

# The effect of mupirocin- and fusidic acid–nasal packings, placed after septoplasty, on the nasal bacterial profile

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## ABSTRACT

**Aim:** To examine the effects, after septoplasty, of local antibiotic pomades as an alternative to prophylactic antibiotic use, which is a controversial matter among the otolaryngologists, on nasal flora and bacterial growth.

**Material and Method:** Nasal packings placed after septoplasty surgery to provide septal stabilization and bleeding control pose a risk in terms of infection. In this study, 106 patients, who were examined by comparing mupirocin- and fusidic acid–soaked packings and antibiotic-free packings, were divided into three groups. Nasal cultures were obtained from each patient twice, before the surgery and on the second day immediately after the packings were removed, and the culture results were statistically compared.

**Results:** In the mupirocin group (group 2), postoperative normal flora growth rate was significantly higher than in the fusidic acid group (group 3) and the antibiotic-free group (group 1) ( $p < 0.024$ ). In the mupirocin group (group 2), the gram-positive growth rate in the postoperative period showed a significant decrease when compared with the preoperative period ( $p < 0.05$ ) (5.7%). In the fusidic acid group (group 3), the postoperative gram-positive rate showed a significant decrease compared with the preoperative period ( $p < 0.05$ ). In group 2, the postoperative methicillin-resistant *Staphylococcus aureus* rate showed a significant decrease than in the preoperative period (2.9%) ( $p < 0.05$ ). Similarly, in group 3, the postoperative methicillin-resistant *S. aureus* rate showed a significant decrease compared with that of the preoperative period (11.1%) ( $p < 0.05$ ).

**Conclusion:** Use of mupirocin- and fusidic acid–soaked nasal packings after septoplasty significantly decreased, especially, postoperative gram-positive bacterial growth in nasal cultures. Although systemic antibiotherapy was not administered, the lack of local and systemic infection findings was an important result that we obtained in terms of clinical use. Usage advantages of mupirocin and fusidic acid soaked packings are an easily applicable, cost-effective, and safe method.

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Nasal septum surgery is one of the most common operations performed by otolaryngologists.<sup>1,2</sup> Nasal bleeding is the most common complication after septum surgery. Infections are observed at a lower rate, and they are assessed as a minor complication. However, severe infective complications, such as toxic shock syndrome (TSS) and endocarditis, although rare, have been reported.<sup>1,3,4</sup> Anterior nasal packings are used after septoplasty to prevent epistaxis and to provide the septal stabilization. However, the use of anterior packings causes an increase in local infections. There is not a consensus on the favorite packing material and removal time from the nasal cavity after

many nasal surgical procedures, especially in septoplasty. The type of packing is usually determined by routine practice and the experiences of the surgeon or by departmental choice.

In nasal septum surgery, the use of postoperative antimicrobial prophylaxis is controversial.<sup>5</sup> Even though many investigators do not recommend it, most surgeons have commonly used antibiotics in recent times.<sup>6,7</sup> In addition, the potential pathogenic bacteria in nasal flora play a triggering role in the nasal packing–related infections. Therefore, reduction of the number of potential pathogenic bacteria may decrease the incidence of postoperative infections.<sup>8</sup> Aerobic bacteria of normal nasal flora are *Streptococcus pyogenes*, coagulase-negative staphylococci, *Corynebacteria*, *Micrococcus* species, *Mycoplasma* species, and *Lactobacillus*. Anaerobic bacteria are *Peptostreptococcus*, *Fusobacterium*, *Veillonella*, *Porphyromonas* species, *Bacteroides* species, *Prevotella*, *Actinomyces*, and *Bifidobacterium* spp.<sup>9</sup> *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Haemophilus influenzae*, and *Klebsiella pneumoniae* are known as potential pathogenic bacteria. *S. aureus* is the most important potential pathogenic bacteria and is present in the nasal mu-

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cosa of healthy individuals at the rate of 18–50%, and *S. aureus* is frequently held responsible for TSS.<sup>1</sup>

