

Efficacy of mitomycin C in modified transcanalicular diode laser dacryocystorhinostomy

Eficácia da mitomicina C na dacriocistorrinostomia transcanalicular com laser diodo modificada

Eduardo Damous Feijó¹ , Mirna de Melo Dias¹ , Bruna Angelina Alves de Souza¹ ,
Juliana Alves Caixeta² , Roberto Murillo Limongi³ , Suzana Matayoshi⁴ 

¹ Department of Oculoplastic Surgery, Hospital Oftalmológico de Anápolis, Anápolis, GO, Brazil.

² Department of Otorhinolaryngology, Universidade Federal de Goiás, Goiânia, GO, Brazil.

³ Department of Ophthalmology, Universidade Federal de Goiás, Goiânia, GO, Brazil.

⁴ Department of Ophthalmology, School of Medicine, Universidade de São Paulo, São Paulo, SP, Brazil.

How to cite:

Feijó ED, Dias MM, Souza BA, Caixeta JA, Limongi RM, Matayoshi S. Efficacy of mitomycin C in modified transcanalicular diode laser dacryocystorhinostomy. Rev Bras Oftalmol. 2022;81:e0035.

doi:

<https://doi.org/10.37039/1982.8551.20220035>

Keywords:

Lacrimal apparatus diseases;
Dacryocystorhinostomy;
Dacryocystitis; Lasers, solid-state

Descritores:

Doenças do aparelho lacrimal;
Dacriocistorrinostomia;
Dacriocistite; Laser de estado sólido

Received on:
Sep 21, 2021

Accepted on:
Jan 25, 2022

Corresponding author:

Eduardo Damous Feijó
Avenida Faiad Hanna, 235 – Cidade Jardim
Zip code: 75080-410 – Anápolis, GO, Brazil
E-mail: eduardodff@yahoo.com.br

Institution:

Hospital Oftalmológico de Anápolis,
Anápolis, GO, Brazil.

Conflict of interest:
no conflict of interest.

Financial support:
the authors received no financial support
for this work.



Copyright ©2022

ABSTRACT

Objective: To evaluate the efficacy of mitomycin C in anatomical and functional success after modified transcanalicular diode laser dacryocystorhinostomy.

Methods: A prospective, double-blinded, randomized placebo-controlled study compared the effect of topical mitomycin C on modified transcanalicular diode laser dacryocystorhinostomy. Group 1 had modified transcanalicular diode laser dacryocystorhinostomy with topical saline, while Group 2 had modified transcanalicular diode laser dacryocystorhinostomy with topical mitomycin C. Success was defined as anatomical patency and relief of symptoms at the end of 6 months.

Results: Six months after surgery, Group 1 (30 patients) showed anatomical and functional success rates of 86.7% and 83.3%, respectively. Group 2 (32 patients) showed anatomical and functional success rates of 87.5% and 84.3%, respectively. There was no statistically significant difference between the groups 1 and 2 ($p = 1.000$).

Conclusion: The use of mitomycin C did not improve the anatomical and functional success rates of modified transcanalicular diode laser dacryocystorhinostomy compared to placebo.

RESUMO

Objetivo: Avaliar a eficácia da mitomicina C no sucesso anatômico e funcional após dacriocistorrinostomia transcanalicular com laser de diodo.

Métodos: Estudo prospectivo, duplo-cego, randomizado e controlado por placebo. Comparou o efeito da mitomicina C tópica na dacriocistorrinostomia transcanalicular com laser de diodo. No Grupo 1, foi utilizada apenas solução salina tópica, enquanto no Grupo 2 foi utilizada mitomicina C tópica. O sucesso foi definido como permeabilidade da via lacrimal e alívio dos sintomas ao final de 6 meses.

Resultados: Seis meses após a cirurgia, o Grupo 1 (30 pacientes) apresentou taxas de sucesso anatômico e funcional de 86,7% e 83,3%, respectivamente. O Grupo 2 (32 pacientes) apresentou taxas de sucesso anatômico e funcional de 87,5% e 84,3%, respectivamente. Não houve diferença estatística significante entre os Grupos 1 e 2 ($p=1,000$).

