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Abstract

Introduction: The primary aim of this prospective study was to evaluate headache severity before and after surgery in patients with chronic rhinosinusitis without polyps (CRSsNP), chronic rhinosinusitis with polyps (CRSwNP), deviated nasal septum (DNS), and inferior turbinate hypertrophy (ITH). Our secondary aim was to compare the improvement of headache symptoms in these different patient groups.

Methods: We enrolled 154 patients with CRSsNP, 130 patients with CRSwNP, 144 patients with DNS with or without ITH, and 69 patients with only ITH. Problems with headaches were reported on a visual analogue scale (VAS) preoperatively and six months postoperatively.

Results: Patients with CRSsNP reported significantly more headaches on the VAS than the other patient groups. Headsaches improved significantly after surgery (p<0.001) but they improved more in CRSsNP patients than in other patient groups. Postoperatively, there were no significant differences in headache problems between the groups. The CRSsNP group reported 50 (standard deviation [SD] 29) on the VAS preoperatively and 25 (SD 26) postoperatively, the CRSwNP group reported 28 (SD 30) versus 18 (SD 25), the DNS group reported 31 (SD 30) versus 17 (SD 24), and the ITH group reported 31 (SD 32) versus 19 (SD 25). Subgroup analyses identified gender as a factor that has an influence on the headache. Female patients reported a mean VAS score of 49 (SD 31) preoperatively and 28 (SD 28) postoperatively. Male patients reported a mean VAS score of 29 (SD 29) preoperatively and 15 (SD 22) postoperatively.

Conclusion: In this study, we have shown that patients with CRSsNP report more headache-related problems preoperatively than patients diagnosed with CRSwNP, DNS, or ITH. All patient groups exhibit a significant improvement in their headache problems and report milder symptoms postoperatively. Female patients tend to report more headaches than men.

Introduction

Nasal obstruction is defined as a discomfort manifesting in a feeling of insufficient airflow through the nose [1]. A number of conditions can lead to nasal obstruction, such as allergic rhinitis, acute or chronic rhinosinusitis, polyps, adenoid hypertrophy, deviated nasal septum (DNS), inferior turbinate hypertrophy (ITH), nasal trauma, foreign objects, or tumors. Many of these diagnoses also give rise to other symptoms, such as nasal secretion, facial or sinus pain or pressure, headache, reduced sense of smell, snoring, difficulty in sleeping, nasal voice, or sneezing.

Treatment of nasal obstruction depends on the causative etiology. Pharmacologic therapy, especially intranasal glucocorticoids, is used as a first-line treatment for several conditions of mucosal origin, such as chronic rhinosinusitis (CRS), allergic rhinitis, or nasal polyps [2]. Antibiotics, oral steroids, antihistamines, and allergy vaccinations are also useful treatments for some of these conditions. In case of an inadequate response, surgery may be considered. Structural causes of nasal obstruction may not respond well to pharmacological treatment, and surgery may be necessary to obtain symptom relief. A combination of both DNS and ITH leading to nasal obstruction is common. Medical treatment of the turbinate hypertrophy component may provide only partial relief. Similarly, surgical treatment may also only provide partial relief with a pharmacologic treatment of a comorbid allergic rhinitis being necessary to fully relieve the symptoms [3].

In the general population, more than 50% of the adults indicate that they have suffered from headache in the last year [4], and almost 5% (9% of women) suffer from chronic daily headache [5]. The causes of headache can be primary or secondary. A primary headache is a headache that occurs...
independently and is not caused by an underlying condition, e.g., migraine, tension, and cluster headache. A secondary headache is a headache that is present because of another condition. Some examples of secondary headaches are headaches attributed to trauma or injury to the head, substance use or misuse, infection, and homeostatic disorders. Another cause of secondary headaches may be attributed to disorders of the nose and sinuses [6].

In 2012, the European Position Paper on Rhinosinusitis and Nasal Polyps was published. The authors suggest that rhinosinusitis rarely causes headaches, except when there is an acute bacterial infection where the sinus in question cannot drain [7]. The subjective assessment of chronic rhinosinusitis is based on symptoms such as nasal blockage, nasal discharge, facial pain, and loss of smell. Nevertheless, headache is a common complaint among many patients diagnosed with chronic rhinosinusitis [8], and headache has been controversially reported to improve after surgery [9] or to remain stable [10]. Nguyen et al. found that in patients with nasal polyps requiring surgery one-half of the patients reported moderate/severe facial pain/headache before surgery and that surgery improved these symptoms [11].