Mupirocin (pseudomonic acid A) is an antibiotic produced by *Pseudomonas fluorescens* and is effective against gram-positive cocci and gram-positive and gram-negative bacilli, and a limited number of gram-negative bacteria such as *Neisseria gonorrhoeae* and *H. influenzae*.<sup>10,11</sup> Fusidic acid is a steroid antibiotic obtained from the *Fusidium coccineum* culture filtrates, and, because it does not show a cross resistance with  $\beta$ -lactams, primarily *S. aureus* and *S. epidermidis*, it is also effective against the strains of these bacteria that are resistant to methicillin.<sup>12,13</sup> In our clinic, septoplasty is frequently performed, and anterior nasal packing and postoperative antibiotic prophylaxis are applied. The purpose of our study was to compare the effects of two different antibiotic pomade-soaked polyvinyl acetate (Merocel, Mystic, CT) packings and antibiotic-free packings on nasal bacterial profile.

## METHODS

This study was designed as a prospective controlled study. A total of 106 patients who underwent septoplasty between February 2015 and June 2015 in the otorhinolaryngology clinic were included in the study. Approval was received from Istanbul Education and Research Hospital Ethics Committee (resolution dated January 23, 2015; no. 596). Written consents of all the patients were obtained. The patients were randomly divided into three groups according to the days that the surgery was performed: group 1 was composed of the operations performed in the first two days of the week, group 2 was composed of the third and fourth days of the week, and group 3 was composed of the fifth day of week. Expandable hydroxylated polyvinyl acetate (Merocel) packing was preferred for all the patients. Nasal packing without an antimicrobial agent was used in the 35 patients in the group 1. Mupirocin-soaked Merocel packing was used in 35 patients in the group 2. Fusidic acid-soaked Merocel packing was used in 36 patients in the group 3. Nasal cultures were taken, before surgery, from the middle meatus area in all the patients by using the same method. No systemic antibiotic was administered to any of the patients in the perioperative period. Packings in all the patients were removed on the second postoperative day and then nasal cultures were repeated by using the same method, and were sent to assessment for microbiologic analysis through the sterile transport system. Pre- and postoperative nasal bacterial profiles were compared. The patients with chronic and active sinusitis, any immune system disorder, diabetes, autoimmune disease, a history of previous sinonasal surgery, and pediatric septal deviation were excluded from the study.

Samples were collected from patients both pre- and postoperatively and inoculated into 5–10% sheep

blood agar (Salubris Biotech, Istanbul, Turkey) medium plaques. All the plaques were incubated under aerobic conditions at 37°C for 24–48 hours. All plaques were evaluated in terms of bacterial growth in the blood agar at the end of incubation, colony morphology, hemolysis features, and Gram stain feature. Biochemical typing of the bacteria that are located in gram-positive cocci morphology was identified by using conventional methods. The presence of catalase enzyme activity was monitored with hydrogen peroxide; the presence of coagulase enzyme activity was monitored with clumping factor research and the tube coagulase test at 2, 4, and 24 hours. Methicillin susceptibility of strains exhibiting catalase and coagulase enzymatic activities was evaluated by using Kirby-Bauer disk diffusion method in accordance to directions from Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) and in Muller Hinton agar (GBL, Istanbul, Turkey) by using Cefoxitin disks (30 $\mu$ g, Bioanalyse, Ankara, Turkey). In order to type all gram-positive cocci not exhibiting catalase activity and causing beta hemolysis in blood agar, the BBL Streptocard Enzyme Latex Test kit (BD Bioscience, San Jose, CA) was used. For the isolated gram-negative bacilli, they were identified by using Vitek II Compact device with a fully automated system (BioMerieux SA, Marcy l'Etoile, France) at the species level.