Conclusão: O uso de mitomicina C não melhora as taxas de sucesso anatômico e funcional do dacriocistorrinostomia transcanalicular com laser de diodo em comparação ao placebo.

INTRODUCTION

Dacryocystorhinostomy (DCR) is the gold standard treatment for primary acquired nasolacrimal duct obstruction (PANDO). There are two different approaches to DCR: external (EX-DCR) and endoscopic approach (EN-DCR). Recently, transcanalicular diode laser DCR (TL-DCR) has been described to treat PANDO. Previous studies showed that laser assisted DCR success rates ranges from 74% to 85%.⁽¹⁻³⁾

The modified TL-DCR (MT-DCR) published by Feijó et al. consists of removing a flap of the nasal mucosa prior to laser osteotomy, to avoid the thermal injury, fibrosis, and excessive scarring of the nasal mucosa, which could lead to anatomical or functional failure.⁽²⁾ Mitomycin C has been used as an adjuvant in lacrimal drainage procedures to avoid scars and stenosis. However, the efficacy of this drug in TL-DCR and MT-DCR may be uncertain⁽²⁻⁴⁾.

The aim of this study was to determine the effects of MMC in MT-DCR regarding anatomical and functional success.

METHODS

This is a prospective, double-blinded, randomized and placebo-controlled study. This study was performed between January 2017 to November 2019. All patients signed the informed consent term, and the study was approved by the local research ethics committee (CAAE: 56843016.4.0000.5083). The study was conducted in accordance with Helsinki Declaration (as revised in 2013).

Inclusion criteria were patients who presented chronic tearing and clinical confirmation of PANDO, by Jones test, Zappia-Milder test, probing, syringing and dacryocystography. The cases of stenosis or indeterminate obstruction were investigated with magnetic resonance looking for secondary lacrimal obstruction.

Exclusion criteria were: age under 18 years old, secondary lacrimal obstruction, history of facial trauma, canalicular obstruction, trichiasis, ectropion, entropion, dry eye disease, extrusion of the silicon tube before 8 weeks, and abnormalities in the nasal fossa identified by otorhinolaryngologist (nasal synechiae, nasal polyps, severe nasal septum deviation and/or middle turbinate hypertrophy, with middle meatus blockage). All procedures were performed by the same surgeons (an oculoplastic surgeon and an otorhinolaryngologist). A 940nm Orlight diode laser was used coupled to a 20-gauge (G) fiberoptic probe.

To achieve a 15% difference between the groups, and after adopting the 95% confidence interval and power of 80%, the estimated sample size was 64 patients.

Data were collected regarding gender, age, side, operation time. On the day of the procedure, the patients were randomized by the numbered sealed manila envelopes. The registered nurse (not involved in the study) chose the envelope that defined whether the patient would be part of Group 1 or 2 and then prepared the substance to be applied at a cotton piece. Neither the surgeons nor the patient had access to the information about the substance used in each patient.

Anesthesia

All patients received topical anesthesia with 1% tetracaine drops and nasal anesthesia with 20% lidocaine spray; cotton pieces with 5% naphazoline solution were placed in the nasal mucosa for 5 minutes. After venous sedation, infraorbital and infratrochlear nerve blocks with 2% lidocaine and 0.75% bupivacaine were performed.

Surgical technique

The upper and lower lacrimal puncta were dilated with a lacrimal punctum dilator, followed by lacrimal syringing with 0.9% saline solution. The insertion of the 20G endolaser probe connected to the 940-nm diode laser was made through the superior canaliculus, reaching the medial wall of the lacrimal sac and the lacrimal bone. The nasal cavity was visualized with a 30° 4mm rigid nasal endoscope (Storz®). The location of the lacrimal sac was identified intranasally using transillumination. A vertical incision was made using a sickle edge blade in the nasal mucosa immediately anterior to the maxillary line and was extended from the projection of the line of insertion of the middle turbinate to the upper portion of the inferior turbinate. Two relaxing incisions perpendicular to the first incision were made, and a nasal mucosal flap was lifted using a Freer elevator. The flap was incised at its posterior portion, and a rectangular portion of the nasal mucosa was removed. The osteotomy was performed using the diode laser parameters of 5W and continuous mode and performed close to the axilla of the middle turbinate. The size of the osteotomy was approximately 6mm x 6mm.⁽²⁾ After this, patients were then treated according to the simple randomization prepared before the surgery. They were allocated into the control group (Group 1: MT-DCR + placebo) or treatment group (Group 2: MT-DCR + MMC).