The European Position Paper on Rhinosinusitis and Nasal Polyps also suggests that other conditions often considered inducing headache are not sufficiently validated as causes of a headache. These include DNS, ITH, atrophy of sinus membranes, and mucosal contact [7]. For instance, one study found no improvement in headaches after septoplasty [12], while other studies describe an association between chronic headache and nasal stenosis [13,14]. A study from 2008 reported that 83% of patients indicated a significant improvement in headache severity after surgery to correct nasal septum abnormalities and the associated reactive mucosal hypertrophy of the inferior turbinate, suggesting a correlation between septum deviation and referred headache [15].

The primary aim of this prospective study was to evaluate problems with headaches before and after surgery in patients with CRS with nasal polyps (CRSwNP), CRS without nasal polyps (CRSsNP), DNS, or ITH. As a secondary aim, we wanted to compare the headache improvement in different patient groups after surgery and evaluate if the following factors have an influence on the headache: allergies, asthma, obstructive sleep apnea syndrome (OSAS), smoking, and gender.

**Materials and Methods**

**Ethics, consent, and permissions**

This prospective study has been conducted during the period from January 2012 to July 2016 and has been approved by the Committee for Medical Research Ethics in Norway (2015-367/REK NORD). All patients signed a written consent prior to inclusion in the trial.

**Study population**

The patients were referred to the Ears, Nose, and Throat (ENT) department at St. Olavs Hospital/Trondheim University hospital by general practitioners, ENT specialists, or from other hospitals in the region. All patients were examined at the outpatient clinic by a variety of surgeons. The definition of chronic rhinosinusitis and nasal polyps [7] in combination with computed tomography (CT) of the sinuses and endoscopy of the nasal cavity were used to diagnose chronic rhinosinusitis and nasal polyps. Patients with nasal blockage due to DNS and ITH were diagnosed using anterior rhinoscopy and endoscopy of the nose. In these cases, supplementary CT was performed when necessary [16]. When surgery was indicated, the patients were asked to participate in the current study. Exclusion criteria were an age less than 18 years and language problems causing difficulties to comprehend the questionnaires.

We included 565 patients with one or more diagnoses. Patients were asked to fill out a self-reporting form preoperatively and six months after surgery. Sixty-eight patients were excluded because they did not return the self-reporting form postoperatively, thus leaving us with a total of 497 patients: 154 patients with CRSsNP, 130 patients with CRSwNP, 144 patients with DNS with or without ITH, and 69 patients with only ITH.

We have chosen to present the patients with DNS with or without ITH as one group called DNS because all patients in this group had a DNS that needed correction and we considered the nasal septoplasty procedure to be the main surgical intervention when combined with a radiofrequency therapy (RFT) for the ITH. These DNS patients were operated in general anesthesia. All patients in the ITH group had a fairly straight nasal septum and, therefore, underwent only RFT under local anesthesia. Both CRS groups underwent sinus surgery in general anesthesia.

**Visual analogue scale**

Headaches were reported on a 100 mm visual analogue scale (VAS) where 0 mm represents no symptoms and 100 mm represents “worst thinkable troublesome”. The score represented how much problems the patients have had with headaches in the last two weeks before reporting. The symptom severity is considered mild from 0 to 30, moderate from 30 to 70, and severe from 70 to 100 [7].

**Statistical analysis**

A power calculation showed that with 296 patients in each group, we could detect a difference of 10 on the VAS (SD 25) with 80% power and a significance level of 0.01 (alpha). To be able to detect a difference of 20 on the VAS with the same assumptions as above, we needed a total of 78 patients.

