The Laryngoscope

Pain Management Following Otological Surgery: A Prospective Study of Different Strategies

Valerie Dahm, MD; Justin T. Lui, MD; Joseph M. Chen, MD; Alex Kiss, PhD; Amr F. Hamour, MD; Trung N. Le, MD, PhD; Vincent Y. Lin, MD, FRCSC

Objectives: The aim of this study was to prospectively assess pain and associated analgesic consumption after otological surgery comparing two prescription patterns.

Study Design: A prospective nonrandomized consecutive cohort study.

Methods: 125 adult patients undergoing ambulatory otologic surgery-cochlear implantation and endaural middle ear surgery, were assigned (according to surgeon's preference) and prospectively studied in two arms: 1) acetaminophen 500 mg + ibuprofen 400 mg; 2) acetaminophen 500 mg + codeine 30 mg. Pain levels, medication dose, disposal patterns of opioids, and suspected side effects were evaluated.

Results: All patients reported mild to moderate pain. There was a statistically significant reduction of pain from day to day, which was on average 0.26 lower than the day before. Sufficient pain control could be achieved with both drug regimens with no significant difference in pain levels. Only 50% of patients who were prescribed opioids used them. Additionally, the median tablet intake was 3 tablets while 10 to 20 tablets were prescribed. The majority of patients (97%) did not dispose of these drugs safely.

Conclusion: Adequate analgesia was achieved in both arms of this study. Pain control following otologic surgery with a combination of acetaminophen and nonsteroidal anti-inflammatory drugs is recommended unless contraindications or chronic opioid use are present. If opioids such as codeine (30 mg) are prescribed, the amount should be reduced as low as possible, such as five tablets, based on our studied population.

Key Words: Pain, nonopioids, opioids, pain control, otologic surgery.

Level of Evidence: 3

***Laryngoscope*, 132:204–211, 2022**

INTRODUCTION

The opioid crisis has been a major scourge with both healthcare and social challenges over the past 25 years. Several previous studies have shown that opioids are often prescribed in excess for acute postoperative pain.[1–4] Boyd et al and Qian et al. showed that approximately 1/3 to 2/3 of prescribed opioids are used after otologic surgery.[4,5]

Over prescription leads to a facilitated availability for improper use without medical control.[1–3,6] This fact is underlined by the "2010 National Survey on Drug Use and Health" stating that 71% of prescription drugs used nonmedically are obtained from friends and relatives- 55% for free, 11% with payment, and about 5% stolen.[7,8] A number of obstacles remain to effectively change prescribing habits and patient acceptance; there is a lack of evidence on postoperative pain control with nonopioid medications to allay the fear of undertreating pain. Prescribing patterns vary substantially between different countries, raising the suspicion that pain after otologic surgery can be controlled without opioids.[9] Setting clinical practice guidelines for postoperative pain management will require a larger pool of data from our specialty.

The aim of this study was to prospectively assess pain and associated analgesic consumption after otologic surgery comparing two arms: acetaminophen/ibuprofen and acetaminophen/codeine. Disposal patterns of prescribed opioids and suspected side effects were evaluated.

MATERIAL AND METHODS

The study was conducted in compliance with the Sunnybrook Institutional Research Ethics Board (REB# 3335). Informed written consent was given by each patient before participating.

125 adult patients were included in this prospective study. These patients underwent either cochlear implantation (CI) or endaural surgery at a single institution by one of three surgeons (J.C., T.L., and V.L.). Five patients were lost to follow-up. One patient did not feel comfortable to continue with the study and dropped out. Details on all 119 included patients are summarized in Table I. All patients were consecutively enrolled over a 6-month period between October 2020 and March 2021, details are shown in the flow diagram. Inclusion criteria were

From the Department of Otolaryngology—Head and Neck Surgery, Sunnybrook Health Sciences Centre (V.D., J.T.L., J.M.C., A.F.H., T.N.L., V.Y.L.), University of Toronto, Toronto, Ontario, Canada; Department of Research Design and Biostatistics, Sunnybrook Research Institute (A.K.), University of Toronto, Toronto, Ontario, Canada.

