XML:ver:5.0.1 5 jena | PRP : 50365 | Prod.Type:FTP pp.1–5(col.fig.:NIL) | ED:Dibyendu PAGN: SCAN:

ARTICLE IN PRESS

Available online at www.sciencedirect.com

ScienceDirect

ELSEVIER

Pathology – Research and Practice ▮ (▮▮▮▮) ▮▮▮–▮▮▮

PATHOLOGY RESEARCH AND PRACTICE

www.elsevier.de/prp

ORIGINAL ARTICLE

The postoperative histologic changes in the nasal mucosa following treatment with amoxycilline or rifampicin: Preliminary findings

Mahmoud R. Hussein[a,b,c,*,1], Eman E. Abu-Dief[a,b,c], Badawy S. Badawy[a,b,c], Mohamed Abdulkader[a,b,c]

[a]Department of Pathology, Faculty of Medicine, Assiut and Sohage Universities, Egypt
[b]Department of Histology, Faculty of Medicine, Assiut and Sohage Universities, Egypt
[c]Department of ENT, Faculty of Medicine, Assiut and Sohage Universities, Egypt

Received 7 December 2007; accepted 23 April 2008

Abstract

This study examines the postoperative histologic changes in the nasal mucosa following treatment with amoxycilline or rifampicin. Three groups of nasal mucosal biopsies were obtained from 20 patients having undergone nasal surgery (partial middle turbinectomy). The first group was obtained immediately before surgery (control group). The second and third groups were taken postoperatively (after the first and 6 weeks of amoxycilline or rifampicin therapy, 10 patients each). The histologic changes in the nasal mucosa and the density of seromucinous glands were examined using histochemical methods and image analyzer.

Amoxycilline treatment was associated with squamous metaplasia and a statistically significant reduction in the percent area of the seromucinous glands compared to the control group ($p<0.05$). Rifampicin therapy was associated with minimal reduction in the density of the seromucinous glands and absence of metaplastic changes.

In nasal surgeries, rifampicin but not amoxycilline had a beneficial effect on postoperative nasal mucosa status.

Keywords: Chronic sinusitis; FESS

Introduction

The nasal cavity is lined by stratified squamous and respiratory-type pseudostratified columnar epithelium separated by transitional epithelium in some places. The nasal secretions are heterogeneous substances composed of secretory products derived from 100,000 small seromucinous glands and goblet cells. The anterior part of the nose has a relatively high secretory capacity [2,7]. These secretions contain antimicrobial molecules as a first-line of host defense mechanism against microbial invaders. Lysozymes and lactoferrin stored in and secreted from serous glands, are the most abundant antimicrobial proteins of the nasal fluid. They are effective against both gram-positive and gram-negative bacteria [7,8,3].

Nasal surgeries are associated with formation of massive nasal crusts, which may last for several months. The reduction of postoperative crustations enhances the healing process and the integrity of the nasal respiratory

*Corresponding author at: Department of Pathology, Faculty of Medicine, Assiut and Sohage Universities, Egypt. Tel.: +20 93 583 166; fax: +20 88 333327.
E-mail addresses: mrcpath17@gmail.com, mrh17@gawab.com (M.R. Hussein).
[1]Former address: University of Wisconsin Medical School and William S. Middleton Memorial Veteran Hospital, Madison, WI 53705, USA. Tel.: 1 608 256 1901x17818.

0344-0338/$ - see front matter © 2008 Elsevier GmbH. All rights reserved.
doi:10.1016/j.prp.2008.04.015

epithelium. Amoxycilline is the drug of choice as a postoperative antibiotic in nasal surgeries. It inhibits cell-wall synthesis [3,5]. Rifampicin is an antimicrobial agent that inhibits nucleic acid synthesis. It kills the microorganisms adherent to the foreign materials. It is used as a synergistic agent for the treatment of Gram-positive infections [6,4]. Two rationales are behind the use of rifampicin and amoxycilline. Rifampicin is the drug of choice in Rhinoscleroma. Its administration is associated with halting of the granulomatous inflammation and even development of atrophic changes in the nasal mucosa. Based on this observation, the authors assumed that rifampicin can halt the hyperplastic and inflammatory changes in the nasal mucosa following surgeries. The authors have chosen to compare the results of rifampicin therapy with those of amoxycilline, as the latter is the drug of choice in the treatment of upper respiratory tract infections.