Descriptive results are presented as the mean with standard deviation (SD) and the median. Our data displayed a slightly skewed distribution checked with histogram and normal Q-Q plot, so we chose to control the results by calculating the median as well as the mean. There were some outliers that we chose to keep in the data set. In the statistical analyses, we used paired sample t-tests to compare mean values pre- and postoperatively and one-way analysis of variance (ANOVA) to compare mean values between groups pre- and postoperatively.
A Bonferroni post hoc test was applied when necessary. We also did regression analyses using a general linear model. All statistical analyses were performed using IBM SPSS statistic 24 (SPSS Inc, Chicago, Illinois, USA). A p-value of less than 0.01 was considered significant.

Results

Demographics

Table 1 shows the baseline demographics of the patient groups. As we see from the table, the gender distribution is not equal in all groups, as there are more female patients in the CRSsNP group and more men in all other groups. Furthermore, the patients in the CRSwNP group seem to be older than those in the other groups.

Headaches on the visual analogue scale before and six months after surgery

We found that prior to surgery patients with CRSsNP had significantly more headache-related problems compared to other patient groups. The headaches, reported on the VAS, improved significantly after surgery for all four groups (Table 2 and Figure 1), but the headaches improved more in CRSsNP patients than in other patients. After surgery, there was no significant difference in headaches between the groups.

Subgroup analyses

As shown in Table 1, all patient groups include patients with other comorbidities, such as allergy, asthma, or OSAS. Some patients are smokers, and there is an unequal gender distribution among the groups. Therefore, we performed subgroup analyses to clarify if these conditions were of importance for the reported headache symptoms given on the VAS.

Allergy

Airborne allergies were presented by 224 patients. We found no statistically significant difference between allergic and non-allergic patients regarding headaches on the VAS before or after surgery. Preoperatively, both the allergic and non-allergic patients had a mean VAS score of 36 (p=0.971; median 30 and 28, respectively). Postoperatively, the average VAS score was 20 (median 7) for the allergic patients and 19 (median 7) for non-allergic patients (p=0.993).

Asthma

There were 114 of the included patients that reported asthma. We compared the mean preoperative and postoperative VAS values of these patients with those of the non-asthmatic patients and found no significant difference. Preoperatively, the patients with asthma had a mean score of 37 (median 33), and the non-asthmatic patients had a mean score of 36 (median 28; p=0.845). Postoperatively, the average VAS score was 22 (median 10) for asthmatic patients and 19 (median 6) for the non-asthmatic patients (p=0.890).

Obstructive sleep apnea syndrome

In the dataset, 31 patients reported that they had moderate to severe OSAS and had received continuous positive airway pressure (CPAP) treatment for their condition. We found no significant difference on the VAS preoperatively and postoperatively while controlling for CPAP treatment (p=0.593 and p=0.657, respectively). The mean VAS values in the OSAS patients were 33 (median 30) preoperatively and 15 (median 6) postoperatively. The equivalent values for the non-OSAS patients were 36 (median 30) and 20 (median 7).

Table 1: Demographic data of the different groups.

|                  | CRSsNP (n=154) | CRSwNP (n=130) | DNS (n=144) | ITH (n=69) | Total (n=497) |
|------------------|----------------|----------------|-------------|------------|---------------|
| Mean age (range) | 43 (18-80)     | 47 (19-84)     | 41 (18-78)  | 38 (18-66) | 43 (18-84)    |
| Female %         | 58.4%          | 30.8%          | 20.8%       | 34.8%      | 37.0%         |
| Allergies        | 64             | 68             | 64          | 28         | 224           |
| Asthma           | 22             | 57             | 23          | 12         | 114           |
| Smoking          | 17             | 15             | 16          | 8          | 56            |
| OSAS             | 3              | 7              | 16          | 5          | 31            |

CRSsNP, Chronic rhinosinusitis without nasal polyps; CRSwNP, Chronic rhinosinusitis with nasal polyps; DNS, Deviated nasal septum; ITH, Inferior turbinate hypertrophy; OSAS, Obstructive sleep apnea syndrome.

