ORIGINAL CONTRIBUTION

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Cefuroxime as a prophylactic preoperative antibiotic in septoplasty. A double blind randomized placebo controlled study*

Markus Lilja[1], Antti A. Mäkitie[1], Veli-Jukka Anttila[2], Pentti Kuusela[3], Matti Pietola[1], Maija Hytönen[1]

[1] Department of Otorhinolaryngology – Head and Neck Surgery, Helsinki University Central Hospital, Helsinki, Finland
[2] Department of Medicine, Division of Infectious Diseases, Helsinki University Central Hospital, Helsinki, Finland
[3] Department of Bacteriology and Immunology, Haartman Institute, University of Helsinki, Helsinki, Finland

SUMMARY

Background: *Prophylactic antibiotics are often used in septoplasty. However, the number of controlled studies, especially randomized double blind placebo controlled studies on the effect of antibiotics in septum surgery, is very low.*

The ***purpose of the present study*** *was to investigate if intravenous cefuroxime given as preoperative antimicrobial prophylaxis 30 minutes prior to surgery diminishes the risk of infection after septoplasty during the first postoperative month among patients with normal immune function.*

Methods: *This study was a double-blind placebo controlled randomized study and patients were randomized to either an antibiotic prophylaxis-group or placebo-group.*

Results: *In the antibiotic-group, the infection rate was 2.2% (2/92) and in the placebo-group 8.3% (8/96), which is not statistically different. All three deep incisional Surgical Site Infection (septal abscess) occurred in the placebo-group. The preoperative crusting or purulent secretion, or Staphylococcus aureus in the bacterial swab increased the risk of postoperative infection significantly.*

Conclusions: *We recommend the use of one dose of 1500 mg intravenous cefuroxime prior to septoplasty in patients having crusts or purulent secretion in the nasal cavities or if the operation is expected to be prolonged.*

Key words: nose, postoperative infection, septal deformity, complication, Staphylococcus aureus

INTRODUCTION

Septoplasty is one of the most common operations performed at ear-, nose- and throat hospitals. The incision wound for this operation is classified as a clean-contaminated surgical wound [(1)]. Consequently, transient bacteraemia is sometimes found pre- and postoperatively [(2,3)]. There is large variability in the reported number of infections after septoplasty, ranging from 0.46% to 12% [(4)].

Septoplasty incision is made into the anterior part of septum, the area where *Staphylococcus aureus* (*S. aureus*) is commonly found. *S. aureus* is a pathogen frequently causing postoperative infections. In an healthy adult population, the incidence of persistent nasal carriage of *S. aureus* ranges between 20 and 30% [(1)]. Intermittent carriage rate can be even 75% [(5)]. The carriage of *S. aureus* is a significant risk factor for postoperative wound infection for example in cardiologic and orthopaedic surgery [(6-8)].

The use of prophylactic antibiotics in septoplasty varies. In a survey of practice habits in USA regarding the use of antibiotics after septoplasty, 66% of respondents used antibiotics routinely and responders who used packing and/or splints were even more likely to use antibiotics [(9)]. Older physicians used more frequently prophylactic antibiotics after septoplasty than the younger ones [(10)]. At our hospital, the reported incidence rate of infections after septoplasty has decreased during a decade from 12% to 4.2%, while the use of antibiotics at the same time has increased from 21% to 41%, respectively [(10,11)].

Altogether, the number of controlled studies, especially randomized double blind placebo controlled studies on the effect of antibiotics, is very low. Some authors recommend the use of antibiotic prophylaxis. The route of the antibiotic used varies: it can be nasal antibiotic packing [(12)], or administration per os

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and intravenously [13]. The conclusion in two review articles, however, is that there is no benefit from prophylactic antibiotics in nasal surgery even if nasal packing is used when there is no predisposing factor for infection [4,14].
Caniello et al. compared three septoplasty groups: without antibiotics, cefazolin during anaesthetic induction, and cefazolin during induction and one week postoperatively [15]. There were 35 patients in this study and there was no statistically significant difference between the groups. Rajan et al. had 200 septorhinoplasty patients divided in two groups: both groups received 2.2 g of amoxicillin-clavulanate as a single intravenous dose 30 minutes prior to surgery [13]. One of the two study groups also received the same antibiotic 1000 mg twice per day per orally for one week. There were three infections in the combined treatment group and none in the single dose group. There was a significant difference in the side-effects in favour of the single dose group (2% vs. 29%). Thus, the authors recommended a single dose prophylaxis.

