AABIP JOURNAL CLUB

TOPICAL MITOMYCIN-C (MMC) IN THE TREATMENT OF LARYNGOTRACHEAL STENOSIS (LTS)

Laryngoscope / 2020

THE CLINICAL QUESTION

What is the Efficacy of topical mitomycin-C (MMC) in the endoscopic treatment of laryngotracheal stenosis (LTS)?

TAKE HOME MESSAGE

The use of mitomycin-C MMC as a topical adjuvant therapy has no additional benefit in the endoscopic surgical management of laryngotracheal stenosis LTS. Further prospective studies with larger sample size are needed.

BACKGROUND

Topical mitomycin-C (MMC) application is a commonly accepted adjuvant therapy in the surgical treatment for laryngotracheal stenosis (LTS). Most of the published clinical studies of topical MMC in LTS have been retrospective case series or cohort studies and report positive outcomes, supporting the use of MMC as an adjuvant treatment. However, the efficacy of MMC has not been examined in a prospective, randomized clinical trial in humans.

STUDY DESIGN

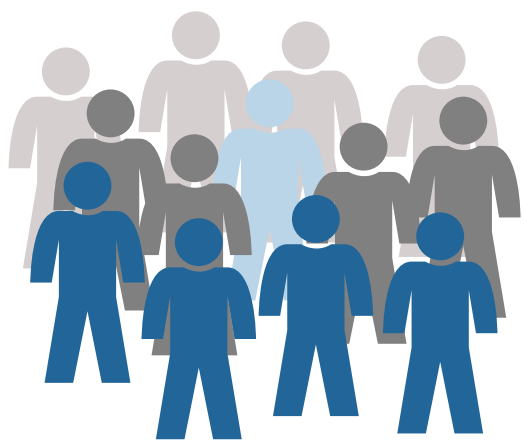
Study design
Prospective, randomized, double-blind, placebo-controlled clinical trial.

Primary outcome
1) Surgical interval

Secondary Outcome(s)
1) Pulmonary function test (Peak inspiratory Flow -PIF)
2) Clinical COPD Questionnaire (CCQ) scores

Intervention(s)
Endoscopic surgical treatment with topical application of MMC or with topical saline. Subsequent surgery was performed as needed based on relapse of stenosis on exam as well as symptom severity

POPULATION

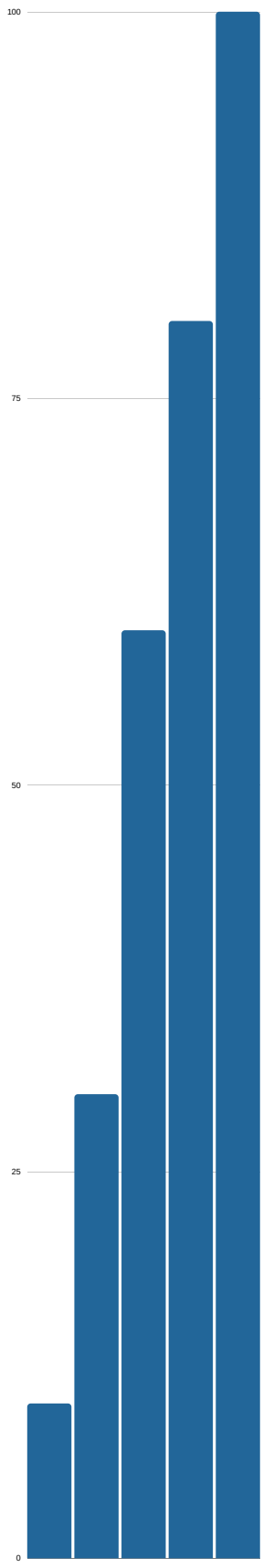


Inclusion criteria
Age greater than 18 years and laryngotracheal stenosis (Idiopathic, Inflammatory, Postintubation) disease amenable to treatment with endoscopic CO2 laser radial incision and balloon dilation.

