Topical application of mitomycin-C in corrosive esophageal strictures

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Abstract

Introduction: Corrosive ingestion is the major cause of esophageal stricture in our country. Mitomycin–C, an anthracycline derived from Streptomyces caespiitosus, has both antineoplastic and antiproliferative properties. Use of mitomycin–C have been well documented in various ophthalmologic procedures and laryngo-tracheal conditions where it has been shown that mitomycin–C inhibited fibroblast proliferation during the postoperative phase without damaging the mucosal and epithelial growth. This preliminary report documents the use of mitomycin–C in caustic stricture esophagus.

Materials and Methods: A prospective study was carried out in ten known patients of caustic esophageal strictures. After taking informed consent patients were subjected to antegrade or retrograde esophageal dilatation under general anesthesia and mitomycin–C was applied topically by a 10 mm cottonoid sponge soaked in mitomycin–C solution (0.4 mg/ml) for 5 minutes at the stricture site. The procedure was repeated at 4 weekly intervals thereafter and need for further dilatation was assessed. Outcomes in terms of symptomatic relief and radiological evaluation were assessed after therapy and results were analyzed for effectiveness of mitomycin–C and compared with retrospective results of previous cases of corrosive ingestion managed at the same institution.

Results: Total number of dilatations required were 34 (mean – 3.4) Two patients required single dilatation while two required six sessions. Symptomatic as well as radiological improvement was present in nine patients.

Conclusions: Use of mitomycin–C seems to improve the outcome in patients of corrosive esophageal strictures. Patients who have undergone esophageal replacement also seem to benefit from mitomycin–C.

Key Words: Caustic esophageal injury, Mitomycin-C

Introduction

Corrosive ingestion is a problem of the industrial age with an increasing trend in the developing countries, although there is no statistical data available from India. Corrosive ingestion is the major cause of esophageal stricture in children. A dilatation program using bouginage remains the mainstay of treatment; recently introduced pneumatic balloons and stenting procedures are also in vogue.[1] Restenosis following scar formation remain the major cause of failure of various dilatation programs.[2]

Mitomycin-C, an anthracycline derived from Streptomyces caespiitosus, has both antineoplastic and antiproliferative properties with the antineoplastic properties similar to alkylating agents, causing cross linking of DNA and inhibiting RNA and protein synthesis. Exact mechanism of its antifibroblastic activity is still elusive but possibly it inhibits fibroblast activity and suppresses fibrosis and scar formation by apoptosis.[3]

Use of Mitomycin-C has been well documented in various ophthalmologic procedures[4,6] and laryngeal/tracheal conditions[3] where it has been shown that Mitomycin-C inhibited fibroblast proliferation during the postoperative phase without damaging the mucosal and epithelial growth.

Treatment of caustic scarred esophagus includes a spectrum from conservative treatment with routine dilatation to substitution of esophagus by stomach or colon using various techniques. Recently, use of Mitomycin-C has been reported in caustic stricture of the esophagus.[7]

Materials and Methods

A prospective study was carried out in patients of corrosive esophageal injury as well as congenital esophageal stenosis to evaluate the effect of Mitomycin-C in these cases. Results were analyzed in terms of clinical improvement and the number of dilatations required to achieve maximum dilator size (#40F) using topical Mitomycin-C. Informed consent was taken and the patients were subjected to rigid esophagoscopy and after anterograde
and/or retrograde dilatations, Mitomycin-C was applied topically by a 10 mm cottonoid sponge soaked in Mitomycin-C solution (0.4 mg/ml) for 5 minutes at the stricture site and the procedure was repeated 4 weekly thereafter till the maximum dilatable size was achieved or there was marked clinical and/or radiological improvement. Post dilatation all patients were administered oral ranitidine and antacid gel in appropriate doses.

Outcomes in terms of symptomatic relief and radiological evaluation and the number of sessions required for easy passage of 40 F dilator were assessed after 4 sessions of therapy and results compared with the retrospective records of patients of corrosive ingestion and were analyzed for effectiveness of Mitomycin-C.

RESULTS

The present study constituted ten children with established esophageal strictures. Of these ten cases, six had been previously operated for the stricture (3 – resection and end to end anastomosis, 2 – reverse gastric tube anastomosis and 1 – stricturoplasty) and four were fresh cases. The age ranged from 2 to 9 years at the time of dilatation and mitomycin-C application. The local application of mitomycin-C was carried out from the first session of dilatation and in the same dose in all patients. The number of sessions required for easy passage of 40 F dilator after post operative application of mitomycin-C locally are shown in Table 1. Overall 34 sessions with topical application of mitomycin-C were required in 10 patients with two patients requiring minimum of 1 session (20%) each and two patients required maximum of 6 sessions (20%) each. Symptomatic and radiological improvement was noted in 9 patients with a single patient having an eccentric anastomosis on barium examination.

DISCUSSION

Accidental ingestion of corrosives represent a major childhood hazard especially in developing countries. Treatment of esophageal stricture following corrosive ingestion is debatable and the three main schools of thought on this issue are as follows: (1) esophageal replacement, possibly associated with esophagectomy, for all corrosive stenoses; (2) conservative management using different protocols of periodic dilatations; (3) surgical treatment confined to those strictures considered “intractable.”[8] Intractability has been defined as failure to respond to a course of esophageal dilatations lasting for a year or more.[9] There are also reports of use of steroids especially high dose dexamethasone in treatment of corrosive strictures with variable results.[10,11] From 1994 to 2003, 97 patients (67 males and 30 females) with an age range of 6 months to 16 years were treated for corrosive injuries at our institute. Primary dilatation was attempted in all cases. Five of these cases were those who were earlier treated for corrosive ingestion by dilatation and who later presented with food bolus impaction. Of the 92 fresh cases there were 5 drop outs and 60 were treated by dilatation alone while in 27 cases dilatation failed. Of the sixty cases who were treated primarily by dilatation (n = 60) successful uncomplicated results were seen in 57 cases (95%) while perforation of esophagus occurred in 3 cases (5%). Of the 57 cases with successful treatment with dilatation alone single session of dilatation was required in 33% (19 of 57), 2-5 session in 17.5% (10 of 57), 6-10 sessions in 28% (16 of 57) and more than 10 sessions (range 11-27) in 21% (12 of 57) of cases.[12] In the present study these results when compared to the results at the same centre prior to use of mitomycin-C are very promising though the number of cases in the present study was less. The use of mitomycin C seems to improve the outcome in patients of corrosive stricture in that stricture becomes supple early, large sized dilators can be passed easily and early and there is early symptomatic and radiological relief.

It is still not clear as to how long the treatment should continue. Till such time that further data becomes available, we recommend that the treatment should continue for at least 6 months since that is the time period required for consolidation and maturation of fibrous tissue. Similarly, the frequency of dilatations during mitomycin-C application therapy will have to be judged on the response of individual patients – if the stricture is found to be supple after a previous dilatation then the next dilatation can be scheduled after a longer time gap. The clinical response to dilatation in terms of relief of dysphagia will also determine the frequency of dilatations.

<table>
<thead>
<tr>
<th>Table 1: Number of sessions required for easy passage of 40 F dilator after application of Mitomycin-C locally</th>
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<tbody>
<tr>
<td>Post operative stricture (n=6)</td>
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<tr>
<td>End to End anastomosis (3)</td>
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<tr>
<td>Reverse gastric tube (2)</td>
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<tr>
<td>Stricturoplasty (1)</td>
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<td>Unoperated corrosive stricture (n= 4)</td>
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Further studies will also be required to assess the results of mitomycin-C application therapy in the presence of gastro-esophageal reflux.

REFERENCES


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