Group 1: modified transcanalicular diode laser dacryocystorhinostomy placebo

Transoperative 0.9% saline solution (placebo) was applied in the region of the ostium using a cotton tip, in the nasal

mucosa for 2 minutes, followed by exhaustive irrigation with approximately 5mL of 0.9% saline solution.

Group 2: modified transcanalicular diode laser dacryocystorhinostomy with mitomycin C

Transoperative 0.02% MMC was applied in the region of the ostium using a cotton tip, in the nasal mucosa for 2 minutes, followed by exhaustive irrigation with approximately 5mL of 0.9% saline solution.

Patency was confirmed by lacrimal syringing with a 0.9% saline solution. Bicanalicular intubation was performed with silicone tube for 8 weeks. No nasal packing material was used.

After the procedure, all patients used antibiotic eye drops associated with corticosteroids four times daily for 1 week. Both nasal irrigations with 0.9% saline solution in the operated nostril and nasal corticosteroid (mometasone) spray were also applied twice a day for 2 weeks.

Follow-up

Postoperative evaluations were masked and performed with lacrimal syringing to confirm patency on the 1st, 7th, and 14th postoperative days, at the moment of silicone intubation removal (8 weeks after surgery) and 6 months postoperatively.

Functional success was defined as the disappearance or improvement of epiphora (Munk criteria zero or one) and confirmed by dye disappearance test. Anatomical success was defined as a positive syringing. The minimum follow-up time was 6 months. Patients with postoperative persistent epiphora underwent nasal endoscopy and dacryocystography to determine the possible cause of failure of the procedure.⁽²⁾

Statistical analysis

Difference between the outcomes of the two techniques was assessed using Fisher's exact test. Other parameters such as gender distribution, age, side, and operation time were evaluated and compared using Fisher's exact test, unpaired student t-test or the Mann-Whitney U test. The statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 22, and p-values less than 0.05 were considered statistically significant.

RESULTS

This study recruited 71 patients, and four were excluded because they refused to participate. After randomization, five patients were excluded due to silicon tube extrusion before 8 weeks (three in Group 1 and two in Group

2). The sample consisted of 62 patients with unilateral obstruction.

Group 1 had MT-DCR with placebo (30 patients), while Group 2 (32 patients) had MT-DCR with MMC.

Data from 62 patients were analyzed: Group 1 (MT-DCR + placebo) was composed by 30 lacrimal drainage systems of 30 patients (26 women and four men) with an average age of 63.4 years. Group 2 (MT-DCR + MMC) was composed of 32 lacrimal drainage systems of 32 patients (27 women and five men) with an average age of 57.8 years. Operation time was 2.5 minutes in Group 1 and 22.4 minutes in Group 2 (p=0.9). Patient data are summarized in table 1.

Table 1. Patient data and anatomical success of the procedures

	Group 1 (n=30)	Group 2 (n=32)	p-value
Gender (female /male)	26/4	27/5	1.000
Age (years)	63.47	57.88	0.151
Side (right/left)	19/11	14/18	0.137
Duration (minutes)	22.5	22.41	0.909
Surgical success	26 (86.7%)	28 (87.5%)	1.000
Failure	4 (13.3%)	4 (12.5%)	1.000

Six months after surgery, Group 1 showed anatomical and functional success rates of 86.7% (26/30) and 83.3% (25/30), respectively. Group 2 showed anatomical and functional success rates of 87.5% (28/32) and 84.3% (27/32), respectively. Despite the percentage variation, there was no statistically significant difference between the groups.