## Statistical Method

Minimum, maximum, frequency, and ratio values were used for the descriptive statistics of data. The distribution of the variables was measured by using the Kolmogorov-Smirnov test. The  $\chi^2$  test was used for the analysis of qualitative data, and when the conditions of the  $\chi^2$  test were not met, Fisher's exact test was used. The McNemar test was used for the analysis of repeated measures. A value of  $p < 0.05$  was accepted as significant. The SPSS 22.0 (IBM Corporation, Armonk, NY) program was used in the analyses.

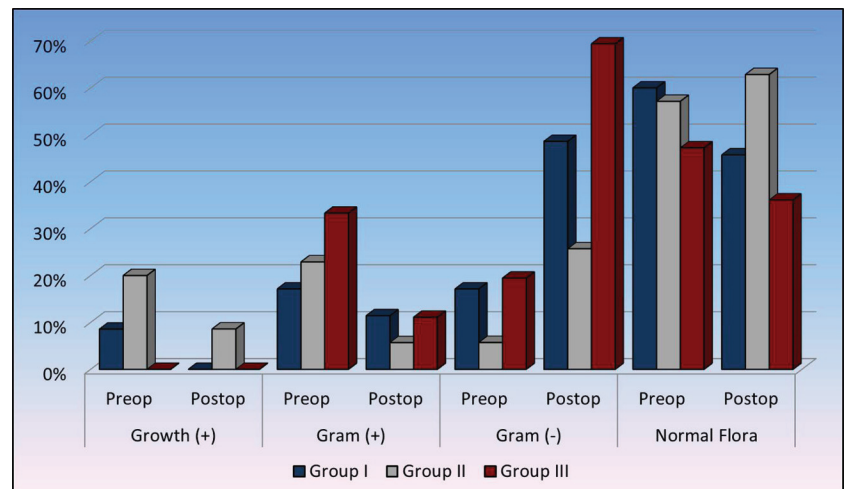
## RESULTS

Fifty-six of the 106 patients included in the study were men and 50 were women, and their average age was 30.5 years (ranging in age of 18 to 55 years old). In all three groups, gram-positive, gram-negative, and normal flora rates in the preoperative period did not show any significant difference ( $p > 0.05$ ). In all three groups, the growth rate in the postoperative period did not show any significant difference ( $p > 0.05$ ). In the mupirocin group (group 2), the gram-positive growth rate in the postoperative period showed a significant decrease compared with the preoperative period

**Table 1 Pre- and postoperative growth, normal flora, gram-positive (+) and gram-negative (-) bacteria distribution among the groups**

Nasal Culture	Group 1 (antibiotic-free), no. (%)	Group 2 (with mupirocin), no. (%)	Group 3 (with fusidic acid), no. (%)	<i>p</i>
<b>Preoperative</b>				
Growth (+)	32 (91.4)	28 (80.0)	36 (100.0)	<0.005
Growth (-)	3 (8.6)	7 (20.0)	0 (0.0)	
Gram (+)	6 (17.1)	8 (22.9)	12 (33.3)	>0.05
Gram (-)	6 (17.1)	2 (5.7)	7 (19.4)	>0.05
Normal flora	21 (60.0)	20 (57.1)	17 (47.2)	>0.05
<b>Postoperative</b>				
Growth (+)	35 (100.0)	32 (91.4)	36 (100.0)	>0.05
Growth (-)	0 (0.0)	3 (8.6)	0 (0.0)	
Gram (+)	4 (11.4)	2 (5.7)*	4 (11.1)*	>0.05
Gram (-)	17 (48.6)*	9 (25.7)*	5 (69.4)*	<0.05
Normal flora	16 (45.7)	22 (62.9)	13 (36.1)	0.024

\*Within-group pre- and postoperative change,  $p < 0.05$ .  
The  $\chi^2$  test (Fisher's exact test)/McNemar test.



**Figure 1.** Pre- and postoperative nasal culture changes.

(5.7%) ( $p < 0.05$ ). In the fusidic acid group (group 3), the postoperative gram-positive rate showed a significant decrease compared with the preoperative period (11.1%) ( $p < 0.05$ ). In the antibiotic-free group (group 1), there was no statistically significant change in the gram-positive growth rate in the postoperative period (Table 1 and Fig. 1).