Studies directly relating to the morphologic changes in the nasal mucosa following treatment with amoxycilline or rifampicin have not yet been published, nor have the effects of these agents on the density of seromucinous glands been examined. This study tries to address these issues.

Materials and methods

The experimental design was approved by the Institutional Research and Ethics Committee of the Faculty of Medicine, Sohag University, Egypt. Informed consent was obtained from the patients before participation in this study.

Patients and clinical assessment

This study included 20 patients with nasal lesions (partial middle turbinectomy), recruited from the Department of Ear, Nose and Throat surgery, Sohag University, Sohag, Egypt. The clinical findings were evaluated before and at the end of the first and sixth week of amoxycilline (10 patients, 1500 mg/day) or rifampicin therapy (10 patients, 600 mg/day). None of the patients had systemic disease, allergy, or was receiving any drugs until the time of the study. The mucosa of the

Table 1. The percent areas of the seromucinous glands

Aspects	Thickness of the nasal mucosa	Squamous metaplasia	Ulceration	PAS (serous glands)	Alcian blue-stained area (mucinous glands)
Untreated (control)	Normal	Absent	Absent		
Mean ± SEM				18.36 ± 1.58	24.40 ± 2.7
Median				19.70	
Range				15.2–20.20	21.7–27.10
Amoxycilline treatment					
First week	Markedly increased (+ + +)	Present	Present		
Mean ± SEM				10.07 ± 2.56	4.77 ± 0.46
Median				10.25	4.85
Range				4.80–15.00	3.6–5.8
Sixth week	Markedly increased (+ + +)	Present	Present		
Mean ± SEM				6.50 ± 0.81	6.75 ± 0.76
Median				6.65	6.90
Range				3.20–9.30	3.2–9.3
Rifampicin treatment					
First week	Mildly increased (+)	Absent	Absent		
Mean ± SEM				15.46 ± 1.13	22.2 ± 1.48
Median				16.50	21.30
Range				13.20–16.7	20–25.1
Sixth week	Mildly increased (+)	Absent	Absent		
Mean ± SEM				14.7 ± 2.00	16.63 ± 4.68
Median				16.60	20.50
Range				10.7–16.8	7.3–22.1
p-Value	–	–	–	<0.05	<0.05

The histological sections were stained with PAS and Alcian blue. The percent areas of the nasal mucosa containing seromucinous glands were determined using Image Analyzer.

Please cite this article as: M.R. Hussein, et al., The postoperative histologic changes in the nasal mucosa following treatment with amoxycilline or..., Pathol. Res. Practice (2008), doi:10.1016/j.prp.2008.04.015

middle turbinate was healthy in all patients before surgeries. The biopsies were taken from the middle turbinate (same site in all patients). The findings of the clinical examinations were evaluated with respect to crusting and the patient nasal comfort [3].

Histological evaluations

Three groups of nasal mucosal biopsies (respiratory nasal epithelium) were obtained from 20 patients having undergone nasal surgeries. The first group was obtained immediately before surgery (control group). The second and third groups were taken postoperatively (first and six week after amoxycilline or rifampicin therapy). The biopsy specimens were obtained under complete aspetic conditions, fixed in 10% neutral buffered formalin and processed for hematoxylin and eosin as well as periodic acid schiff (PAS) and Alcian blue staining. In each case, two observers examined the histological changes in the covering epithelium, seromucinous glands and blood vessels in at least six different sections. In each section, at least five different fields were evaluated. The positive control specimens consisted of normal salivary glands.

Quantification of the percent area of the seromucinous glands

The histological sections were stained with PAS and Alcian blue. The percent areas of the seromucinous glands were determined by using image analyzer. Two observers evaluated the percent areas of the seromucinous glands in five different fields; in areas showing the most intense staining. The values were reported as the mean values of the percent areas of seromucinous glands ± standard error of mean.

Statistical analysis

Statistical comparison among different groups was done using analysis of variance (ANOVA). Calculations were done using the statistical package SPSS for windows, version 10.0. Statistical significance was defined as $p < 0.05$.