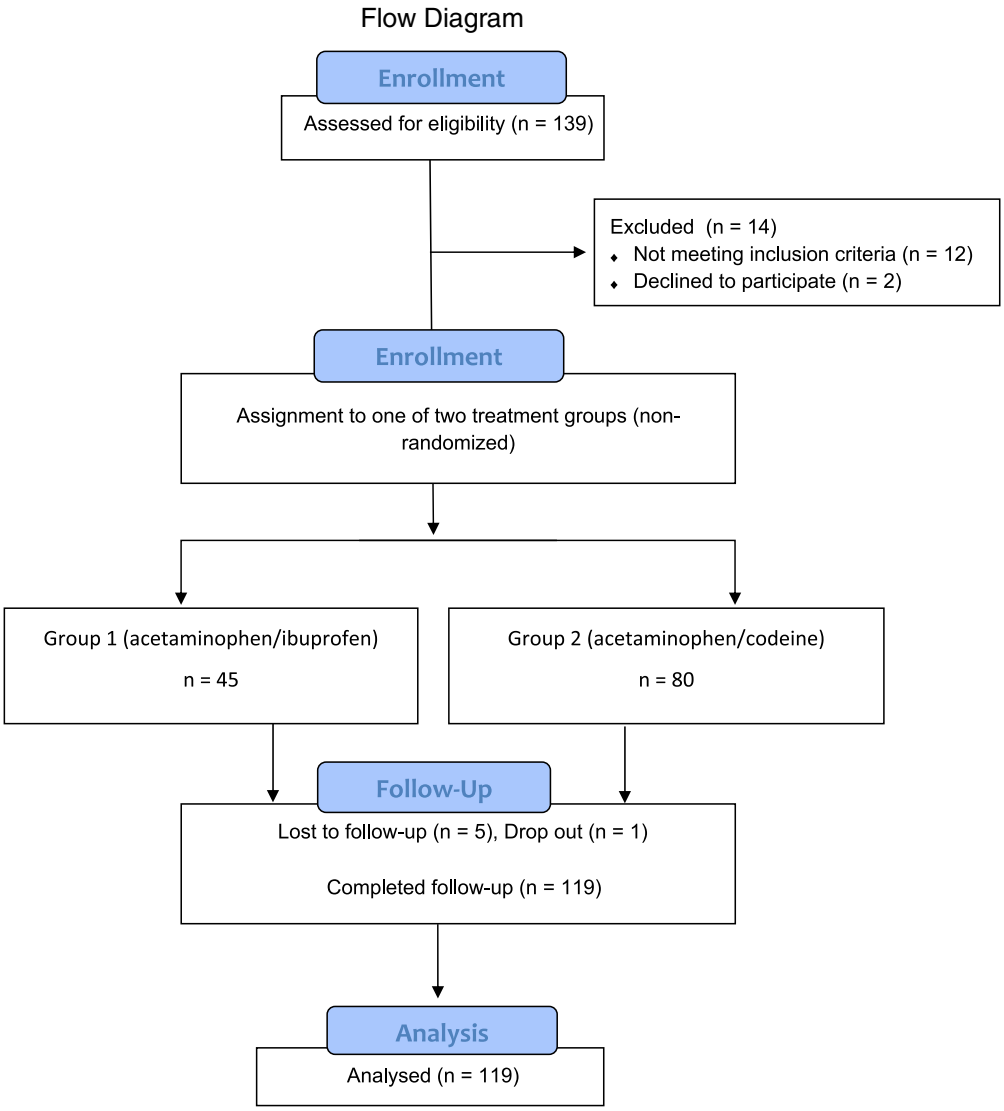
Editor's Note: This Manuscript was accepted for publication on August 20, 2021.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

Meeting: Part of the results of this study were presented at CI2021.

Send correspondence to Vincent Y. Lin, MD, FRCSC, Department of Otolaryngology—Head and Neck Surgery, Sunnybrook Health Sciences Centre, University of Toronto, 2075 Bayview Ave, Toronto, Ontario M4N 3M5, Canada. E-mail: vincent.lin@sunnybrook.ca

DOI: 10.1002/lary.29845



[Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

patients older than 18 years, undergoing endaural surgery (stapedotomy or tympanoplasty with tragal cartilage harvest only) or CI, and willingness to participate in the study. Exclusion criteria were patients using opioids daily, or those lacking English proficiency to answer questionnaires.