In all three groups, the growth rates of gram-negative bacteria in the postoperative period increased compared with the preoperative period in a statistically significant way ( $p < 0.05$ ). In groups 1 and 3, the growth rates of gram-negative bacteria were significantly higher than in group 2 ( $p < 0.05$ ). No significant difference was found between groups 1 and 3 in terms of the postoperative growth of gram-negative bacteria ( $p > 0.05$ ). In group 2, the postoperative normal flora growth rate was significantly higher than in groups 1

and 3 ( $p = 0.024$ ). However, in all three groups, the rate of postoperative normal flora did not show any change compared with the preoperative period. In group 1, the postoperative bacterial growth rate, gram-positive bacteria, and normal flora bacterial growth rate did not show a significant change compared with the preoperative period ( $p > 0.05$ ) Fig. 1.

In all three groups, the pre- and postoperative methicillin-resistant *S. aureus* (MRSA) growth rate did not show a significant difference ( $p > 0.05$ ). In group 1, the postoperative MRSA rate did not show a significant change compared with the preoperative period ( $p > 0.05$ ). In group 2, the postoperative MRSA rate showed a significant decrease compared with the preoperative period (2.9%) ( $p < 0.05$ ). Similarly, in group 3, the postoperative MRSA rate showed a significant decrease compared with the preoperative period (11.1%)

Table 2 Pre- and postoperative comparison of MSSA and other bacteria groups among the groups

MRSA Results	Group 1, no. (%)	Group 2, no. (%)	Group 3, no. (%)	<i>p</i>
Preoperative				>0.05
MRSA (+)	6 (17.1)	7 (20.0)	11 (30.6)	
Other bacteria*	29 (82.9)	28 (80.0)	25 (69.4)	
Postoperative				>0.05
MRSA (+)	4 (11.4)	1 (2.9)#	4 (11.1)#	
Other bacteria*	31 (88.6)	34 (97.1)	32 (88.)	

MSSA = Methicillin-sensitive *Staphylococcus aureus*; MRSA = methicillin-resistant *Staphylococcus aureus*; (+) = positive.  
 \*Bacteria other than MRSA.

#Denotes significant change within-group pre- and postoperative change,  $p < 0.05$ .

The  $\chi^2$  test (Fisher's exact test)/McNemar test.

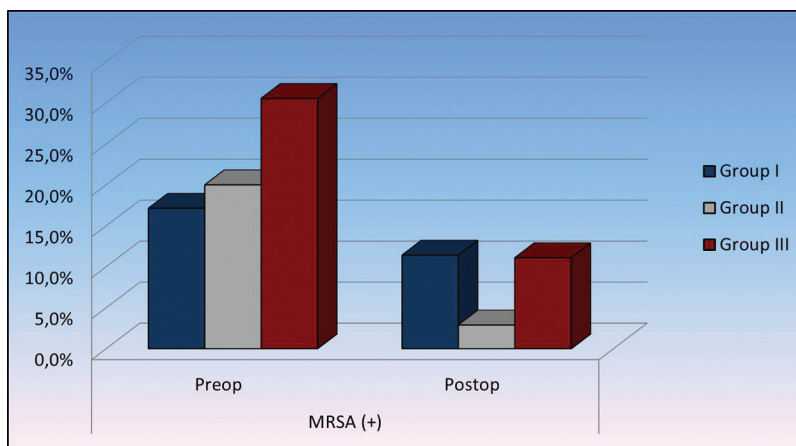


Figure 2. Methicillin-resistant *Staphylococcus aureus* (MRSA) changes.

( $p < 0.05$ ) (Table 2 and Fig. 2). In terms of the growth of methicillin-sensitive *S. aureus* (MSSA), no significant difference was found between the pre- and postoperative periods in all three groups ( $p > 0.05$ ). (Table 3 and Fig. 3). There was no postoperative marked pain, bleeding, septal hematoma, abscess formation, or systemic complications in any of the groups.