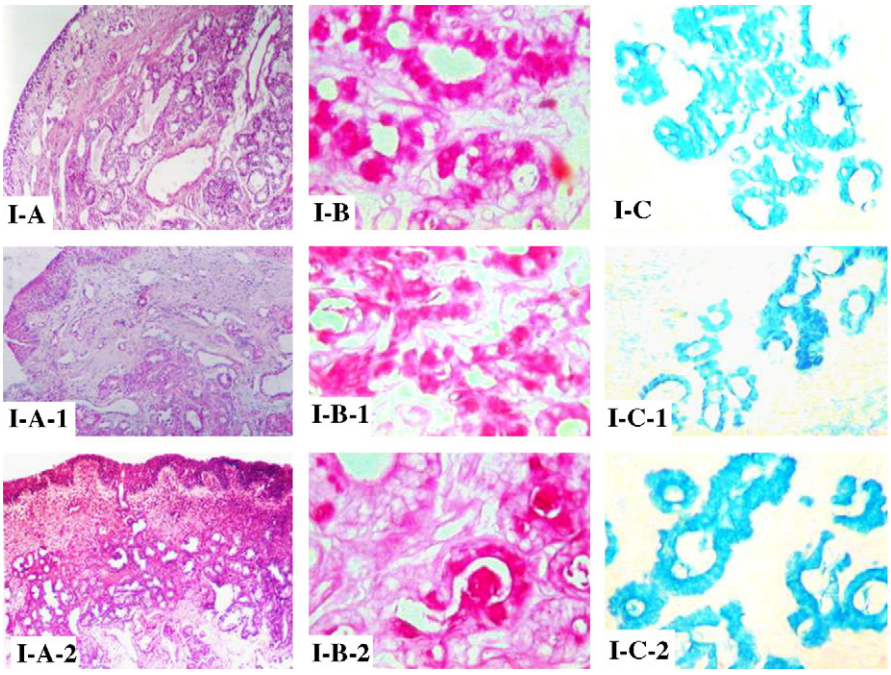

Fig. 1. Histochemical changes in the Schneiderian membrane associated with Rifadine therapy. (1-A-C): In the control (preoperative) group, the nasal cavity is lined by respiratory type pseudostratified columnar epithelium that contained some goblet cells (H&E). Strong positive PAS staining and Alcian blue staining were observed both in the goblet cells and in the cells of the mucous (PAS) and in a serous (Alcian blue) portion of the submucosal seromucinous glands; (1-A.1-C.1 and I-A.2-C2): in the Rifadine-treated group (1-A.1-C.1: first week and I-A.2-C2: sixth week), the nasal cavity was lined by a mildly thickened respiratory-type pseudostratified columnar epithelium without squamous metaplasia or ulceration (H&E). Strong positive PAS staining and Alcian blue staining were observed both in the goblet cells and in the cells of the mucous (PAS) and in a serous (Alcian blue) portion of the submucosal seromucinous glands. Compared to the control group, the percentage areas of these cells were mildly reduced. H&E stains (left panel), ×100; PAS stain (middle panel): ×400; and Alcian blue (right panel): ×200.

Please cite this article as: M.R. Hussein, et al., The postoperative histologic changes in the nasal mucosa following treatment with amoxycilline or..., Pathol. Res. Practice (2008), doi:10.1016/j.prp.2008.04.015

Results

In the rifampicin-treated group, more nasal comfort (nasal obstruction) and less crustations were observed compared to the amoxycilline-treated group.

Histochemical changes in the nasal mucosa

In the control (untreated) group, the nasal cavity was lined by respiratory type pseudostratified columnar epithelium that contained some goblet cells. Seromucinous glands were seen in submucosa. Strong positive PAS and Alcian blue stainings were observed both in the goblet cells and in the cells of the mucous (PAS stain) and serous (Alcian blue stain) portion of the submucosal seromucinous glands. The percent area of these glands was 18.36 ± 1.58 and 24.40 ± 2.7 for PAS and Alcian blue, respectively.

Amoxycilline therapy was associated with a significant reduction in the percent areas of the seromucinous glands

In the amoxycilline-treated group, the nasal cavity was lined by a markedly thickened pseudostratified columnar epithelium compared to the control (untreated) group. The mucosa showed focal squamous metaplasia and ulceration. The percent areas of the seromucinous glands were statistically significantly reduced as opposed to the untreated group ($p < 0.05$).