There were no postoperative complications such as hemorrhages, false passage, granuloma, canalicular damage or orbital bruise.

Ophthalmological, lacrimal duct and nasal endoscopy examinations of the eight patients (four Group 1 and four Group 2) with anatomical and functional failure revealed cicatricial ostium closure in six patients (four Group 1 and two Group 2) and common duct obstruction in two patients (both Group 2).

DISCUSSION

This study evaluated the efficacy of MMC in MT-DCR, to prevent scar formation and maintain the patency of the osteotomy.

External DCR is the classic technique for the treatment of PANDO. The use of transcanalicular laser for the osteotomy reduces significantly the operating time and the risk of bleeding.⁽²⁻⁴⁾ Cicatricial ostium closure at the osteotomy area is the most common cause of failure of this surgical technique.⁽⁵⁾

MMC is commonly used by ophthalmologists during glaucoma filtering procedures, pterygium excision, and DCR.^(5,6) MMC has antiproliferative and antifibroblastic activity.⁽³⁻⁵⁾ The ultrastructural effects of MMC are many, including epithelial, glandular, and vascular tissue changes. These effects may help to enhance the success of DCR by preventing cicatricial changes of the ostium.^(5,7)

In this study, the concentration of intraoperative MMC was 0.2mg/mL for 2 minutes, applied topically to surgical rhinostomy using a cotton tip.

There is still no consensus regarding the standard dosage of MMC (it may range from 0.05mg/mL to 0.5mg/mL) nor the application time (ranging from 2 to 15 minutes).⁽⁸⁾ It is necessary to define the best concentration and time exposure to inhibited proliferation of fibroblasts in response to injury without causing extensive apoptosis and side effects. Two studies showed that it is sufficient to use a concentration of 0.2mg/mL MMC for a duration of 3 minutes^(4,9,10) or less.⁽¹¹⁾ Another study observed the effect of MMC exposure (0.4mg/mL) for 5 minutes and reported cell regrowth in 24 to 72 hours.⁽¹²⁾ The longer the duration of MMC application, the greater is the effect on fibroblasts and subsequent healing but studies show that a concentration of MMC over 1.0mg/mL does not increase its effectiveness.⁽⁶⁾ The authors highlight those studies were conducted in vitro (cultured human nasal mucosa fibroblast) and that the results probably may not be the same in vivo.

Mitomycin C has been used in different routes of application:^(4,5) topical intraoperative application, intramucosal circumostial injection of MMC during DCR, multiple topical applications of MMC postoperatively in endonasal DCR^(8,11,13). These applications appear to be a safe and effective adjunctive modality after endocanalicular laser DCR in PANDO. The surgical success rates ranged between 80% and 95%.

In our study we did not observe bleeding, poor epithelization, mucosal or bone necrosis, neither infection, as already reported.^(4,8,14,15)

This study reported that, although the success rate of MT-DCR with MMC was higher than the surgery without MMC, the difference was not significant as the one noticed in other studies that concluded the MMC has no beneficial effect on the success rate in TCL-DCR.^(4,5) On the other hand, this is not observed in all studies since some demonstrate that EN-DCR surgery had a significantly higher success rate compared to the same surgery without MMC.⁽¹⁶⁾ Intrasurgical application of topical MMC during EN-DCR with diode laser is said to reduce excessive scarring on the ostium area.^(14,15) However, it seems that the benefit of using MMC in EN-DCR would be less significant than that in EX-DCR.⁽⁶⁾

CONCLUSION

In this study, both groups had remarkably high anatomical and functional success rates. To the best of our knowledge, this is the first double-blinded, randomized, and comparative controlled study that evaluated the efficacy of MMC in anatomical and functional success in MT-DCR. The limitations of this study are the short sample size and relatively short follow-up period.

