

# Preemptive analgesia for endoscopic sinus surgery: a retrospective study\*

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## Abstract

**Background:** Chronic rhinosinusitis (CRS) is a common disease, and endoscopic sinus surgery (ESS) is widely performed. However, there is no consensus regarding postoperative pain control after ESS, and postoperative opioid abuse is a problem in many countries. Acetaminophen is reportedly effective for postoperative pain control. Preemptive analgesia has received more attention lately, wherein pain is prevented before it occurs. In this study, we assessed the use of acetaminophen for preemptive analgesia during the perioperative period in ESS.

**Methodology:** This is a retrospective study of 175 patients who underwent ESS, septoplasty, and bilateral inferior turbinate mucosal resection at our hospital from April 2016 to February 2018. In total, 82 patients received 1,000 mg of acetaminophen during surgery and 4 hours after the first dose, while 93 patients did not receive it routinely. We compared these two groups. The primary outcome was the need to use additional analgesics prescribed by the ward physician and the secondary outcomes included postoperative pain, postoperative bleeding, reoperation, blood pressure, and body temperature.

**Results:** The use of additional oral and intravenous analgesics was significantly reduced in the patients who received acetaminophen perioperatively.

**Conclusion:** Preemptive analgesia during the perioperative period of ESS could lead to satisfactory postoperative pain control.

**Key words:** ESS, preemptive analgesia, postoperative analgesia, acetaminophen, postoperative pain

## Introduction

Chronic rhinosinusitis (CRS) is a common inflammatory condition of the nasal cavity and paranasal sinuses<sup>(1)</sup>. Endoscopic sinus surgery (ESS) is widely performed for CRS resistant to conservative treatment.

Previous studies indicated that pain levels after ESS surgery should be low, with minimal analgesic use<sup>(2)</sup>. However, it is similarly reported that patients who underwent common ear, nose, and throat (ENT) operations delayed their return to work because of postoperative pain<sup>(3)</sup>. In reality, it is not uncommon for patients to complain of pain after ESS.

Poorly controlled postoperative pain in adult patients leads to cardiopulmonary complications, prolonged hospital stay, and subsequent development of chronic pain<sup>(4)</sup>. Research regarding

the use of opioids in post sinus surgery indicated that opioids are overprescribed for operations that are not particularly painful, resulting in potential narcotic abuse and misuse<sup>(5)</sup>. Moreover, additional prescription of pain medication could also become a burden on health care providers.

Therefore, it is important to focus on preventing postoperative pain in ESS. The postoperative scheduled use of non-selective or selective NSAIDs, cyclooxygenase (COX) 2 inhibitors, and acetaminophen (oral or intravenous) in laparoscopic cholecystectomy has been shown to improve postoperative analgesia and reduce the consumption of systemic opioids and their dose-dependent adverse effects<sup>(6)</sup>. In the field of rhinology, it has been reported that intravenous acetaminophen after ESS provided adequate pain relief in most patients who have undergone ESS<sup>(7)</sup>.

Although there are several reports about ESS postoperative pain control, there is still no standardisation due to the small number of subjects involved in many of these studies.

Recently, more attention has been paid to preemptive analgesia, wherein pain is prevented before it occurs. Preemptive analgesia is an anti-nociceptive treatment that prevents the establishment of altered processing of afferent inputs that amplify postoperative pain<sup>(7)</sup>. However, the effectiveness of analgesics in the perioperative period of ESS to achieve preemptive analgesia is unclear. To prove the importance of preemptive analgesia in ESS, we assessed the effect of regularly prescribed analgesics during the perioperative period on the requirement of additional analgesics and the achievement of adequate postoperative pain control.

## Materials and methods

This study was approved by the ethics committee of our institution and the requirement for informed consent was waived since this was a retrospective cohort study. This is a retrospective study of 175 adult patients (older than 20 years of age) who all underwent bilateral ESS, septoplasty, and bilateral inferior turbinate mucosal resection in our hospital, from April 2016 to February 2018. Exclusion criteria included cases of aspirin-exacerbated respiratory disease (AERD), hepatic disease, unilateral ESS, and those wherein submucosal nasal turbinate resection or septoplasty alone was performed.