Exclusion criteria
Pregnant women, Patients with glottic, supraglottic, cartilage involvement

Baseline characteristics
N= 15, Nine subjects were randomized to the placebo group and six subjects to the MMC group. Between the two groups, there were no statistically significant differences in age, gender, age of onset, site of disease, history of prior LTS surgeries, number of LTS surgeries, or prior treatment with MMC or Kenalog. Eleven out of the fifteen subjects had idiopathic LTS, three patients had granulomatosis with polyangiitis with LTS and only one patient had postintubation LTS. Given the recent focus on idiopathic LTS as an inflammatory disorder, fourteen out of the fifteen subjects in this study could be considered as having an inflammatory etiology with only one postintubation LTS patient. Three subjects did not have complete 24-month follow-up. One patient in the MMC group withdrew after 9 months and two surgeries.

OUTCOMES



Primary outcome

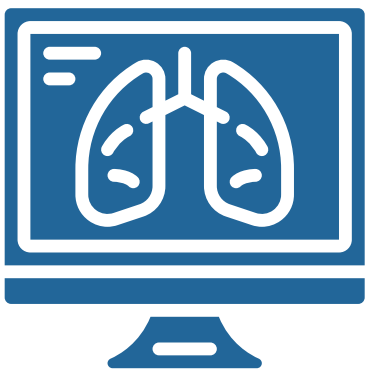
1. Surgical interval - There were six surgeries in the placebo group and two surgeries in the MMC group that did not have a subsequent surgery, and therefore, a surgical interval could not be calculated. Only a total of seven patients (4 in MMC group and 3 in the placebo group) underwent a subsequent surgery. Among the seven patient who underwent a subsequent surgery the average interval for each patient was 17.9 months in the placebo group and 17.4 months in the MMC group (P = .95).

Secondary outcomes

1. Pulmonary function test (Peak inspiratory Flow PIF) - There was no difference in magnitude of peak inspiratory Flow (PIF) improvement between groups. The average magnitude of PIF change was 1.3 L/s and 1.1 L/s for the placebo and MMC groups, respectively (P = .64).
2. Clinical COPD Questionnaire (CCQ) scores - The average magnitude of symptom improvement was 2.4 and 2.2 for the placebo and MMC groups, respectively (P = .73). The percent improvement in CCQ score was 73% in the placebo group and 69% in the MMC group (P = .53).

Adverse events - None

COMMENTARY



1. Kenolog usage during the interventions is a confounding factor making the actual effect of placebo and topical mitomycin-C (MMC) questionable.
2. Low statistical power (because of low sample size) = 15
3. Of the total fifteen patients, nine were randomized to the placebo group, with the remaining six subjects enrolled in the MMC group. Of these patients six in the placebo group and two in the MMC group that did not have a subsequent surgery, and therefore, a surgical interval could not be calculated. Only a total of seven patients (4 in MMC group and 3 in the placebo group) underwent a subsequent surgery. This makes the study much smaller than what it was already.
4. Nine patients had undergone previous endoscopic surgery prior to enrollment.
5. Cross-over patients: From MMC to no MMC - Three patients had endoscopic surgical treatment for LTS including topical MMC prior to study enrollment, but were then randomized to the placebo group. This makes the results in these patients more questionable.

Given all of the above limitations, the conclusions drawn from this study are probably not firmly applicable to general practice. Further studies with larger sample size with longer period of enrolment and follow up comparing combination therapy (steroids + MMC) vs single agent vs placebo are needed.

FUNDING

- None

SUGGESTED READING

1. Rosow DE, Barbarite E. Review of adult laryngotracheal stenosis: pathogenesis, management, and outcomes. Curr Opin Otolaryngol Head Neck Surg 2016;24:489–493.
2. Roediger FC, Orloff LA, Courey MS. Adult subglottic stenosis: management with laser incision and mitomycin-C. Laryngoscope 2008;118:1542–1546.
3. Simpson CB, James JC. The efficacy of mitomycin-C in the treatment of laryngotracheal stenosis. Laryngoscope 2006;116:1923–1925.

ARTICLE CITATION

Yung KC, Chang J, Courey MS. A randomized controlled trial of adjuvant mitomycin-C in endoscopic surgery for laryngotracheal stenosis. Laryngoscope. 2020;130:706-711.

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