture management. In the last decade, intralesional steroid injections have become first line treatment in the management of refractory strictures, especially in cases of oesophageal peptic strictures.2-7 Studies in the management of complex strictures, such as anastomotic8-10 and radiation-induced11-13 strictures, have also shown that steroid injections in combination with endoscopic dilatations have
largely reduced the need for repeated dilatations and increased the intervention free interval between dilatations. Fewer studies have shown similar positive outcomes in managing strictures in pyloric stenosis and Crohn’s.12–15

Triamcinolone and other steroids have historically been used in the treatment of dermatological scars such as keloids and burns.16,17 On a microscopic level, similarly to scars, stricture formation is thought to be inhibited by steroids, as it interferes with collagen synthesis and reduces the transcriptions of matrix protein genes such as fibronectin and procollagen, as well as reducing synthesis of alpha2-macroglobulin, an inhibitor of collagenase.

Hence steroid injections are thought to further reduce the formation of strictures as it impairs fibrotic healing.

Currently there is no published data in New Zealand to support the efficacy of intralesional triamcinolone use in refractory oesophageal strictures.

The aim of this investigation was to objectively examine the use of intralesional triamcinolone injections in the endoscopic management of refractory oesophageal strictures.

Patients and methods

The study was approved by the Northern X Regional Ethics Committee. The study patient population comprised of 25 patients (15 men, 10 women: mean age 75.08 [SD=14.78] years; range 41–95 years), with refractory oesophageal strictures of differing etiologies treated between June 2004 to January 2012. Seventeen patients had peptic, 1 anastomotic, 4 radiation-induced and 3 eosinophilic oesophagitis related strictures. Refractory strictures in this study were defined as anatomic restriction due to fibrosis requiring more than 3 sessions of dilatation to maintain lumen of at least 14 mm or inability to maintain a satisfactory luminal diameter for 4 weeks once the target diameter of 14 mm had been achieved.18 Prior to dilatations, all patients were receiving proton pump inhibitors averaging 40–80 mg equivalent of omeprazole and advised lifestyle anti-reflux measures.

All patients underwent oesophageal dilatations at Counties Manukau Health Gastroenterology service to relieve dysphagic symptoms. Before dilatations, patients were sedated by intravenous administration of midazolam and fentanyl after topical lignocaine spray. Standard gastroscopes were used, however the technique of dilatation was variable between endoscopists.

Savary-Gilliard and CRE (through the scope) balloon were the most commonly used dilators. When intralpersal steroids were used, dilatations were combined with triamcinolone acetonide (40mg/mL, diluted 1:1 with saline solution) injections in four quadrants using a 23 gauge, 5mm long sclerotherapy needle in aliquots of 0.5mL at the proximal margin of the stricture and into the strictured segment. Most subsequent dilatation procedures were scheduled in 4–6 weeks until endoscopic resolution of strictures and improvement in patient’s symptoms, or earlier if patients returned with further dysphagia.

The primary investigator manually went through databases (Endoscribe, Provation, Concerto and hardcopy of clinical notes) to retrieve the site(s), number(s), nature and location of stricture(s) that were dilated, and recorded data for each patient. Each endoscopic procedure with and without triamcinolone injection for each patient for the relief of dysphagic symptoms was examined and data extracted. The data regarding patient demographics and stricture characteristics are available in Table 1.

The total number of dilatations prior to receiving triamcinolone injection and the total number of dilatations with triamcinolone injections until resolution of stricture or cessation of dilatations were recorded. Duration of endoscopic therapy was divided into two: the total number of months from the first endoscopic dilatation for dysphagic symptoms until the first dilatation with triamcinolone injection, and the total number of months from the first dilatation with triamcinolone injection until the endoscopic dilatation therapy ceased.

The maximal stricture diameter attained with each endoscopic treatment with and
without triamcinolone injections was also recorded. Clinical records were searched for any reported adverse events related to the endoscopic treatment.

Effectiveness of triamcinolone injections in improving clinical outcomes for patients with refractory oesophageal strictures was thought to: i) reduce the number of endoscopic dilatations required once triamcinolone injection therapy was commenced; ii) decrease the total duration of endoscopic therapy required; and iii) allow attainment of higher maximal stricture diameter once triamcinolone therapy was commenced.

The periodic dilatation index (PDI) was used to objectively define efficacy of intralesional steroid injections. Most patients received 80 mg Triamcinolone at each procedure. PDI was defined by the number of dilatations required over the duration of time in months.

Not enough objective data was available to elucidate symptom-free intervals between endoscopic dilatations. The refractoriness of the strictures was judged entirely from endoscopic appearances. Since the preliminary results of this series, we have started a prospective database of all refractory strictures and incorporated dysphagia scores to improve objective assessment and also to reduce operator bias.

Data regarding effects of intralesional triamcinolone injections can be seen in Tables 2 and 3.

### Results

Inferential analysis of data was carried out using SAS statistical software, version 9.3. Poisson regression, with a logarithmic link function, was carried out on the primary outcome of PDI against time with patient ID as random effect to account for the over dispersion in the model. The absolute rates with 95% confidence interval before and after triamcinolone injection use was 0.32 [0.22–0.47] and 0.15 [0.097–0.22] respectively. The raw data, as seen in Table 2, also support this reduction in PDI after triamcinolone injections. Rate ratio of PDI before and after intralesional triamcinolone injection use was 1.45 with 95% confidence interval [0.30 -0.68] and p-value of 0.0005. This shows a statistically significant reduction in PDI, and hence, the efficacy of triamcinolone injections in reducing the number of dilatations required over time in months. Subgroup analysis did not demonstrate a similar effect in strictures related to eosinophilic oesophagitis.