## DISCUSSION

Merocel is one of the most common nonabsorbable nasal packing materials, although it has disadvantages, such as pain, discomfort, bleeding upon removal, nasal obstruction, and mucosal edema. However, bioresorbable materials, *e.g.*, NASOPORE (fully synthetic biodegradable; Polyganics, Groningen, the Netherlands), one of the most commonly used dissolvable materials, tended to induce excessive granulation tissue formation during the early stages of wound healing after surgery.<sup>14</sup> When compared with Merocel, NASOPORE significantly reduced pain *in situ* and upon removal. Even so, in our current study, based on previous experiences, we preferred Merocel rather than biodegradable material. Weber *et al.*<sup>15</sup> reported that retention intervals for materials such as Merocel, paraffin gauze, gauze, fingerstalls, and silastic splints ranged from 24

to 72 hours. We preferred that packings in all the patients be removed at 48 hours after surgery.

It was reported that, after anterior packing is placed after nasal surgery, the rate of nasal local infection is 0.5–12% and that subclinical bacteremia may be observed at the rate of 12%.<sup>1</sup> Accumulation of hemorrhagic fluid and secretions in the operation area causes the packings to be converted into a suitable medium for bacterial growth. Mucosal damage that occurs during the operation may play a role in the pathogenesis of TSS by enabling the transfer of bacteria to the blood.<sup>16,17</sup> TSS is produced by *S. aureus*, at 10–30% of toxin 1.<sup>18–20</sup> The incidence of TSS is given as 0.0002% after nasal surgery.<sup>21,22</sup> However, it could not be shown that antibiotic use decreases the incidence of TSS.<sup>4,21</sup>

Although systemic antibiotic use after nasal surgery is controversial, numerous otolaryngologists prefer prophylactic antibiotic treatment to reduce the risk of this complication because toxic shock potentially is a serious situation.<sup>2,23</sup> Also, it is used to try to reduce the infection complications by soaking antibiotic pomades to the gauze strip nasal packings. In our study, systemic antibiotics were not used, and mupirocin, fusidic acid, and antibiotic-free Merocel packings were used,

Table 3 Pre- and postoperative comparison of MSSA and other bacteria groups among the groups

MSSA Results	Group 1, no. (%)	Group 2, no. (%)	Group 3, no. (%)	<i>p</i>
Preoperative				>0.05
MSSA (+)	2 (5.7)	1 (2.9)	0 (0.0)	
Other bacteria*	33 (94.3)	34 (97.1)	36 (100.0)	
Postoperative				>0.05
MSSA (+)	1 (2.9)	1 (2.9)	0 (0.0)	
Other bacteria*	34 (97.1)	34 (97.1)	36 (100.0)	

MSSA = Methicillin-sensitive *Staphylococcus aureus*; (+) = positive.

\*Bacteria other than MSSA.

The  $\chi^2$  test (Fisher's exact test)/McNemar test.

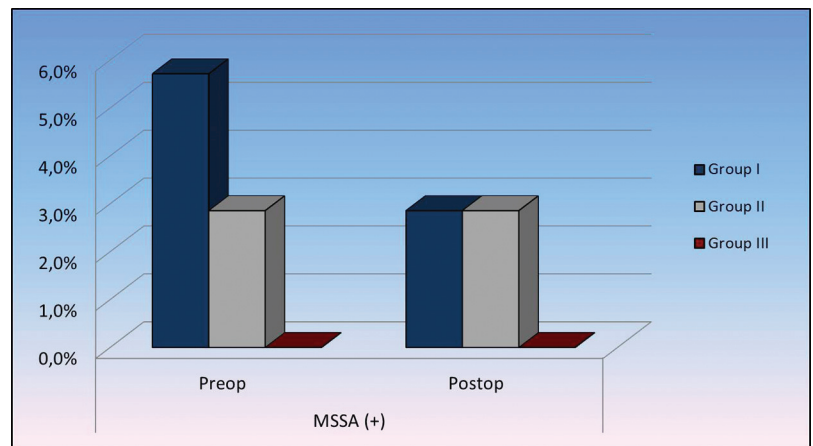


Figure 3. Methicillin-sensitive *Staphylococcus aureus* (MSSA) changes.