According to Guideline for Prevention of Surgical Site Infection (SSI) antimicrobial prophylaxis should be used in all operations or classes of operations in which the use has been shown to reduce SSI-rates based on evidence from clinical trials, and in operations after which incisional or organ/space SSI would represent a catastrophe [1]. Antimicrobial agents should be administered intravenously, but the majority of studies demonstrate that antimicrobial prophylaxis after wound closure is unnecessary [1,16,17]. Prolonged use of antibiotics is also associated with risk of resistant bacteria or antibiotic related diarrhoea [16]. The recommended timing of the single-shot antibiotic prophylaxis varies from 120 minutes to immediately before the operation [17].

The first and main purpose of the present study was to investigate if intravenous cefuroxime given as preoperative antimicrobial prophylaxis diminishes the risk of infection during the first postoperative month after septoplasty among patients with normal immune function. The second aim was to study whether the positive culture finding of *S. aureus* from the preoperative nasal sample increases the risk of postoperative infections.

PATIENTS AND METHODS

The study was carried out from November 2006 to January 2008. The original study population consisted of 200 adult septoplasty or septocolumelloplasty patients operated on at the Department of Otorhinolaryngology – Head and Neck Surgery, at the Helsinki University Central Hospital. All patients had a preoperative visit when clinical status, endoscopy and rinomanometry without and with decongestion were done. Washing-out period since the last respiratory infection was one month. Septoplasty involved correction by mobilizing, straightening and re-inserting the cartilaginous (and the bony) septum. No submucous resection operations were done. Patients could also have inferior turbinate(s) radiofrequency thermal ablation (RFA) or turbinate resection during the operation. The operation was performed under local or general anaesthesia. Written informed consent was obtained from all study subjects.

The exclusion criteria of the study were: 1) disease that increases the infection risk, i.e. for example diabetes, leucopenia, neutropenia, HIV-infection, hypogammaglobulinemia), 2) rhinoplasty operation, 3) septoplasty in combination with sinus surgery, and 4) age < 18 years.

Altogether 200 patients were included in this study. This study was a double-blind placebo controlled randomized study and patients were randomized to Antibiotic prophylaxis group (Ab-group, 100 patients) and Placebo-group (100 patients). The randomization envelopes were prepared at the hospital pharmacy. The envelope was opened and active medication or placebo was given to the patient accordingly by a nurse who did not otherwise participate either in the operation or the postoperative treatment of the patient. Half of the patients received one dose of 1500 mg cefuroxime (Zinacef®, GlaxoSmithKline) and the other half (placebo group) 100 ml of NaCl solution intravenously. The dose was given during 5-10 minutes starting 30 minutes prior to the surgical incision. If the patient had cephalosporin allergy, clindamycin 600 mg (Dalacin®, Pfizer) was the alternative preparation.

A swab sample was taken 1-2 hours before the operation from the vestibulum of the nasal cavity for immediate bacterial culture. Local anaesthesia was applied also in operations performed under general anaesthesia to gain vasoconstriction. Before administering the local anaesthetic, the surgeon graded the status of the nasal cavity. Amount of watery secretion, coloured/purulent secretion, crusting, and mucous membrane oedema in the nasal cavities were graded separately using a scale of 0 to 3 points. There were no restrictions or directions for the surgeon regarding the surgical procedure, use of postoperative packing or nasal splints.

The septoplasty could be done as day-case surgery, i.e. the patient was admitted 2 hours before the operation and discharged 3 to 5 hours after the operation, or the patient stayed overnight at the ward. In day-case septoplasties, the patient came the next morning for removal of the nasal packing. If the patient stayed overnight at the hospital, the packing was removed before the patient was discharged. The next follow up visit was arranged no later than after 3 months.

Table 1. Criteria for a postoperative septoplasty infection.

1) Infection occurred during the first 30 postoperative days and
2) Signs of infections
   a) prominent submucosal swelling and flush of the septum mucosa or
   b) pus in the hemitransfixation wound or
   c) septal abscess or haematoma and fever
   d) symptoms of possible general infection (fever, malaise, headache etc.)