At enrollment, patients were asked if they were ever treated for substance abuse. Additionally, they were asked to rate their pain on a numeric rating scale (NRS) between 0 and 10. These scales are validated tools used to assess postoperative pain scores.[10] The NRS we provided to patients included the following explanation: 0 = *pain free*, 1 = *very mild*, 2 = *discomforting*, 3 = *tolerable*, 4 = *distressing*, 5 = *very distressing*, 6 = *intense*, 7 = *very intense*, 8 = *utterly horrible*, 9 = *excruciating/unbearable*, 10 = *unimaginable/unspeakable*. Further, the NRS included a graphical summary of four main levels of pain: 0—no pain, pain intensity between 1 to 3 was summarized as mild pain, 4 to 6 as moderate pain, and 7 to 10 as severe pain. Patients with a pain level above 0 indicating chronic or acute pain before surgery were also included in the study.

Pain Medication

Patients were not randomized to treatment groups. The two main treatment regimens represent the surgeon's preferences: 1) acetaminophen 500 mg (q4h—quaque quarta hora—every 4 hours) + ibuprofen 400 mg (q4h); 2) acetaminophen 500 mg (q4h) + codeine 30 mg (q6h). Patients were told to take pain medication as needed. About 30 mg of codeine was chosen as it is the equivalent dose of Tylenol #3, a commonly prescribed combination of acetaminophen and codeine. Patients were instructed to use acetaminophen as first-line oral therapy, while reserving ibuprofen or codeine for breakthrough pain. In the second arm, about half of the patients were prescribed 10 tablets of codeine and the other half 20 tablets of codeine as per surgeon's preference.

In the second arm, in those patients who underwent a CI, 5 ml of bupivacaine 0.25% was injected along the postauricular incision at the end of surgery by one of the two surgeons in that group. This application of local anesthetic at the end of surgery represents the surgeon's preference. Patients' profiles are depicted in Table I.

TABLE I.
Patient Demographics According to Oral Analgesics Prescription.

		Acetaminophen/Ibuprofen		Acetaminophen/Codeine		Total	
Number of patients		42		77		119	
Endaural	CI	18	31	32	45	50	69
Female	Male	21	21	38	39	59	60
Left	Right	19	23	37	40	56	63
Median Age in years		56.5 yr (IQR 46.8–67.3)		56.0 yr (IQR 44.0–70.5)		56.0 yr (IQR 45.0–69.0)	
Median BMI kg/m^2		26.7 kg/m^2 (IQR 22.8–29.9)		26.4 kg/m^2 (IQR 23.1–29.1)		26.6 kg/m^2 (IQR 23.0–29.4)	
Percentage (number) of patients with chronic disorders or relevant daily medication							
Hx of pain		21% (n = 9)		23% (n = 18)		23% (n = 27)	
Pain medication		14% (n = 6)		9% (n = 7)		11% (n = 13)	
Pregabalin		2% (n = 1)		4% (n = 3)		3% (n = 4)	
ASA		10% (n = 4)		14% (n = 11)		13% (n = 15)	
Depression		12% (n = 5)		7% (n = 5)		8% (n = 10)	
Pain level > 0		7% (n = 3)		5% (n = 4)		6% (n = 7)	
History of substance abuse		0% (n = 0)		0% (n = 0)		0% (n = 0)	
Tobacco (current smokers)		7% (n = 3)		8% (n = 6)		8% (n = 9)	
Alcohol (at least 1×/week)		43% (n = 18)		48% (n = 37)		46% (n = 55)	
Illicit drugs		2% (n = 1)		5% (n = 4)		4% (n = 5)	

Hx (history) of pain includes all patients stating that they had a pain disorder such as arthritis, musculoskeletal pain, or migraines. Pain medication includes patients who take regular pain medication due to one of the mentioned diagnoses. Pain level > 0 implies the presence of pain preoperatively as reflected by a subjective numerical rating above 0.
ASA = acetylsalicylic acid.

Diary and Questionnaires

Patients were instructed to make daily entries in their survey documents for a minimum of 7 days or as long as they had pain. In their diary, they recorded maximum daily pain level (as measured on a NRS from 0 to 10), and the number of tablets taken of each analgesic medication. At follow-up (Day 10–15), patients were asked to fill out a final questionnaire. Patients were queried about nonincisional pain, and the need to take additional pain medication. In Arm 2, patients reported how many codeine tablets remained.