and the number of postoperative gram-negative bacteria statistically increased, similar in all three groups. This increase was significantly higher in groups 1 and 3 than in group 2. The efficacy of mupirocin on gram-negative bacteria was assessed as compatible with this situation. In addition, the postoperative nasal flora growth rate in the patients in whom mupirocin packings were used was significantly higher than in the other groups. In our study, also, the statistical decrease in the postoperative MRSA positivity in groups 2 and 3 compared with the preoperative period supported that, especially, mupirocin and fusidic acid were effective in the treatment of MRSA.

Over the past several years, there has been increased interest in the use of topical antibiotics instead of oral antibiotics in sinonasal surgery procedures, and, for that purpose, mupirocin has been safely used worldwide. As for fucidic acid, after many years of use, the most common adverse effects reported are minor and are related to the gastrointestinal tract. The adverse effects such as hepatotoxicity (reversible), skin reactions, and allergic contact dermatitis have been rarely reported.<sup>24</sup> However, no toxic effect on olfactory neuroepithelium has been reported in literature.

In the study conducted by Karaman *et al.*,<sup>25</sup> with 115 patients, the investigators showed that the use of cefa-

zolin prophylaxis and 0.02% nitrofurazone-soaked Merocel packing decreased the gram-negative, MSSA, and normal flora structure, and systemic or topical antibiotic use did not cause any significant change in the number of *S. aureus*. Nasal bacterial flora is stabilized in a period of at least 3 months. In the study by Karaman *et al.*,<sup>25</sup> nasal cultures were taken at the third month after septoplasty. However, because the complications that may occur during packing use were observed in the early stage, the reason for taking the culture immediately after removal of packing was because of the changes in nasal flora in the early period due to nasal packings.

In the study by Mehraj *et al.*,<sup>26</sup> with a population of 405 out-of-hospital adults in the northern Germany region, these investigators found that the prevalence of *S. aureus* nasal carriage was 85 patients (21.9%) and that the prevalence of MRSA was 5 patients (1.29%). They determined 54 different MSSA types within the isolated 85 *S. aureus* strains.<sup>26</sup> In our study, no significant difference was found between the pre- and postoperative periods in all three groups in terms of MSSA growth ( $p > 0.05$ ). This result can be associated with the wide range of MSSA types. Although similar results were obtained regarding MRSA prevalences in other European countries (England, 1.1%; France,

1.02%; Italy, 0.12%), the studies conducted in the continent of Asia reported that MRSA prevalence was 5.3% in India, 3.6% in China, and 2.8% in Pakistan.<sup>27–32</sup> In a study conducted in Turkey, *S. aureus* nasal carriage was observed in 4% the hospital personnel.<sup>33</sup>

This study was the first comparative study that assessed pre- and postoperative nasal bacterial profiles by using topical antibiotic nasal Merocel packings. This study can be developed further in later research by performing nasal culturing from higher number of patients of both early and late stages and by statistical examinations on bacterial colony examinations from patient samples. We are of the opinion that the results obtained will decrease the use of systemic antibiotherapy.

## CONCLUSION

The use of mupirocin- and of fusidic acid-soaked nasal packings after septoplasty significantly decreased the growth of postoperative gram-positive bacteria in nasal culture. In addition, the use of topical antibiotic packings did not change the nasal flora. These results made us think that, because the use of mupirocin- and of fusidic acid-soaked packings was easy and cost effective, and also that there was no need for the use of systemic antibiotic, these packings may be preferred.

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