One hundred and seventy-five (N=175) patients were divided to two groups. Since the regular use of acetaminophen during ESS surgery was started in our hospital in February 2017, patients that underwent surgery before and after that time were classified into group 1 and group 2, respectively. We chose acetaminophen because it was easy to use in the field of anesthesiology and had a few side effects. There were 82 patients in group 1 and 93 patients in group 2. Patients in group 1 received 1,000 mg of acetaminophen twice: during surgery and 4 hours after the first dose. The interval between the doses was 4 hours. Patients in group 2 did not receive acetaminophen in the perioperative period. The primary outcome measured was the need for additional analgesics (oral or intravenous), and secondary outcomes were postoperative pain (pain when leaving the operating room), postoperative bleeding, reoperation, blood pressure, and body temperature after the surgery. We collected data on additional analgesic administration, postoperative bleeding, and reoperation (during the first two days after surgery) from the patients' medical records. Additional analgesics were administered by the ward physician in response to the patient complaint of pain. Other parameters, such as pain, blood pressure, and body temperature when leaving the operating room, were retrieved from the anesthesiology charts. The status of postoperative pain was assessed by the anesthesiologist and classified as "painful" or "painless." The temperature

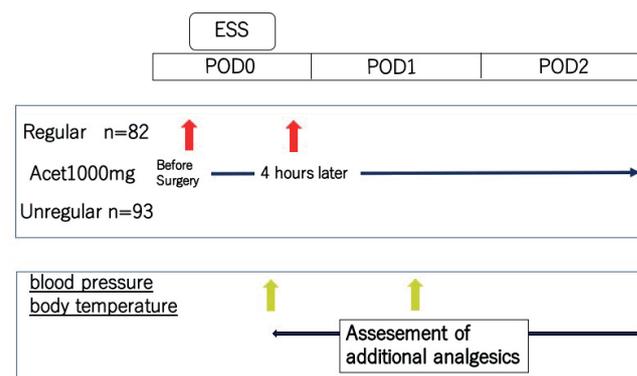


Figure 1. Postoperative management protocol for ESS. Patients in group 1 received 1,000 mg of acetaminophen twice: during surgery and 4 hours after the first dose. Group 2 patients did not receive acetaminophen in the perioperative period.

and blood pressure were recorded approximately one hour after the surgery and one day after surgery (Figure 1). The anesthesiologist used 100 µg of fentanyl during induction of anesthesia, and remifentanyl was administered continuously at 0.1-0.2 µg/kg/min to reduce intubation stimulation.

## Statistical analysis

Patient characteristics and variables were analysed using the Statistical Package for Social Sciences version 24 (IBM Corp; Armonk, NY, USA). The differences in analgesic administration (oral or intravenous) and postoperative pain, postoperative bleeding, and reoperation were analysed using a t-test. The differences in blood pressure and body temperature were analysed using the Pearson  $\chi^2$  test. We considered the difference to be statistically significant if the two-sided P-value was less than 0.05. Data are expressed as number of cases or mean with the standard deviation.

## Results

Table 1 shows the baseline characteristics of the patients. There were no significant differences in sex, age, height, body weight, history of diabetes or asthma, smoking history, and blood pressure (before or after surgery) between the two groups (Table 1). Additional oral analgesics were needed in 19 of 82 patients (23.1%) in group 1 and in 43 of 93 patients (46.2%) in group 2 ( $p=0.001$ ). Additional intravenous analgesics were administered in 15 of 82 patients (18.3%) in group 1 and 32 of 93 patients (34.4%) in group 2 ( $p=0.016$ ). The use of additional analgesics was significantly reduced in group 1.

Postoperative pain was significantly reduced in group 1 ( $p=0.028$ ). Similarly, body temperature on postoperative day one (POD1) was significantly lower ( $p=0.031$ ) in group 1 than in group 2. No significant difference was observed in postoperative bleeding, reoperation, blood pressure, and body temperature (postoperative). There were no serious adverse events including

Table 1. Baseline characteristics of the patients.

