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ORIGINAL ARTICLE

On ciprofloxacin concentration in chronic rhinosinusitis

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KEYWORDS
Chronic rhinosinusitis;
Nasal polyps;
Topical antibiotic;
Nasal gel;
Nasal drops

Abstract
Objective: Considering that all the evidence indicates that chronic rhinosinusitis without nasal polyps (CRSsNP) and chronic rhinosinusitis with nasal polyps (CRSwNP) are distinct entities, the aim of this study was to compare the concentrations obtained in plasma and in sinonasal mucosa with oral and nasal topical ciprofloxacin, in patients with and without nasal polyps, without evaluating the effectiveness of the use of an antibiotic.
Methods: Prospective clinical study with single-blind randomization. The population consisted of patients with chronic rhinosinusitis with eligible for endonasal surgery, over 18 years old. It took place between January 2010 and December 2014. A single preoperative dose of ciprofloxacin (oral or nasal topic- spray, gel or drops) was given and samples of plasma and nasal mucosa (inferior turbinate, middle turbinate, ethmoid and maxillary sinus) were collected prior to surgery. The plasma and mucosal ciprofloxacin concentrations were assayed with high performance liquid chromatography (HPLC) with fluorescence detection (FD).
Results: The oral ciprofloxacin achieved better mucosal concentrations but had a significant plasmatic expression in all patients. None of the topical formulations achieved measurable ciprofloxacin plasmatic levels. Among the topical formulations, the gel had the best mucosal results, despite the existence of polyposis.

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PALABRAS CLAVE
Rinosinusitis crónica;
Pólipos nasales;
Antibiótico tópico;
Gel nasal;
Gotas nasales

Acerca de la concentración de ciprofloxacino en la rinosinusitis crónica

Resumen
Objetivo: Considerando todas las evidencias de que la rinosinusitis crónica sin poliposis nasal (RSCsPN) y la rinosinusitis crónica con poliposis nasal (RSCcPN) son entidades distintas, el objetivo de este estudio fue comparar las concentraciones obtenidas en el plasma y en la mucosa nasal con ciprofloxacino oral y tópico nasal en pacientes con y sin pólipos nasales, sin evaluar la efectividad del uso del antibiótico.
Métodos: Estudio clínico prospectivo con asignación aleatoria. La población se componía de pacientes con rinosinusitis crónica propuestos para cirugía endonasal, mayores de 18 años. Se desarrolló entre enero de 2010 y diciembre de 2014. Se administró una dosis única preoperatoria de ciprofloxacino (oral o tópico nasal, en aerosol, gel o gotas) y se recogieron muestras de plasma y mucosa nasal (cornetes, etmoides y seno maxilar) antes de la cirugía. La concentración de ciprofloxacino en el plasma y en la mucosa se ensayó mediante cromatografía líquida de alto rendimiento con detección de fluorescencia.
Resultados: El ciprofloxacino oral logró las concentraciones mucosas más altas pero tuvo una expresión plasmática significativa en todos los pacientes. Ninguna de las formulaciones tópicas ha generado niveles plasmáticos de ciprofloxacino medibles. Entre las formulaciones tópicas, el gel fue el que presentó mejores resultados mucosos, a pesar de la existencia de poliposis.

Introduction

Chronic rhinosinusitis is a symptomatic inflammation of the paranasal sinuses and nasal cavity that lasts more than 12 weeks, with or without acute exacerbations.[1] US National ambulatory care data from 2006 to 2010 revealed that rhinosinusitis accounted for more outpatient antibiotic prescriptions than any other diagnosis.[2]

CRS is primarily an inflammatory disease, with occasional exacerbations associated with infection. Treating only the acute exacerbations leaves the underlying condition untreated, likely contributing to an increased frequency of exacerbations. CRS is associated with sinus edema and impaired mucociliary clearance. With edema-related obstruction and retained mucus, bacterial infection can more easily set up within the sinuses.[3]

Current consensus classifies chronic rhinosinusitis (CRS) into two subgroups: chronic rhinosinusitis without nasal polyps (CRSsNP) and chronic rhinosinusitis with nasal polyps (CRSwNP).[1] In the past few years, there are a growing number of investigators showing the differences between the sub-types of CRS, stating them as two distinct entities. These differences are becoming proved in many characteristics of the diseases, beyond their phenotype.[4] For instance, its already demonstrated that CRSwNP and CRSsNP have distinct disease markers (cytokines, mediators, and cellular profiles).[4,5] These findings are already affecting the treatment approaches for CRS.

It remains unknown why do polyps develop in some patients but not in others.

Based on the phenotype and on the different expression of the inflammatory cytokines and remodeling patterns, we can distinguish CRSwNP from CRSsNP.[4,5]

The nasal polyps are poorly vascularized structures. Several authors claim that polyps have a normal basal membrane vascularization, but they seem to have an increased expression of vascular permeability factor and have a lack of vasoconstrictor innervation. These factors may play a significant role either in their formation and in its edema or in reducing venous drainage.[6–8] Does this interfere with local antibiotic concentration?

The current treatments for rhinosinusitis are aimed to reduce the inflammation, controlled the infection and restore the mucociliary clearance within the sinuses.

The more commonly responsible microbiological agents for rhinosinusal infection are sensitive to first line antibiotics, but there are some patients infected with resistant bacteria (Pseudomonas or MRSA). Furthermore, one of the more consensual etiologic factors is the presence of biofilms in the nasal mucosa. It is known that biofilms perpetuate the inflammation and the mucociliar disfunction, and therefore, to treat CRS, it is necessary to eradicate the biofilms. Desrosiers demonstrated, in vitro, that a much higher concentration of antibiotic is required to achieve a bactericidal effect on bacteria of biofilms, than the necessary to have bactericidal effect on planktonic bacteria.[9] It questions the effectiveness of oral/systemic antibiotics, leading to the hypothesis that topical nasal antibiotic therapy may be more effective, since it may allow that a higher amount of the active substance reaches the desired location with insignificant systemic absorption and, therefore, without any side effect for patients. There are already some studies concluding that nasal topical antibiotics, used in acute rhinosinusitis (ARS) and in CRS, provoke no side effects to patients.[10] However, there are only a few studies comparing the several available topical presentations and there