Braz J Otorhinolaryngol. 2016;xxx(xx):xxx–xxx

Brazilian Journal of
OTORHINOLARYNGOLOGY
www.bjorl.org

ORIGINAL ARTICLE

The potential role of amlodipine on experimentally induced bacterial rhinosinusitis☆

Arzu Tatar[a,*], Mukadder Korkmaz[b], Muhammed Yayla[c], Elif Polat[d], Hakan Uslu[e], Zekai Halici[f], Secil N. Parlak[d]

[a] *Ataturk University, Medical Faculty, Department of Otorhinolaryngology, Head and Neck Surgery, Erzurum, Turkey*
[b] *Ordu University, Medical Faculty, Department of Otorhinolaryngology, Head and Neck Surgery, Ordu, Turkey*
[c] *Kafkas University, Medical Faculty, Department of Pharmacology, Kars, Turkey*
[d] *Ataturk University, Medical Faculty, Department of Embryology and Histology, Erzurum, Turkey*
[e] *Ataturk University, Medical Faculty, Department of Medical Microbiology, Erzurum, Turkey*
[f] *Ataturk University, Medical Faculty, Department of Pharmacology, Erzurum, Turkey*

Received 16 January 2016; accepted 9 August 2016

KEYWORDS
Rhinosinusitis;
Non-antibiotic;
Amlodipine;
Antioxidants;
Guinea pig

Abstract
Introduction: For the treatment of rhinosinusitis antibiotics are used frequently. Concerns have been raised regarding the adverse effects of antibiotics and growing resistance. The lack of discovery of new antibiotic compounds has increased the necessity for exploration of non-antibiotic compounds that have antibacterial activity. Amlodipine is a non-antibiotic compound with anti-inflammatory activity.
Objective: In this study we aimed to investigate the potential role of amlodipine in treatment of rhinosinusitis by evaluating its effects on tissue oxidative status, mucosal histology and inflammation.
Methods: Fifteen adult albino guinea pigs were inoculated with *Staphylococcus aureus* and treated with saline, cefazolin sodium, or amlodipine for 7 days. The control group was five healthy guinea pigs. Animals were sacrificed after the treatment. Histopathological changes were identified using Hematoxylin-Eosin staining. Inflammation was assessed by Polymorphonuclear Leukocyte (PMNL) infiltration density. Tissue levels of antioxidants (superoxide dismutase, glutathione) and an oxidative product (malondialdehyde) were determined.
Results: In rhinosinusitis induced animals, amlodipine reduced loss of cilia, lamina propria edema and collagen deposition compared to placebo (saline) and although not superior to cefazolin, amlodipine decreased PMNL infiltration. The superoxide dismutase activity and glutathione levels were reduced, whereas the malondialdehyde levels were increased significantly

☆ Please cite this article as: Tatar A, Korkmaz M, Yayla M, Polat E, Uslu H, Halici Z, et al. The potential role of amlodipine on experimentally induced bacterial rhinosinusitis. Braz J Otorhinolaryngol. 2016. http://dx.doi.org/10.1016/j.bjorl.2016.08.006

* Corresponding author.
E-mail: arzutatar@atauni.edu.tr (A. Tatar).

http://dx.doi.org/10.1016/j.bjorl.2016.08.006

in all three-treatment groups compared to the control group. Amlodipine treated group showed significantly increased superoxide dismutase and glutathione levels and decreased malondialdehyde levels compared to all treatment groups.
Conclusion: The non-antibiotic compound amlodipine may have a role in acute rhinosinusitis treatment through tissue protective, antioxidant and anti-inflammatory mechanisms.

PALAVRAS CHAVE
Rinossinusite;
Não antibiótico;
Amlodipina;
Antioxidantes;
Cobaia

O papel potencial da amlodipina na rinossinusite bacteriana induzida experimentalmente

Resumo
Introdução: Antibióticos são frequentemente utilizados para o tratamento de rinossinusite. Questões têm sido levantadas sobre os efeitos adversos dos antibióticos e a resistência crescente. A falta de descoberta de novos compostos antibióticos aumentou a necessidade da exploração de compostos não-antibióticos que possuem atividade antibacteriana. A amlodipina é um composto não-antibiótico com atividade anti-inflamatória.
Objetivo: O objetivo desse estudo foi investigar o papel potencial da amlodipina no tratamento da rinossinusite, avaliando seus efeitos sobre o estado oxidativo do tecido, histologia da mucosa e inflamação.
Métodos: Quinze cobaias albinas adultas foram inoculadas com Staphylococcus aureus e tratadas com solução salina, cefazolina, ou amlodipina durante 7 dias. O grupo controle incluiu cinco cobaias saudáveis. Os animais foram sacrificados após o tratamento. Alterações histopatológicas foram identificadas utilizando-se a coloração de Hematoxilina-Eosina. A inflamação foi avaliada pela densidade de infiltração de leucócitos polimorfonucleares (LPMN). Foram determinados os níveis teciduais de antioxidantes (superóxido dismutase, glutationa) e um produto de oxidação (malondialdeído).
Resultados: Em animais com rinossinusite induzida, a amlodipina reduziu a perda dos cílios, edema da lâmina própria e deposição de colágeno em comparação com o grupo placebo (solução salina) e embora não seja superior à cefazolina, a amlodipina diminuiu a infiltração de LPMN. Os níveis de atividade da superóxido dismutase e glutationa foram reduzidos, enquanto os níveis de malondialdeído foram significativamente aumentados nos três grupos de tratamento em comparação com o grupo controle. O grupo tratado com amlodipina apresentou aumento significativo dos níveis de superóxido dismutase e glutationa e diminuição dos níveis de malondialdeído em comparação com todos os grupos de tratamento.
Conclusão: O composto não-antibiótico amlodipina pode ter um papel no tratamento da rinossinusite aguda através de mecanismos protetores de tecido, antioxidantes e anti-inflamatórios.

Introduction

Rhinosinusitis is characterized by inflammation of the sinus and nasal mucosa. It is one of the most common health problems and accounts for more outpatient antibiotic prescriptions than any other diagnosis.[1] Both host and environmental factors play a role in the development of rhinosinusitis. The pathophysiology causing acute rhinosinusitis involves a series of changes that lead to obstruction of the sinus ostia, swelling and inflammation of the mucosa, mucous stasis, impaired mucociliary clearance, and microbial infection. The goals of treatment are to reduce inflammation, eradicate infection, improve drainage and aeration of nasal and sinus mucosa, and restore mucociliary function.[2] Common medical therapies for acute rhinosinusitis include antibiotics, nasal saline irrigation, decongestants, antihistamines, mucolytics, topical or systemic corticosteroids, and anti-inflammatory drugs. Little evidence supports the use of decongestants and antihistamines, although they may help to reduce rhinorrhoea and nasal congestion. Nasal irrigation with saline is usually used in acute rhinosinusitis and may improve mucociliary clearance but evidence is limited to support its use.[3,4]

Antibiotics are commonly prescribed for treatment and their use has been suggested to shorten the time to cure acute bacterial rhinosinusitis; however, concerns have been raised regarding the adverse effects of antibiotics, including resistance. A meta-analysis of randomized controlled