Variable	Group 1 n=82	Group 2 n=93	P Value
Sex			
male	54	72	0.089
female	28	21	
Age (year)	47.7±12.7	45.1±11.8	0.607
Diabetes	5	2	0.189
Asthma	12	12	0.740
Smoking	35	41	0.852
Height (cm)	168.9±7.77	169.5±9.0	0.638
Body weight (kg)	65.3±9.81	67.7±13.5	0.180
Blood pressure (preoperative)	115.6±17.4	116.3±14.8	0.780
Body temperature (preoperative)	36.3±0.3	36.4±0.4	0.392

Table 2. Primary and secondary outcomes of study participants.

Variable	Group 1 n=82	Group 2 n=93	P Value
Additional analgesics			
oral	19 (23.1%)	43 (46.2%)	0.001*
intravenous	15 (18.3%)	32 (34.4%)	0.016*
Postoperative pain	9 (10.9%)	22 (23.6%)	0.028*
Postoperative bleeding	2	0	0.132
Reoperation	1	0	0.288
Blood pressure (±SD)			
Postoperative†	124.3±13.2	125.0±16.6	0.766
POD1‡	118.9±14.7	131.7±13.46	0.404
Body temperature (±SD)			
Postoperative†	36.6±0.4	36.6±0.4	0.442
POD1‡	36.9±0.5	37.1±0.5	0.031*

\*P < 0.05. †Postoperative pain= pain approximately one hour after the surgery. ‡POD: Postoperative day. SD= Standard deviation.

liver damage related to the intervention (Table 2).

## Discussion

In this study, our results showed that routine perioperative administration of acetaminophen significantly reduced postoperative pain and the need for additional oral and intravenous analgesics. In addition, suppression of body temperature (POD1) was observed. Supposedly, the preemptive analgesia reduced the postoperative requirement of additional analgesics, which will improve the patient's quality of life and may lighten the burden on medical staff by reducing the prescription of analgesics. It has been previously proposed that prescribing scheduled acetaminophen could effectively control postoperative pain after ESS without the need for opioid analgesics(9). However, in this study, regular administration of the drug was started postoperatively rather than perioperatively. Postoperative pain was evaluated by the use of additional analgesics rather than the patient. The route and timing of administration were different; however, we believe that the present study also suggests the benefits of acetaminophen use at regular intervals in the perioperative period.

A survey of 1,770 members of the American Rhinologic Society (ARS) showed that most healthcare providers were prescribing opioids<sup>(10)</sup>. In another study, a total of 64 patients had a mean ± SD narcotic use of 7.7 ± 7.6 tablets during the first 7 days after surgery<sup>(11)</sup>. Therefore, opioids are presently being overprescribed for ESS, especially in the United States (US), and abuse and misuse are becoming a problem. Supposedly, perioperative administration of acetaminophen could help solve this challenge. Preemptive analgesia was proposed by Wall in 1988<sup>(12)</sup>. It was described how C-fiber afferent volleys from deep tissues trigger prolonged changes in cord excitability. Once this is established, large doses of narcotics will have to be administered to suppress

central hyperexcitability. However, if a small amount of narcotics is administered before the successive triggers occur, central hyperexcitability would not have occurred initially. Briefly, the possibility that preemptive preoperative analgesia will prolong the drug effects was mentioned. In 1996, Kissin advocated a theory about preemptive analgesia<sup>(13)</sup>, suggesting that analgesia is more effective before invasive stimulation than after, and the pain control in the perioperative period suppresses postoperative pain. This is consistent with our study results that perioperative administration was more effective in controlling pain after ESS.

Patients with AERD were excluded from this study because careful drug selection is necessary for these patients. AERD is a clinical tetrad of nasal polyps, chronic hypertrophic eosinophilic sinusitis, asthma, and sensitivity to medications that inhibit cyclooxygenase-1 (COX-1) enzymes<sup>(14)</sup>. Additionally, acetaminophen is considered to have a COX-inhibitory effect; hence, it should be used carefully in these patients. 34% of patients with aspirin-intolerant asthma in the US who received a single 1,000-1,500 mg dose of acetaminophen showed decreased lung function<sup>(15)</sup>. Therefore, COX-2 inhibitors, such as celecoxib and pentazocine, are recommended for these patients. Similarly, the American Academy of Otolaryngology–Head & Neck Surgery (AAO-HNS) clinical practice guideline (CPG) priorities multimodal, nonopioid analgesia as first-line therapy and recommends that opioids be reserved for severe or refractory pain<sup>(16)</sup>. Anesthesiologists and pain specialists can play a significant role in this effort.