Table 2: Headaches on the VAS for the different groups preoperatively and postoperatively.

| Groups        | Mean VAS preoperatively (SD) | Median VAS preoperatively | Mean VAS postoperatively (SD) | Median VAS postoperatively | p-value |
|---------------|-----------------------------|----------------------------|-------------------------------|----------------------------|---------|
| CRSsNP (n=154)| 50 (29)                     | 54                         | 25 (26)                       | 14                         | <0.0005 |
| CRSwNP (n=130)| 28 (30)                     | 17                         | 18 (25)                       | 4                          | <0.0005 |
| DNS (n=144)   | 31 (30)                     | 21                         | 17 (24)                       | 5                          | <0.0005 |
| ITH (n=69)    | 31 (32)                     | 17                         | 19 (25)                       | 5                          | <0.0005 |

CRSsNP, Chronic rhinosinusitis without nasal polyps; CRSwNP, Chronic rhinosinusitis with nasal polyps; DNS, Deviated nasal septum; ITH, Inferior turbinate hypertrophy; SD, Standard deviation; VAS, Visual analogue scale.

Figure 1: Boxplot of headaches on the VAS for the different groups before and after surgery. The box indicates the 25th and the 75th percentile. The dark line in the boxes is the median, and the T-bars extend to 1.5 times the height of the box or to the minimum or maximum values. The points above them are the outliers.
Smoking

Preoperatively, 56 patients reported that they were daily smokers. The other patients reported either that they smoked occasionally (39 patients), that they had never smoked (241 patients), or that they had quit smoking (154 patients). The smokers had a mean preoperative VAS of 46 (median 49), while the other patients had a VAS of 35 (median 27). Regression analyses showed that smokers had a 10 mm higher VAS score preoperatively than non-smokers (p=0.019). Postoperatively there was with a p-value of 0.232 no difference. After surgery, smokers had a VAS of 24 (median 15), and non-smokers had a VAS of 19 (median 7).

Gender

There were 313 male and 184 female patients. Preoperatively, the female patients reported a mean VAS of 49 (SD 31, median 51). The male patients reported a mean VAS of 29 (SD 29, median 17). Postoperatively, the female patients reported a mean VAS of 28 (SD 28, median 19), and the male patients reported a mean VAS of 15 (SD 22, median 4; Figure 2). The difference between the genders was highly significant (p<0.005) both pre- and postoperatively.

The four diagnosis groups were also analyzed separately according to gender. We found that females reported significantly more headaches than men preoperatively in all groups except those with CRSsNP. In this group, male and female patients reported equal headache symptoms preoperatively. Postoperatively we only found a significant difference between genders in the CRSwNP group (Table 3, Figure 3).

Discussion

In this study, we found that patients with CRSsNP reported a higher headache score preoperatively than the other patient groups. The other three patient groups described approximately the same level of headache problems preoperatively. Surgery seems to reduce headache symptoms in all patient groups. All four groups reported a statistically significant reduction in headaches postoperatively. The patients with CRSsNP had the largest improvement. After surgery, all groups reported milder symptoms on the VAS.

We found that patients with CRSsNP reported more headaches than patients with CRSwNP. This is supported by findings from other studies [17,18]. Even though the role of infection in CRS is unclear [19], a possible explanation for the difference in headaches in these CRS groups may be an increased susceptibility for infection and inflammation of the sinonasal mucosa in CRSsNP patients compared to CRSwNP patients [17]. Fahy and Jones found that patients with CRSwNP rarely have facial pain except if it is concurrent with purulent secretion and infection [20]. Pain is one of the cardinal signs of inflammation, and some patients may misinterpret this pain as a headache.

Other reasons for headaches in patients with CRS can be a misdiagnosed primary headache or the fact that patients with CRS also have additional problems with primary headaches. These patients cannot expect the same results on headache after surgery as patients without primary headaches. Studies have found that migraines often affect the nose and paranasal sinus areas and can be misinterpreted by the patients to be symptoms caused by rhinosinusitis [21,22]. A multispecialty consensus group found indications that a majority of individuals who believe, either because of self-diagnosis or a physician’s diagnosis, that they suffer from sinus headaches actually have headaches that fulfill the criteria for a migraine according to the International Headache Society (IHS) criteria [23]. A Norwegian study found that the 1-year prevalence of migraine was 12% (16% in women and 8% in men) in the general population [24]. Another type of headaches the patients may interpret as sinus headaches is a version of tension-type headaches called midfacial segment pain. The pain these patients experience is described as a feeling of pressure, and some patients might feel that their nose is blocked when they have no nasal airway obstruction. Midfacial segment pain is symmetric, and it might involve areas of the nasion (the root of the nose), under the bridge of the nose, on either side of the nose, the peri- or retro-orbital regions, or across the cheeks [25]. Because of the similarity of the symptoms in these conditions, it is most important that CRS is diagnosed based on a combination of symptoms and the findings of an endoscopy or a CT of the sinuses. We had some outliers in our data postoperatively (Figure 1), and these outliers may represent patients with primary headaches. There were 29 outliers in our data, which means that at least 5.8% of our patients had significantly more headaches than expected after surgery. This could represent patients with primary headache problems that did not respond to the surgical treatment of their condition.