Chronic Disorders and Relevant Daily Medication

Musculoskeletal pain, arthritis, and migraine were summarized in history of pain. Both diagnoses (history of pain and depression) were chosen (ticked off on a questionnaire) by included patients and did not necessarily mean that daily treatment for these diagnoses was received. Consequently, medications such as regular pain medication and antidepressants are shown in separate rows in Table I. Pain medication summarizes regular acetaminophen, cox-2 inhibitor, cox-inhibitors, other weak opioids, pregabalin, or acetylsalicylic acid (ASA).

Surgery

Technical variations among the three surgeons were minimal. Cochlear implantation was carried out in a standard fashion with a postauricular incision, mastoidectomy, posterior tympanotomy, and round window

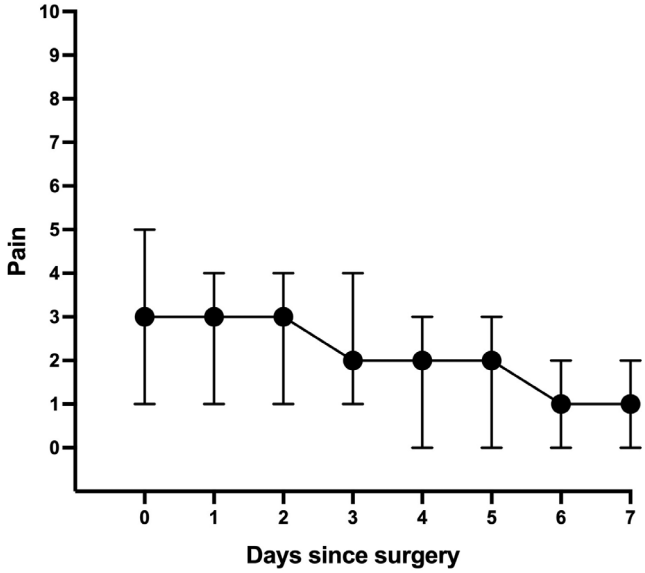


Fig. 1. Median pain levels over the first week of surgery on a numeric rating scale 0 to 10. Error bars denote interquartile range.

electrode insertion. The receiver stimulator and the magnet were placed under a musculoperiosteal flap. The skin incision was closed with sutures and staples.

Middle ear surgeries were performed via an endaural approach through a small incisural incision; self-retaining retractors were used for exposure. Surgical procedures were limited to stapedotomies or tympanoplasties. For tympanoplasties, tragal cartilage and perichondrium were harvested for reconstruction. Limited drilling was

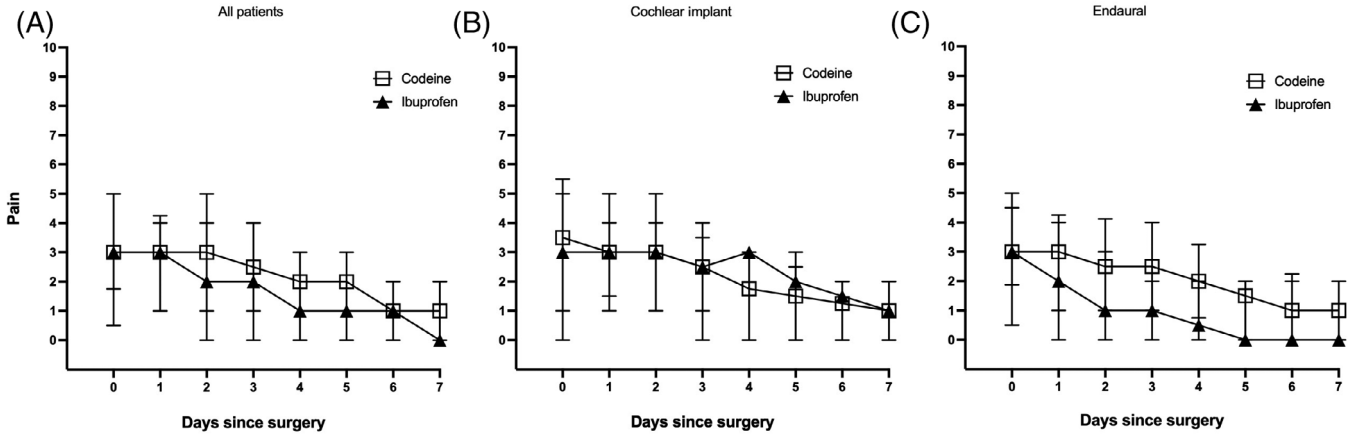


Fig. 2. Pain levels Arm 1 versus Arm 2. Median pain levels of all patients (A), cochlear implantation (B), or endaural surgery (C) over the first week of surgery on a numeric rating scale 0 to 10. Error bars denote interquartile range.