Our study had several limitations. First, the evaluation of postoperative pain was probably inaccurate because subjective evaluation was not performed. For example, in a previous study, postoperative pain was assessed using an 11-point-numeric rating scale<sup>(9)</sup>. Second, analgesics may have been prescribed for

pain that was not ESS-related. Finally, our study did not consider other analgesics administered during surgery by the anesthesiologists. Thus, drug selection should also be performed in collaboration with the anesthesiologist for accurate evaluation.

## Conclusion

We conclude that acetaminophen administration during the perioperative period of ESS resulted in better postoperative pain control. Preemptive analgesia was achieved, leading to a smoother postoperative recovery for the patient and easing the workload of the concerned medical staff. Nevertheless, further

research is needed to standardise pain management after ESS surgery.

## Authorship contribution

DN, EM: concept of study, collection of data, analysis of results, write up of manuscript, critical review of all contents; TT, YH, SH and KO: concept of study; HK, NO: critical review of all contents.

## Conflict of interest

None of the authors declares any conflict of interest.

## References

1. Fokkens WJ, Lund VJ, Mullol J, et al. European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. *Rhinology* 2012; 50: 1-12.
2. Wise SK, Wise JC, DelGaudio JM. Evaluation of postoperative pain after sinonasal surgery. *Am J Rhinol* 2005; 19: 471-477.
3. Chidambaram A, Nigam A, Cardozo AA. Anticipated absence from work ('sick leave') following routine ENT surgery: are we giving the correct advice? A postal questionnaire survey. *Clin Otolaryngol Allied Sci* 2001; 26: 104-108.
4. Gabriel RA, Swisher MW, Sztain JF, et al. State of the art opioid-sparing strategies for postoperative pain in adult surgical patients. *Expert Opin Pharmacother* 2019; 20: 949-961.
5. Karkos PD, Constantinidis J. Are opioids necessary in post sinus surgery care? *Curr Opin Otolaryngol Head Neck Surg*. 2021; 29:27-30.
6. Taniguchi H, Takenouchi M, Imaura M, et al. Postoperative scheduled intravenous acetaminophen in patients undergoing laparoscopic cholecystectomy in Japan. *M J Anes* 2018; 1: 009.
7. Kemppainen T, Kokki H, Tuomilehto H, et al. Acetaminophen is highly effective in pain treatment after endoscopic sinus surgery. *Laryngoscope* 2006; 116: 2125-2128.
8. Kissin I. Preemptive analgesia. *Anesthesiology* 2000; 93:1138-1143.
9. Kemppainen TP, Tuomilehto H, Kokki H, et al. Pain treatment and recovery after endoscopic sinus surgery. *Laryngoscope* 2007;117:1434-1438.
10. Gray ML, Fan CJ, Kappauf C, et al. Postoperative pain management after sinus surgery: a survey of the American Rhinologic Society. *Int Forum Allergy Rhinol*. 2018; 8: 1199-1203.
11. Ndon S, Spock T, Torabi SJ, et al. Patterns in pain and opiate use after endoscopic sinus surgery. *Otolaryngol Head Neck Surg* 2020; 162: 969-978
12. Wall PD. The prevention of postoperative pain. *Pain* 1988; 33: 289-290.
13. Kissin I. Preemptive analgesia: why its effect is not always obvious. *Anesthesiology*. 1996; 84: 1015-1019.
14. Lee RU, Stevenson DD. Aspirin-exacerbated respiratory disease: evaluation and management. *Allergy Asthma Immunol Res* 2011; 3(1): 3-10.
15. Settignano RA, Schrank PJ, Simon RA, Mathison DA, Christiansen SC, Stevenson DD. Prevalence of cross-sensitivity with acetaminophen in aspirin-sensitive asthmatic subjects. *J Allergy Clin Immunol* 1995; 96(4): 480-485.
16. Cramer JD, Barnett ML, Anne S, et al. Nonopioid, multimodal analgesia as first-line therapy after otolaryngology operations: Primer on nonsteroidal anti-inflammatory drugs (NSAIDs). *Otolaryngol Head Neck Surg*. 2020.

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