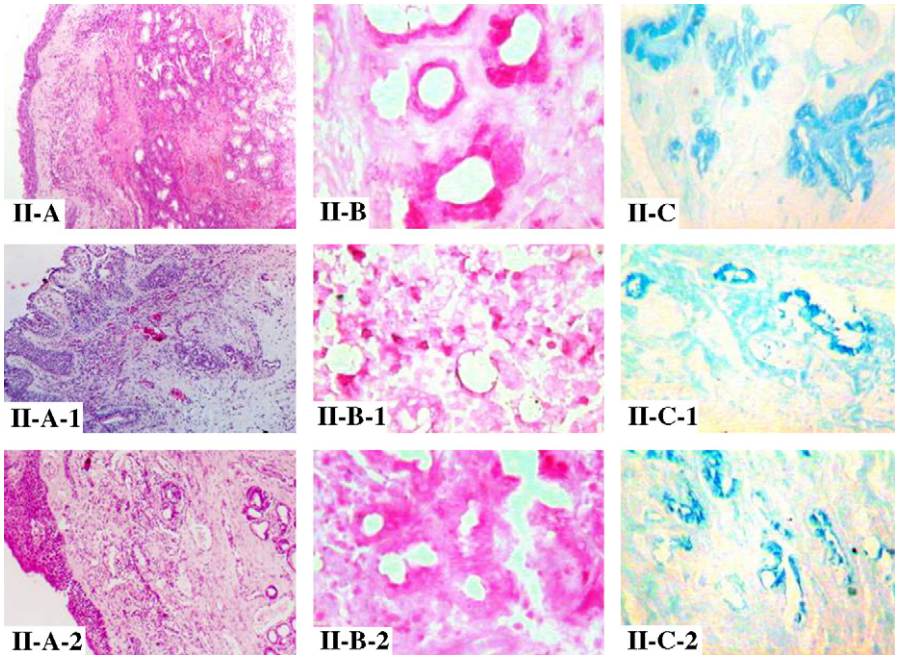

Fig. 2. Histochemical changes in the Schneiderian membrane associated with Amoxycilline therapy. (II-A-C): In the control (preoperative) group, the nasal cavity is lined by respiratory-type pseudostratified columnar epithelium containing some goblet cells. Strong positive PAS staining and Alcian blue staining were observed both in the goblet cells and in the cells of the mucous (PAS) and in serous (Alcian blue) portion of the submucosal seromucinous glands; (II-A.1-C.1 and II-A.2-C2): In the amoxycilline-treated group (II-A.1-C.1: first week and II-A.2-C2: sixth week), the nasal cavity was lined by a markedly thickened respiratory type pseudostratified columnar epithelium with focal squamous metaplasia and ulceration (H&E). Strong positive PAS and Alcian blue staining were observed both in the goblet cells and in the cells of the mucous (PAS) and in a serous (Alcian blue stain) portion of the submucosal seromucinous glands. Compared to the control group, the percentage areas of these cells were markedly reduced. H&E (left panel), × 100; PAS (middle panel): × 400; and Alcian blue (right panel): × 200. Histochemical changes in the nasal mucosa following rifampicin therapy. (II-A-C): In the control (preoperative) group, the nasal cavity is lined by respiratory type pseudostratified columnar epithelium containing some goblet cells (H&E). Strong positive PAS staining and Alcian blue staining were observed both in the goblet cells and in the cells of the mucous (PAS stain) and in a serous (Alcian blue stain) portion of the submucosal seromucinous glands; (II-A.1-C.1 and II-A.2-C2): In the Rifadine-treated group (II-A.1-C.1: first week and II-A.2-C2: sixth week), the nasal cavity was lined by a mildly thickened respiratory type pseudostratified columnar epithelium without squamous metaplasia or ulceration (H&E). Strong positive PAS staining and Alcian blue staining were observed both in the goblet cells and in the cells of the mucous (PAS stain) and in a serous (Alcian blue stain) portion of the submucosal seromucinous glands. Compared to the control group, the percentage areas of these cells were mildly reduced. H&E (left panel), × 100; PAS (middle panel): × 400; and Alcian blue (right panel): × 200.