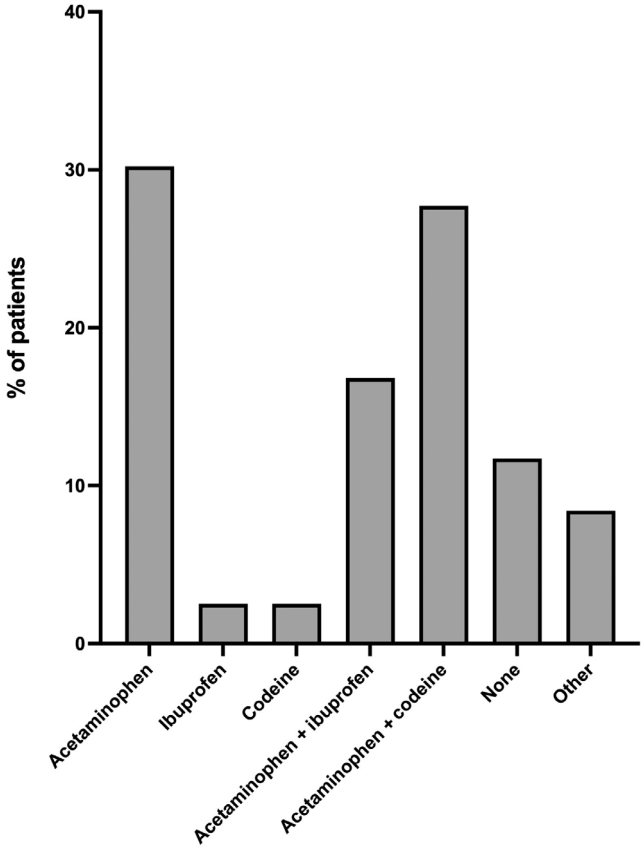


Fig. 3. Percentage of patients taking specific drugs/drug combinations for pain control. Patients were added to the Acetaminophen = Ibuprofen group if they, for example, took daily acetaminophen and one single ibuprofen tablet as well as if both medications were taken regularly.

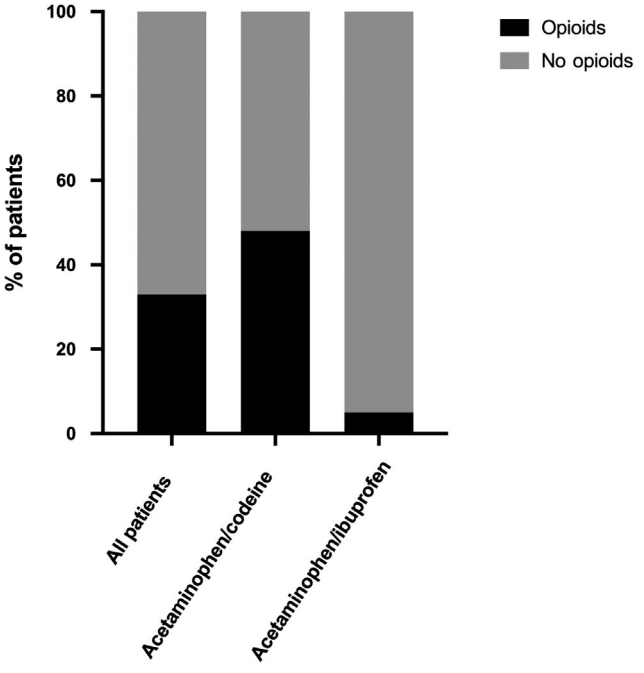


Fig. 4. Percentage of patients taking opioids and nonopioid pain medications of all patients and according to prescription group.

performed for access to the middle ear. Endaural and tragal incisions were closed with absorbable sutures.