Furthermore, the raw data seen in Table 3 show an increase in the maximum dilated...
diameter of strictures after the introduction of triamcinolone injections. A linear regression model was applied to investigate if improvement in maximal diameter of strictures impacted PDI for strictures. It was found not to be significant at the 5% level even after adjusting for confounders such as age and location of stricture site (proximal, mid and distal) with a p-value of 0.17. This was thought to be primarily due to restricted sample size.

All 25 patients included in this retrospective study tolerated the procedures well, and no adverse events were documented at follow up time.

## Discussion

There are only a small number of studies in current literature that support the use of intralesional triamcinolone steroid injections for the treatment of benign refractory oesophageal strictures. Our study results, comprising 25 patients, have indicated that triamcinolone injections are efficacious in reducing the number of endoscopic dilatations required and decreased the total duration of endoscopic therapy in peptic, anastomotic and radiation induced strictures. Strictures related to Eosinophilic oesophagitis did not show any difference. Furthermore, triamcinolone injections allowed higher maximal stricture diameters to be achieved once therapy was commenced. This result was observed across strictures of different etiologies.

One limitation to our retrospective study is potential operator bias affecting the data collated. After successful interim results of treating refractory oesophageal strictures with triamcinolone injections, the refractory nature of some strictures were anticipated by endoscopists depending on the endoscopic appearance and the length of the stricture, and triamcinolone injections were commenced earlier. This may have affected the dilatation intervals and some patients may have had anticipated dilatations depending on endoscopic

<table>
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<th>Variables</th>
<th>Peptic n=17</th>
<th>Anastomotic n=1</th>
<th>Radiation induced n=4</th>
<th>Other (EO*) n=3</th>
<th>Total n=25</th>
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<tr>
<td>No of dilations</td>
<td>Before: 3.12, After: 1.41</td>
<td>Before: 1, After: 3</td>
<td>Before: 3.25, After: 5.25</td>
<td>Before: 2.67, After: 3.0</td>
<td>Before: 3.0, After: 2.28</td>
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<td>Periodic dilation index (PDI)</td>
<td>Before: 0.65, After: 0.27</td>
<td>Before: 1, After: 0.05</td>
<td>Before: 0.50, After: 0.28</td>
<td>Before: 0.16, After: 0.39</td>
<td>Before: 0.58, After: 0.28</td>
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*EO: Eosinophilic Oesophagitis

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<th>Variables</th>
<th>Peptic n=17</th>
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appearances. Furthermore, as 3 different endoscopists carried out the dilatation procedures, there may have been slight operator bias, although procedures were largely standardised.

Overall, this study adds to the growing evidence of the efficacy of triamcinolone intralesional injections on benign refractory oesophageal strictures with positive results in favour of triamcinolone injection use to improve patient outcomes in most etiologies, except eosinophilic oesophagitis. The use in this condition needs to be explored further. There were no adverse events related to the use of triamcinolone injection. This may encourage endoscopists to use this therapy as adjunct to dilatation at an earlier stage.

In recent times alternative methods of treating refractory oesophageal strictures, such as removable stents, biodegradable stents and experimental incisional therapies, have evolved. The use of removable or biodegradable stents is associated with a high rate of adverse reactions and migration.

Non-randomised studies examining the use of self-expanding plastic stents in the treatment of refractory benign oesophageal strictures have shown high complication rates, including migration (22%–81%), chest pain (11%), bleeding (8%), and perforation (5.5%). The relief of dysphagic symptoms is sustained only in a minority of patients, and in a small number of patients, tissue hyperplasia can impact on the removability of stents. The use of self-expanding, fully-covered metal stents has been reported, however also yield disappointing results in regards to its efficacy in relieving long-term dysphagic symptoms (<20%).

We have used 3 types of stents for refractory strictures at our unit. Two patients received biodegradable stents, with successful resolution of stricture in one (50%). One Poliflex plastic stent (Migrated) and 2 self-expanding metal stents (Niti-S Taewoong Medical Korea), one migrating and the other successful. The use of incisional therapies and argon plasma coagulation is reported in small numbers and has not gained widespread use. In view of the relative ineffectiveness of these newer endoscopic therapies for these strictures, the use of intralesional triamcinolone injections is a cheap and simple endoscopic method of managing refractory and difficult to treat strictures. The treatment did not show efficacy in the subgroup of eosinophilic oesophagitis and the paucity of numbers of anastomotic and radiation induced strictures in our sample would warrant further exploration of the use in these situations.

Our study clearly indicates benefit for peptic strictures and should be adopted as the first choice of treatment of such cases and could be attempted in other etiologies. Encouraged by these results, we enroll all patients with refractory oesophageal strictures prospectively into a database and also record the dysphagia scores and have educated the endoscopists regarding the correct injection technique of triamcinolone injection and also have incorporated the use of removable self-expanding metal stents with antimigratory mechanism [EndoMAXX Oesophageal stent (Merit Medical Endotek USA)].
REFERENCES:


