MITOMYCIN: EFFECTS ON LARYNGEAL AND TRACHEAL STENOSIS, BENEFITS, AND COMPLICATIONS

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The management of laryngeal and tracheal stenosis continues to challenge us, despite advances in surgical techniques and better understanding of the wound healing process. Injury to the airway mucosa is the inciting event, regardless of the cause of the stenosis. Mitomycin-C is an antineoplastic antibiotic that acts as an alkylating agent by inhibiting DNA and protein synthesis. It can inhibit cell division, protein synthesis, and fibroblast proliferation. Topical application of mitomycin-C (0.4 mg/mL) was used as an adjuvant treatment in the endoscopic laser management of laryngeal and tracheal stenosis in 15 patients. Fourteen patients (93%) have shown improvement of their airway and resolution of their preoperative symptoms. After a mean follow-up of 18 months, no complication was noted with regard to the application of mitomycin-C. This study gives promising findings on the efficacy and safety of mitomycin-C as an adjuvant treatment in the management of selected cases of laryngeal and tracheal stenosis.

KEY WORDS — endoscopic surgery, laryngeal stenosis, laser surgery, mitomycin-C, subglottic stenosis, tracheal stenosis.

INTRODUCTION

Treatment of laryngeal and tracheal stenosis remains one of the most difficult and perplexing problems in the area of head and neck surgery. Scar formation and restenosis remains the main cause of failure in the surgical management of airway stenosis. Modulation of the wound healing process to prevent excessive scar formation can play a major role in improving the success rate and decreasing the need for further surgery.

Mitomycin-C is an antiproliferative agent that can inhibit fibroblast proliferation and activity. It has been successfully used as an adjuvant treatment in a number of ophthalmologic procedures to decrease scar formation and restenosis.

A multicenter prospective clinical trial was undertaken in an effort to evaluate the efficacy and safety of the topical application of mitomycin-C in the prevention and treatment of airway stenosis. Mitomycin-C was used as an adjuvant treatment in the endoscopic laser management of laryngeal or tracheal stenosis in 15 patients. The preliminary results of some of these patients have been reported.[1]

MATERIALS AND METHODS

Fifteen patients underwent endoscopic laser management of laryngeal or tracheal stenosis and the topical application of mitomycin-C at New England Medical Center and The Children's Hospital, Boston, between January 1998 and December 1999. There were 8 male patients and 7 female patients. The patients' ages ranged from 2 to 78 years (mean, 32 years). The patients presented with preoperative symptoms of dyspnea interfering with routine daily activity, poor voice quality and vocal fatigue, and/or the inability to cap their tracheotomy tube. Included were 3 cases of glottic stenosis, 10 cases of subglottic stenosis, and 2 cases of tracheal stenosis (see Table).

Glottic Stenosis. One patient (No. 1) presented with a congenital anterior glottic web. Two patients (Nos. 2 and 3) were referred with posterior glottic stenosis and arytenoid fixation: 1 patient had undergone a tracheotomy and laryngofissure for repair of a blunt laryngeal trauma, and the other had undergone a tracheotomy and partial arytenoidectomy for bilateral vocal cord paralysis caused by a brain stem infarct. Only patient 3 was tracheotomy-dependent at the time of our evaluation, with an inability to cap the tracheotomy tube and poor voice quality.

Subglottic Stenosis. Three patients (Nos. 5, 11, and 13) presented with subglottic stenosis due to prolonged intubation because of cardiac surgery, pneumonia, and thalamic infarct, respectively. One patient (No. 4) presented with restenosis after a laryngotracheal reconstruction for a congenital subglottic stenosis (grade IV). No cause could be identified in

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PATIENT DATA

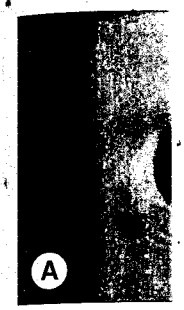
Pt No.	Sex	Age (y)	Location of Stenosis	Etiology	Tracheotomy-Dependent	No. of Procedures	Initial Airway Stenosis	Thickness (mm)	Current Airway Stenosis	Initial Symptoms	Current Status	Follow-up (mo)
1	F	5	Glottic	Congenital web	No	2	60%	4	20%	B	F	12
2	M	14	Glottic	Laryngeal trauma	No	1	4-mm opening		7-mm opening	A, B	F	23
3	M	78	Glottic	Bilateral vocal cord paralysis	Yes	3	2-mm opening		5-mm opening	B, C	D, E	25
4	M	14	Subglottic*	Congenital	Yes	1	80%	4	20%	B, C	D, E	6
5	M	17	Subglottic	Prolonged intubation	No	1	80%	5	30%	A, B	F	13
6	F	33	Subglottic*	Idiopathic subglottic stenosis	No	1	80%	15	20%	A, B	F	25
7	F	38	Subglottic	Idiopathic subglottic stenosis	No	1	50%	12	20%	A, B	F	27
8	F	40	Subglottic*	Idiopathic subglottic stenosis	No	1	80%	4	20%	A, B	F	15
9	F	42	Subglottic*	Idiopathic subglottic stenosis	No	1	50%	7	10%	A, B	F	15
10	F	45	Subglottic*	Idiopathic subglottic stenosis	No	2	70%	10	10%	A, B	F	20
11	M	48	Subglottic	Prolonged intubation	Yes	2	95%	4	40%	A, B, C	D, E	19
12	M	53	Subglottic	Wegener's granulomatosis	No	1	50%	5	10%	A	F	15
13	M	56	Subglottic	Prolonged intubation	No	2	70%	5	30%	A, B	F	29
14	M	2	Tracheal	Prolonged intubation	No	1	70%	5	60%	Prolonged intubation	Tracheotomy	15
15	F	5	Tracheal	Congenital stenosis	No	2	70%	3	10%	A, B	F	13

A — dyspnea on routine daily activity; B — poor voice quality and vocal fatigue; C — inability to cap tracheotomy tube; D — improved voice quality; E — ability to cap tracheotomy tube during day; F — resolution of preoperative symptoms.
*Circumferential scarring.

5 cases (patients 6 through 10), which were classified as idiopathic subglottic stenosis. Wegener's granulomatosis was the cause of subglottic stenosis in 1 patient (No. 12). Only 2 patients from this group (Nos. 4 and 11) were tracheotomy-dependent, with an inability to cap the tracheotomy tube and poor voice quality.

Tracheal Stenosis. One patient (No. 14), with a history of trisomy 21, presented with tracheal stenosis after prolonged intubation because of cardiac and pulmonary status. A second patient (No. 15) presented with tracheal stenosis after laryngotracheal reconstruction for a congenital subglottic and tracheal stenosis.

All patients underwent endoscopic examination and treatment under inhalational general anesthesia provided via a tracheotomy tube, when present, or intravenous anesthesia and Venturi jet ventilation. The airway size and length of stenosis were measured with an open tube ventilating bronchoscope or an endotracheal tube through a laryngoscope. Surgical exposure was obtained by placing the tip of a laryngoscope (Dedo, Healy-Jako, or anterior commissure scope) through the vocal cords for subglottic and tracheal stenosis. The laryngoscope was suspended from a Boston University suspension apparatus, and an operating microscope was used at 16× magnification for all cases. The CO_2 laser at a power setting of 4 to 6 W (time, 0.1 to 0.3 second), in a



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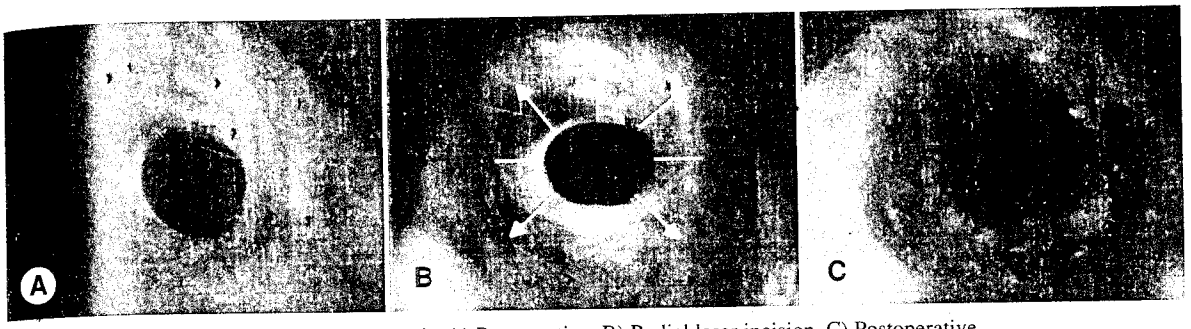

Fig 1. Subglottic stenosis. A) Preoperative. B) Radial laser incision. C) Postoperative.

superpulsed mode (0.25- to 0.3-mm spot size) was used to make radial incisions through the subglottic or tracheal stenosis (Fig 1). Ventilating open tube bronchoscopes were then used for dilation of the stenotic segment. The radial incisions in subglottic or tracheal stenotic areas served to guide the dilating forces in a controlled manner to preserve viable epithelium within the incision.[2] A similar laser setting was used for excision of glottic stenosis (Fig 2). Thereafter, a 10-mm cottonoid sponge was soaked with mitomycin-C 0.4 mg/mL and topically applied to the surgical site for 4 minutes. Then the area was irrigated with 20 to 30 mL of normal saline solution. All patients were observed for a minimum of 24 hours after the procedure. Success was defined as an improvement in the size of the airway and elimination of the preoperative symptoms.

RESULTS

A total of 22 procedures were performed in 15 patients (average, 1.5 procedures): 9 patients had 1 procedure each, 5 patients had 2 procedures each, and 1 patient had 3 procedures. The follow-up ranged from 6 to 29 months, with an average of 18 months. Open tube bronchoscopes and/or endotracheal tubes were used for the measurement of the postoperative length and degree of stenosis under general anesthesia, or the measurements were made with fiberoptic laryngoscopy and still photographs taken by means of a 70° rigid telescope under topical anesthesia. Fourteen patients (93%) showed an improvement in the degree of airway stenosis and resolution of their preoperative symptoms (see Table). The postoperative length of the subglottic or tracheal stenosis could only be measured in patients who underwent general anesthesia because of the need for further surgery. There was no significant improvement noted in the length of the stenosis.

Glottic Stenosis. A total of 6 procedures were performed in 3 patients. Before operation, 1 patient demonstrated a 60% stenosis, and 2 patients had posterior airway openings of 4 and 2 mm, respectively, compared to a postoperative stenosis of 20% and airway openings of 7 and 5 mm, respectively. Two patients are completely asymptomatic with regard to their preoperative symptoms. One patient was tracheotomy-dependent, was unable to cap the tracheotomy tube, and had poor voice quality. Currently, the tracheotomy tube is capped during the day without dyspnea on exertion, and the patient has good voice quality.

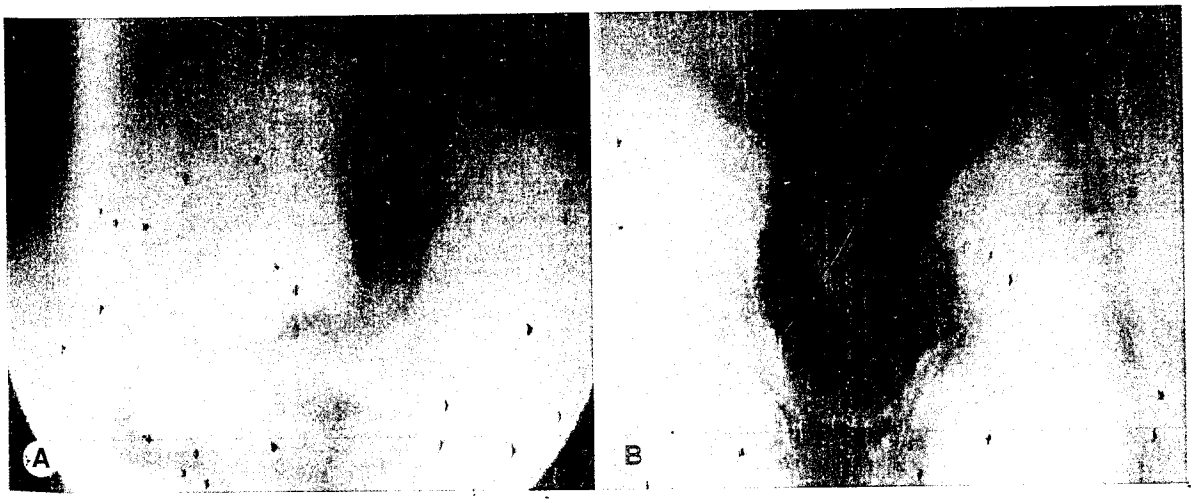

Fig 2. Posterior glottic stenosis. A) Preoperative. B) Postoperative.