Statistical Analysis

Results are detailed as medians with interquartile range (IQR) or mean with standard deviation (SD), where appropriate. A linear mixed model was used to evaluate the slope of pain scores of the first 7 days after surgery (day 0—day of surgery up to postoperative day 7). To calculate the difference of pain scores between the two surgeries, an average pain score over the first 7 days was used and a two-sided t-test was carried out. T-test was used to calculate difference of pain score on day of surgery, and on day 1 after surgery comparing those that received local anesthesia and those that did not. A two-sided t-test was also used to compare patients who drink alcohol to those that do not, body mass index (BMI) > 30 kg/m^2 and ≤ 30 kg/m^2, as well as difference in pain between females and males.

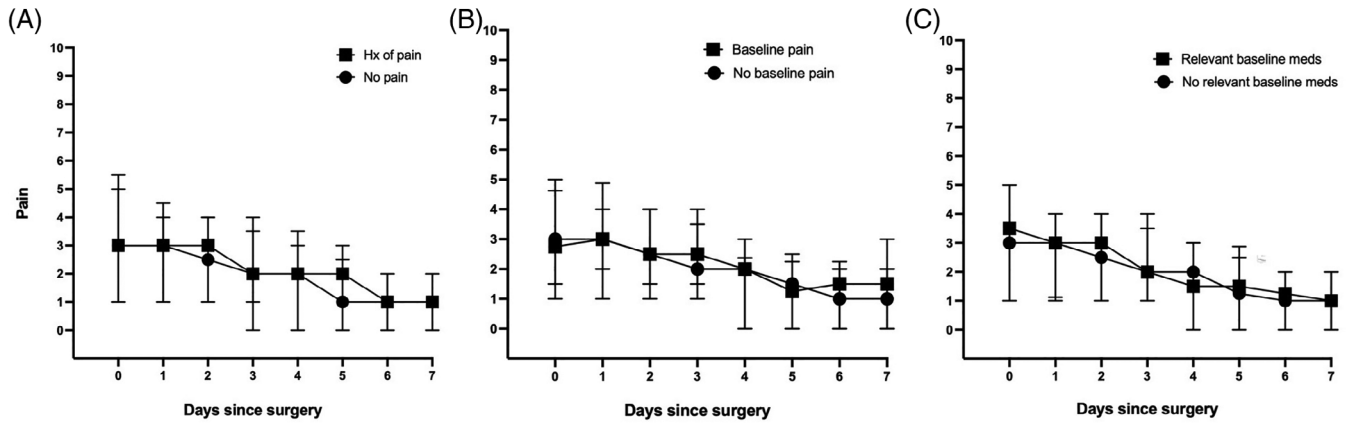


Fig. 5. Comparison of pain levels over the first week of surgery on a numeric rating scale 0 to 10. Error bars denote interquartile range. (A) Median pain levels of patients with and without history of pain disorders (migraine, arthritis, musculoskeletal pain); (B) Median pain levels of patients with and without baseline pain. (C) Median pain levels of patients who were on regular relevant medications (acetaminophen, ibuprofen, pregabalin, ASA)

RESULTS

119 patients were included, of which 50 underwent endaural surgery and 69 underwent CI. Forty-two patients were prescribed acetaminophen and ibuprofen while 77 were prescribed acetaminophen and codeine for postoperative pain control. Median pain duration for all patients was 7 days (IQR 3–9 days).

Median pain levels of all patients over the first week after surgery are shown in Figure 1.

There was a statistically significant reduction of pain from day to day, which was on average 0.26 lower than the day before ($P < .0001$). There was no statistically significant difference between patients undergoing CI and endaural surgery ($P = .23$). Further there was no statistically significant difference of pain levels comparing Arm 1 to Arm 2 ($P = .21$) as seen in Figure 2. Arm 1 and Arm 2 were consequently subdivided in patients undergoing endaural surgery and cochlear implantation. Similarly, there was no difference in pain levels when averaging pain over the first week after surgery (endaural surgery, $P = .22$; cochlear implantation, $P = .62$). Thirty percentage of all patients used only acetaminophen for postoperative analgesia. Twenty-eight percentage took both acetaminophen and codeine. Seventeen percentage used acetaminophen and ibuprofen and 12% did not take or need any pain medication following surgery. Details are depicted in Figure 3. In total, 77 patients (65%) were prescribed opioids (codeine) but only 39 (51%) of these patients used it. Of those who were prescribed non-opioids exclusively, 5% ended up requiring opioids (details are presented down below). Figure 4 shows percentage of all patients and of each group who consumed opioids as postoperative pain therapy.