Table 2. Demographic data and the statistical difference between the study groups.

	Antibiotic-group	**Placebo-group**
Number of patients	92	96
Age (range)	41 (18 -71)	41 (18 -70)
Sex M / F	73 / 19	75 / 21
Operation time (mean ± SD)	49 ± 21 min	50 ± 22 min
Day-case surgery cases	76 (83 %)	81 (84 %)
Additional operations	22	31
RFA	20	28
Concha inferior resection	0	1
Concha media resection	2	1
Valvuloplasty	0	1

The patients were advised to contact the hospital immediately in case of an infection or a suspicion of an infection. If a post-operative infection was diagnosed, a swab sample was taken from the infected area of the septum or nasal cavity for bacterial culture. The doctor treated the infection according to its severity.

In this study, the CDC (Centers for Disease Control and Prevention) – criteria for defining a SSI were used [(1)]. According to these criteria, SSI occurs within 30 days after the operation. The infections are categorized as superficial incisional, deep incisional or organ/space SSI [(1)]. We considered as post-operative surgical site infections those of nasal cavity, septum, nose and/or the face. Other infections occurring within 30 days, for example common cold, were registered but not included in the final analysis. The criteria for a postoperative septoplasty infection are shown in Table 1. If there was discrepancy whether the patient had a postoperative septoplasty infection, the investigators made a consensus decision based on the carefully collected case records data. In case of prominent septal swelling the infection site was drained to differentiate between swelling, abscess and haematoma.
The study was approved by the Research Ethics Board of the Helsinki University Central Hospital.

Statistical analysis
Data analysis and the statistics of the study were done by a professional statistician. Statistical analysis was performed with the Student's t-test in cases where 2 population means where compared. Where the requirement of normal distribution was not met, Mann-Whitney U test was used instead. Pearson's chi-square test and Fisher`s exact test were used when comparing categorical variables. The difference between the groups was considered significant if p was < 0.05.

RESULTS

Altogether 200 patients were included in this study. Afterwards 12 patients were excluded because of the following reasons: 7 patients were treated postoperatively by antibiotic not allowed by the study protocol, 2 patients were treated with antirheumatic drugs, 1 patient had insulin-dependent diabetes, 1 patient underwent sinus surgery in combination with septoplasty and 1 patient underwent only RFA for inferior turbinate reduction. None of the excluded patients developed a postoperative infection. Eight excluded patients were in the Ab-group and 4 in the Placebo-group. Thus, the final analysis consisted of 188 patients whose demographic data are in Table 2. The groups were similar, i.e. there were no statistically significant differences between the groups in age, sex, operation time, day-case surgery rate, pre-operative nasal status or additional operations. Five of the 188 septoplasties were revision operations. In the preoperative swab of the nasal vestibulum, the pathogen was *S. aureus* in 66/188 cases.

The operations were performed by 28 different surgeons (19 specialists and 9 residents). In total, 159 operations were done by a specialist and 25 by residents alone. Two operations were done by a specialist assisted by a resident and another 2 operations were performed by a resident under supervision of a specialist. One hundred fifty seven operations (84%) were day-case surgery. The remaining patients stayed one night at the hospital and were discharged the next morning. One hundred seventy two operations were done under local anaesthesia supplemented with intravenous sedation, and 16 septoplasties under general anaesthesia. The mean operation time was 49 minutes (range 12-116 min). Post-operative nasal packing was used in all operations. The packing was removed the next day after the operation in all but 3 cases. Silicone sheeting splints were used in 57/188 (30%) cases and the most common (33/57) duration of their use was 7 days (range 1-8 days). The splints were fixed with one anterior transseptal Ethicon PDS (polydioxanon) suture.

Postoperative infections
Postoperative infections were found in 10/188 (5.3%) cases. Seven of the infection cases were classified as superficial incisional surgical site infection (SSI) and 3 as deep incisional SSI (septal abscess). None of the patients suffered organ/space SSI. The sample for bacterial culture was taken from 8/10 infected patients when the infection was diagnosed. The most common

Table 3. Swab samples from 8 out of 10 infection patients taken when the infection was diagnosed.