Please cite this article as: M.R. Hussein, et al., The postoperative histologic changes in the nasal mucosa following treatment with amoxycilline or..., Pathol. Res. Practice (2008), doi:10.1016/j.prp.2008.04.015

Rifampicin therapy was associated with minimal reduction in the percent areas of the seromucinous glands

In the rifampicin-treated group, the nasal cavity was lined by a mildly thickened pseudostratified columnar epithelium compared to the control group. Neither squamous metaplasia nor ulceration was seen. The percent areas of the seromucinous glands were minimally reduced relative to the untreated group. A summary of these results is shown in Table 1 and Figs. 1 and 2)

Discussion

Studies examining the morphologic changes in the nasal mucosa following amoxycilline or rifampicin treatment are lacking. In this investigation, we tried to address this issue. Our study demonstrates marked reduction in the percent area of the seromucinous glands following amoxycilline therapy. These findings concur with other groups [1]. This finding may be attributable to the ability of amoxycilline to alter the intracellular cAMP, as well as to suppress DNA and protein synthesis of the serous and mucous-secreting cells [1]. Abdollahi et al. examined the effects of ciprofloxacin (a fluoroquinolone antibiotic) on the structure and functions of the rat submandibular salivary gland. The drug was administered intraperitoneally at various doses. All doses of ciprofloxacin reduced the salivary flow rate, the concentration of salivary total protein, calcium level and DNA contents of the salivary glands. Histologically, structural damage of the seromucinous glands was also observed [1]. In this study, the presence of marked squamous metaplasia following amoxycilline treatment may be attributed to the persistent bacterial effects on the nasal mucosa. Mygind et al. suggested that bacteria in the nasal secretions may affect the ability of the basal cells of the nasal epithelium to synthesize the tonofibrils and desmosomes. This feature causes the respiratory mucosa to metaplize to squamous epithelium. The extension of the metaplastic epithelium down to the glandular ducts impairs the expulsion of secretions from these glands [7]. The dryness of secretions and crust formation blocks the mouths of glandular ducts and impairs the extrusion of the glandular secretions with stasis of secretions within the glands, leading to their atrophy.

Our results indicated that the administration of rifampicin was associated with minimal reduction of the percent area of the seromucinous glands. It is possible that rifampicin has a selective effect on the microbial nucleic acid synthesis but does not affect the DNA synthesis in the seromucinous glands. Recent reports indicated that rifampicin can affect the P-glycoprotein at the nose–brain barrier [4]. Therefore, a hypothesis to be tested is that the administration of rifampicin can affect the composition and transport of the mucin covering the nasal mucosa in a way that markedly decreases the crust formation [4].

Here, we report the morphologic changes in the nasal mucosa following administration of amoxycilline or rifampicin. The intake of rifampicin was associated with reduction of nasal crustations and more nasal comfort compared to amoxycilline. In addition, rifampicin had a beneficial effect on postoperative nasal mucosa histology.

References

[1] M. Abdollahi, B. Minaiee, A.A. Yaaghoubi, Structural and functional changes by Ciprofloxacin of rat submandibular gland, Hum. Exp. Toxicol. 22 (2003) 177–181.
[2] S. Brofeldt, N. Mygind, Viscosity and spinability of nasal secretions induced by different provocation tests, Am. Rev. Respir. Dis. 136 (1987) 353–356.
[3] I. Ercan, B.O. Cakir, M. Ozcelik, S. Turgut, Efficacy of Tonimer gel spray on postoperative nasal care after endonasal surgery, ORL J. Otorhinolaryngol. Relat. Spec. 69 (2007) 203–206.
[4] C.L. Graff, G.M. Pollack, Functional evidence for P-glycoprotein at the nose–brain barrier, Pharm. Res. 22 (2005) 86–93.
[5] P.P. Graziadei, The mucous membranes of the nose, Ann. Otol. Rhinol. Laryngol. 79 (1970) 433–442.
[6] A.K. Lalwani, T.A. Tami, R.H. Gelber, Lepromatous leprosy: nasal manifestations and treatment with minocycline, Ann. Otol. Rhinol. Laryngol. 101 (1992) 261–264.
[7] N. Mygind, S. Brofeldt, B. Ostberg, V. Cerkez, M. Tos, C. Marriott, Upper respiratory tract secretions: pathophysiology, Eur. J. Respir. Dis. Suppl. 153 (1987) 26–33.
[8] K. Schorn, K. Hochstrasser, Biochemical investigations of nasal secretions, Acta Otorhinolaryngol. Belg. 33 (1979) 603–606.

Please cite this article as: M.R. Hussein, et al., The postoperative histologic changes in the nasal mucosa following treatment with amoxycilline or..., Pathol. Res. Practice (2008), doi:10.1016/j.prp.2008.04.015