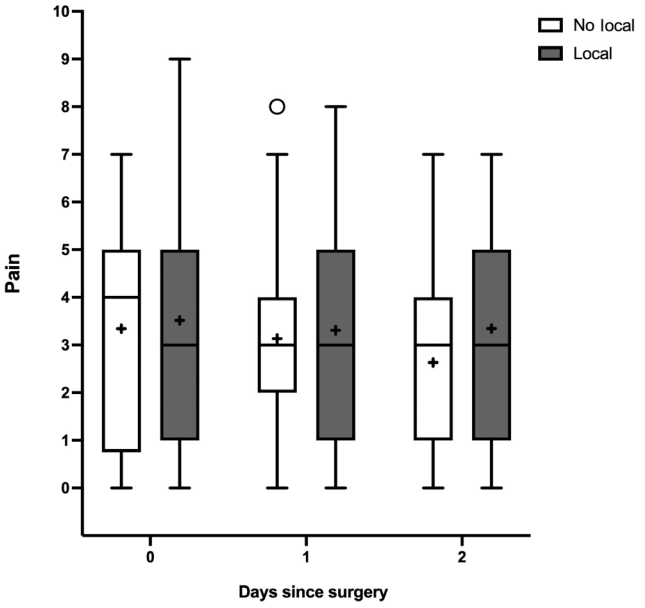


Fig. 6. Difference of pain levels of patients undergoing cochlear implantation with and without long-lasting local anesthetics. Median pain level on the day of surgery and on postoperative day 1 and 2 divided into patients who did receive local bupivicaine at the end surgery and patients who did not. The horizontal line indicates the median, and the x indicates the mean. The boundaries of the box represent the lower and upper quartiles. The whiskers are drawn from the edge of the box to the largest and smallest values that are outside the box but within 1.5 standard deviations. Circles depict outliers.

Pain Levels of Different Patient Groups

There was no difference between pain levels of patients who had a history of a pain disorder (n = 27) such as migraines, arthritis, or any other musculoskeletal pain and those who did not have a pain disorder (n = 92). The same is true for patients who had no baseline pain (n = 112) compared to those who did report to have pain before surgery (n = 7). Lastly, there was no difference between patients on pain medication or other relevant medications (n = 32) such as ASA or pregabalin and patients who did not take any relevant other medication (n = 87). These results are depicted in Figure 5. There was no statistically significant difference between the pain scores of patients who drank alcohol and those that did not drink alcohol ($P = .55$), as well as between patients with a BMI above 30 kg/m^2

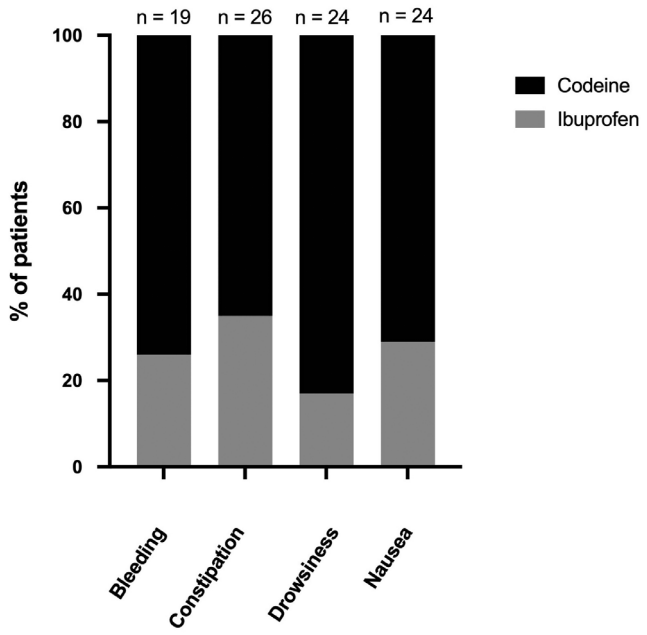


Fig. 7. Reported side effects. Percentage of patients in Arm 1—Ibuprofen and Arm 2—Codeine.

and those with a BMI ≤30 kg/m^2 ($P = .31$). There was no statistically significant difference of pain levels between men and women ($P = .59$).