1	*S. aureus* ++
2	*S. aureus* +++, *Streptococcus pneumoniae* ++
3	*Propionibacterium acnes* +++, *coagulase-negative S. species* ++, *Haemophilus*-like rods ++
4	Group-G beta-haemolytic *Streptococcus* +++, *E. coli* ++, *Bacteroides fragilis* group +
5	*S. aureus* +++, *Ps. aeruginosa* ++, *Streptococcus viridans* ++
6	*S. aureus* +++
7	*S. aureus* ++, *Moraxella catarrhalis* ++, *Klebsiella oxytoca* ++
8	*S. aureus* +++, coagulase-negative *S. species* +++

Table 4. Patient characteristics and operative data, and the statistical difference between the infectious patients (n = 10/ 188) and the non-infection group (n= 178/ 188). * = data available in 164 cases.

	Number of cases	Cases in infection group (n = 10)	Cases in non-infection (n = 178) group	p
Preoperative data				
Female gender	40	4	36 (20%)	0.14
Crusting in nasal cavity	53	6	47 (31%) *	0.078
Purulent secretion in nasal cavity	8	2	6 (4%) *	0.077
Crusting or purulent secretion	57	7	50 (33%) *	0.021
S. aureus in bacterial culture	69	9	60 (34%)	0.00059
Operative data				
Silicone splints > 24 hours	48	3	45 (25%)	0.75
RFA	48	4	44 (25%)	0.28
Overnight stay	31	3	28 (16%)	0.24
General anaesthesia	16	2	14 (8%)	0.18
Surgeon resident	27	2	25 (14%)	0.64
Operation time, average		63 min	48 min	0.055

pathogen was *S. aureus* found in 6/8 cases. In all of these six cases, *S. aureus* was also isolated from preoperative bacterial sample. The microbiological findings in samples taken from infected patients are shown in Table 3. One septum abscess patient needed treatment at a ward.

Within the first 30 postoperative days, 2 patients had rhinosinusitis treated with antibiotics. Both patients had acute sinusitis symptoms and signs (the other had pus in the middle meatus and the other had sinusitis detected by sinus ultrasound). One patient had peritonsillar abscess treated by tonsillectomy and intravenous antibiotics and 1 patient had crusted mucosa of the nasal septum treated by mupirocin nasal ointment. These 4 cases were not classified as SSI.

Infection risk

Patient characteristics and operative data, and the statistical difference between the infectious and non-infectious patients are shown in Table 4. The preoperative crusting or purulent secretion, or *S. aureus* in the bacterial swab increased the risk of postoperative infection significantly. The operation time in the infectious group tended to be longer, p = 0.055. The use of silicone splints, RFA treatment in combination with septoplasty or overnight stay did not seem to have a significant effect on the incidence of infection.

Effect of the antibiotic prophylaxis

None of the study patients had cephalosporin allergy in their patient history. In the Ab-group, the infection rate was 2.2% (2/92) and in the Placebo-group 8.3% (8/96). The difference between the groups was not statistically significant (p = 0.10). All 3 deep incisional SSI (septal abscess) occurred in the Placebo-group.

Complications

Postoperative bleeding occurred in 5 (2.7%) patients during the first 24 hours, 4 cases in Ab- and 1 in the Placebo-group, and 1 of these patients needed additional nasal packing. On the first postoperative day 1 septal haematoma and 1 serous abscess occurred and these were drained. There were no allergic reactions or other side effects caused by the antibiotics. Late complications occurred in 4 cases (2.1%): 2 septal perforations of a few millimetres in size (1 in the Ab- and 1 in the Placebo-group), 1 mild saddle nose deformity (Placebo-group) and 1 sensory disturbance in the nasal tip region (Placebo-group).

DISCUSSION

The use of antibiotics in septoplasty or nasal surgery in general has been much discussed. Some articles recommend antibiotics while some do not. In a review article by Weber et al. (2002) antibiotic prophylaxis was not recommended [14]. In general and according to Guideline for Prevention of SSI, prophylaxis should be used for all operations or classes of operations in which its use has been shown to reduce SSI-rates based on evidence from clinical trials, and operations after which incisional or organ/space SSI would represent a catastrophe [1].