REFERENCES

1. Herzallah I, Marghani O, Alherabi A, Faraj N, Bukhari D. Bilateral simultaneous endoscopic dacryocystorhinostomy: outcome and impact on the quality of life of the patients. *Int Arch Otorhinolaryngol.* 2019;23(2):191-5.
2. Feijo ED, Caixeta JA, Nery AC, Limongi RM, Matayoshi S. A comparative study of modified transcanalicular diode laser dacryocystorhinostomy versus conventional transcanalicular diode laser dacryocystorhinostomy. *Eur Arch Otorhinolaryngol.* 2017;274(8):3129-34.
3. Mor JM, Matthaei M, Schrupf H, Koch KR, Bölke E, Heindl LM. Transcanalicular laser dacryocystorhinostomy for acquired nasolacrimal duct obstruction: an audit of 104 patients. *Eur J Med Res.* 2018;23:58.
4. Ozsutcu M, Balci O, Tanriverdi C, Demirci G. Efficacy of adjunctive mitomycin C in transcanalicular diode laser dacryocystorhinostomy. *Eur Arch Otorhinolaryngology.* 2016;274(2):873-7.
5. Kar T, Yildirim Y, Topal T, Çolakoğlu K, Ünal MH. Efficacy of adjunctive mitomycin C in transcanalicular diode laser dacryocystorhinostomy in different age groups. *Eur J Ophthalmol.* 2016;26(1):1-5.
6. Qian Z, Zhang Y, Fan X. Clinical outcomes of dacryocystorhinostomy with or without intraoperative use of mitomycin C: a systematic review and meta-analysis. *J Ocul Pharmacol Ther.* 2014;30(8):615-24.
7. Ali MJ, Baig F, Lakshman M, Naik MN. Electron microscopic features of nasal mucosa treated with topical and circumostial injection of mitomycin C: implications in dacryocystorhinostomy. *Ophthalmic Plast Reconstr Surg.* 2015;31(2):103-7.
8. Kamal S, Ali MJ, Naik MN. Circumostial injection of mitomycin C (COS-MMC) in external and endoscopic dacryocystorhinostomy: efficacy, safety profile, and outcomes. *Ophthalmic Plast Reconstr Surg.* 2014;30(2):187-90.
9. Nair AG, Ali MJ. Mitomycin-C in dacryocystorhinostomy: From experimentation to implementation and the road ahead: A review. *Indian J Ophthalmol.* 2015;63(4):335-9.
10. Ali MJ, Mariappan I, Maddileti S, Ali MH, Naik MN. Mitomycin C in dacryocystorhinostomy: the search for the right concentration and duration—a fundamental study on human nasal mucosa fibroblasts. *Ophthalmic Plast Reconstr Surg.* 2013;29(6):469-74.
11. Rathore PK, Kumari Sodhi P, Pandey RM. Topical mitomycin C as a postoperative adjunct to endonasal dacryocystorhinostomy in patients with anatomical endonasal variants. *Orbit.* 2009;28(5):297-302.
12. Hu D, Sires BS, Tong DC, Royack GA, Oda D. Effect of brief exposure to mitomycin C on cultured human nasal mucosa fibroblasts. *Ophthalmic Plast Reconstr Surg.* 2000;16(2):119-25.
13. Henson RD, Henson RG Jr, Cruz HL Jr, Camara JG. Use of the diode laser with intraoperative mitomycin C in endocanalicular laser dacryocystorhinostomy. *Ophthalmic Plast Reconstr Surg.* 2007;23(2):134-7.
14. Alañón Fernandez MA, Alañón Fernandez FJ, Martínez Fernández A, Cárdenas Lara M. Resultados de la aplicación de mitomicina en la dacriocistorrinostomía endonasal y endocanalicular con láser diodo [Results the application of mitomycin during endonasal and endocanalicular dacryocystorhinostomy by diode laser]. *Acta Otorrinolaringol Esp.* 2006;57(8):355-8. Spanish.

15. Kumar V, Ali MJ, Ramachandran C. Effect of mitomycin-C on contraction and migration of human nasal mucosa fibroblasts: implications in dacryocystorhinostomy. *Br J Ophthalmol*. 2015;99(9):1295-300.
16. Cheng SM, Feng YF, Xu L, Li Y, Huang JH. Efficacy of mitomycin C in endoscopic dacryocystorhinostomy: a systematic review and meta-analysis. *PLoS One*. 2013;8(5):e62737