Even though studies have shown that sinusitis is very rarely the cause of a headache, we found in our study that patients gained some relief from headache problems after surgery. It is important to keep in mind that the patients in our study did not qualify for surgery based on their headache level; they underwent surgery because of CRS symptoms or...
nasal blockage caused by DNS or ITH. Regardless of the fact that our patients experienced fewer problems with headaches after surgery, indicating that headache symptoms can be reduced by improving the nasal blockage and alleviating the symptoms of CRS. An explanation for this improvement could be a less severe infection and inflammation in CRS patients, or an improved sleep and a more relaxed breathing after surgery in patients with DNS [26] and ITH.

The demographic data show that some of the patients who undergo surgery are daily smokers, and some have coexisting diseases such as allergy, asthma, or OSAS. Subgroup analyses showed that patients with allergies, asthma, or OSAS did not report more headaches on the VAS preoperatively or postoperatively than patients without these conditions. Daily smokers, on the other hand, reported more headaches on the VAS preoperatively than non-smokers but reached the same level of improvement as the other patients after surgery. Nevertheless, other studies have shown that smokers have a higher prevalence of headaches compared with non-smokers [27–29].

Furthermore, we found that gender is of great importance for the headache severity. In our study, women diagnosed with CRSwNP, DNS, or ITH had more headaches preoperatively than men. In the patients diagnosed with CRSsNP, there were no differences between male and female subjects preoperatively.

Postoperatively there was no statistically significant difference between the genders except for patients diagnosed with CRSwNP, where women still had more headaches than men. Even though the other groups showed no statistical difference between the genders postoperatively, we see a tendency to more headaches among female patients also after surgery. The fact that women have more headaches than men is well established [24], especially in patients with migraines [30]. Sex hormones have been shown to be of great importance when trying to explain the difference in headache severity between the genders [30,31]. An explanation for the lack of difference between the genders in the CRSsNP group preoperatively could be that the etiology behind this condition is of greater importance to headaches than gender.

Some could argue that we did not have a control group and, thus, do not know how healthy people report a headache on the VAS. We compared the results from our patients that reported headache scores between 17 and 25 on the VAS postoperatively with headache scores documented by healthy controls in other studies. We found that healthy people present an average headache score between 16 and 20 on the VAS [32,33], indicating that our patients reached after surgery the same headache level as healthy people.

The study had certain limitations, one being that we only had one postoperative time point, which was after six months. A further limitation was that we did not attempt to distinguish between different types of headache; we only looked at how the patients evaluated their problems with headaches the last two weeks before they reported on the VAS. We did not use disease-specific questionnaires to identify primary headache diagnoses, and our questionnaire did not ask about current headaches, chronic daily headaches, or the headache frequency which is important when diagnosing primary headaches.

The major strengths of this study are the prospective study design and the fact that the data show results from an everyday clinical setting. Additional strengths are the number of patients included in the present study and the comparison of four different patient groups. There were only 12% of the patients that failed to appear for the six-month follow-up and, thus, had to be excluded from the analysis, leaving a relatively high number of patients for the analysis.
Conclusions

In this study, we have shown that patients with CRSsNP report more headache-related problems preoperatively than patients diagnosed with CRSwNP, DNS, and ITH. All patient groups exhibited a significant improvement in their headache after surgery, and there were no significant differences in headache complaints between the groups postoperatively. All patient groups reported mild symptoms after surgery, but female patients tended to report more headaches than men.

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Data availability statement

The data on which the findings of this study are based are included in the Supplementary Materials.

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