As far as we know, this study is the first placebo controlled double blind study intended to investigate the effect of one dose of 1500 mg intravenous cefuroxime given 30 minutes prior to septoplasty. The 188 operations included in this study were normal operations at a large university hospital where some 350 septoplasties are done every year. The operations in this study were performed by 28 different surgeons. Thus, the results reflect very well the results in every-day clinical practice.

The number of day case nasal surgery has increased in the past 2 decades. However, there is still large local variation [18]. At our hospital, the number of day case surgery septoplasties and also the number of septoplasties done under local anaesthesia is high. In this study, the number of infections in day case operations and local anaesthesia was lower than in overnight stay- or general anaesthesia cases (4.5% vs. 9.7%, and 4.7% vs. 12.5%) although statistical significance was not reached. Although the septoplasties performed during overnight stay or under general anaesthesia might have been more severe cases, this study suggests that local anaesthesia and day case surgery

may diminish the risk of postoperative nasal infection.

S. aureus is an important bacterial pathogen in both hospital and community. It is a common cause of postoperative infections in elective surgery. To decrease the infection risk for example in cardiac surgery, there are studies going on to develop *S. aureus* – vaccination [19]. This study confirms that *S. aureus* significantly increases the risk of the postoperative infection also in septoplasty. Nine out of the 10 infected patients were carriers of *S. aureus* when the operation was done. In addition, crusts and purulent secretion in the nasal cavity before the operation statistically significantly increased the risk of infection, as did also a long operation time. If prominent crusts or purulent secretion is seen in the nasal cavity one should consider doing the operation at a later date. In 6 out of the 8 cases with a bacterial swab taken during the infection, the pathogen was *S. aureus*. In postoperative infection cases, the choice the antibiotic should be based on the strains in the local environment as there are large differences in the proportion of the resistant bacterial strains in different countries and areas.

The number of infections was nearly 4-fold in the Placebo-group in this study, but the difference was not statistically significant ($p = 0.101$). Probably the size of the study sample was too small to show the statistical significance. Supposing that the proportion of the infections would remain the same in a bigger study group (2/92 and 8/96, respectively) the number of patients in the study should have been 418 to reach statistical significance.

The cefuroxime dose was given during 5-10 minutes starting 30 minutes prior to surgical incision. In a recent prospective study by Weber, the optimal timing for a single-shot cephalosporin was the interval of 59-30 minutes as compared with 120-60 minutes or less than 30 minutes before starting the operation [17]. However, a wide spectrum of operations was presented, and day case surgery patients were excluded. Thus, these results for optimal timing probably cannot be directly applied to septal surgery.

One prophylactic intravenous dose of cefuroxime caused no complications, and neither were there major complications caused by the septoplasty operations. However, this was a study of the postoperative infections and thus the follow-up period was short considering the overall number of complications of septoplasty. The sequela of the nose can be detected at a considerably later date [20]. For example the number of perforations – 2 during the first 3 months – underlines need for a longer follow-up period. According to Bateman and Woolford, the reported number of perforations after septoplasty varies between 1.6-5.4% [21].

Our study is one of the few randomized placebo-controlled antibiotic studies in septum surgery. As we did not reach a statistically significant difference between the two groups, we cannot recommend the prophylactic use of 1 dose of cefuroxime prior to septoplasty in all cases. However, there was a clear tendency in favour for the Ab-group: (2 vs.8 infection cases), and the incidences of infections were 2.2% and 8.3%, respectively. All the 3 deep infections occurred in the Placebo-group. The overall risk of infection was increased: 1) in patients having crusts or purulent secretion seen in the nasal cavities, 2) if the operation was a long one, and 3) in patients who carry *S. aureus* in the nasal cavity. In a recent review article by Georgiou prophylactic antibiotic was recommended for patients who are immunocompromised, suffering from valvular heart disease, or otherwise susceptible to infections [4]. Based on the earlier studies and reviews published and our present study we recommend the use of 1 dose of 1500 mg intravenous cefuroxime prior to septoplasty in patients having crusts or purulent secretion in the nasal cavities or if the operation is expected to be prolonged.

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Markus Lilja, MD, PhD
Department of
Otorhinolaryngology –
Head & Neck Surgery
Helsinki University Central Hospital
P.O.Box 220, FI-00029 HUS
Helsinki
Finland

Tel: +358-50-554 6845
Fax: +358-9-4717 5010
E-mail: markus.lilja@hus.fi