Local Anesthesia

Sixty-nine patients underwent CI, of which 30 received long-acting local anesthetic (bupivacaine) at the end of surgery. Thirty-nine patients did not receive local anesthesia. Difference in pain levels of these two groups on the day of surgery ($P = .76$) and postoperative day one ($P = .78$) are depicted in Figure 6. Additionally, there was no difference of drug usage in the first 24 hours following surgery. Mean drug usage (tablets) is as follows: acetaminophen 1.7 (with): 1.6 (without); Codeine 0.6(with): 0.7 (without). Two of the 30 patients had a temporary facial paresis at the end of surgery due to the bupivacaine injection, which fully resolved by the next day.

Medication Use and Excess Opioids

Ninety-five patients took a median of 11 tablets of acetaminophen (IQR 5–18 tablets). Twenty-seven patients took a median of 7.5 tablets of ibuprofen (IQR 4.25–16 tablets) and 37 patients took a median of 3 codeine tablets (IQR 3–7 tablets). Forty patients were prescribed 10 tablets of codeine, while 36 were prescribed 20 tablets. Mean consumed tablets were 2.43 (± 3.37 SD, range 0–10) in the 10-tablet prescription group, while mean consumed tablets was 2.44 (± 4.23 SD, range 0–16) in the 20-tablet prescription group.

In total, nine patients added pain medication or substituted the prescribed analgesics with other analgesics. Three patients added oxycodone, of which two had oxycodone at home from a prior prescription. Four patients took ibuprofen although they had been prescribed acetaminophen and codeine. One patient decided to use tramadol and celecoxib, which was the patient's usual pain medication for chronic musculoskeletal pain. Another patient took naproxen instead of the prescribed medication. One single patient went to the emergency department, mainly due to dizziness after stapedotomy and was prescribed oxycodone.

In total, 67 patients were left with 855 tablets of excess codeine, translating to nearly 13 tablets per patient. Almost all patients (96%) kept the medication at home. Three patients utilized their pharmacies to dispose of remaining codeine while one patient discarded excess codeine in the garbage.

Other Symptoms and Complaints

Patients were asked if they had any other complaints since the surgery that prompted them to take pain medication. In total, 29 patients complained about headaches, of which 70% had undergone CI and 30% endaural surgery. No other sites of pain were reported.

Nineteen patients reported some bleeding from the wound, 26% of which were in the ibuprofen group, despite only half actually taking ibuprofen. Twenty-six patients complained of constipation, 24 of drowsiness, and 24 of nausea; primarily in the codeine group (65%, 83% and 71%, respectively). These results are depicted in Figure 7. None of the patients reported epigastric discomfort. Further, there was no incident of renal failure during the study period.

DISCUSSION

In this study, we compared pain levels after CI (via postauricular approach) to endaural surgery and pain levels with nonopioid and opioid medications. All included patients had low to moderate pain levels with the maximum pain on the day of surgery and a continuous reduction from day to day over the first week. Further, sufficient pain control was achieved with both prescribed pain regimens (acetaminophen + ibuprofen and acetaminophen + codeine). None of the patients had to see their family physician or visit an emergency department to supplement their pain medication. In a previous study on hospital revisit and complication rates after otologic surgery, only 5% of 16,709 patients needed an unexpected revisit, of which less than 10% were linked to pain.[11] No severe side effects were encountered during the herein presented study period. Constipation, drowsiness, and nausea were associated with codeine use. Only half of the codeine prescriptions were filled while the remaining prescriptions resulted in an excess of 855 tablets. This consumption rate was similar to other investigations.[1] Median codeine tablet use was 3 with an IQR of 3 to 7 tablets, despite being prescribed 10 or 20 tablets, which is similar to previous studies.[2] However, patients who were prescribed more codeine did not take more codeine tablets. Excess codeine was not disposed of safely by the large majority of patients.

Results of the study show that sufficient pain control can be achieved with nonopioid analgesics (i.e. acetaminophen and

ibuprofen). A previous review concluded that combination analgesia after otologic surgery is preferred, as this regimen is noninferior in alleviating postoperative pain when compared to acetaminophen and tramadol.[12,13]

For patients undergoing otologic surgery, in particular, endaural surgery or CI, the use of postoperative opioid prescriptions should be limited. In our study, there was no significant difference between pain levels following endaural surgery compared to cochlear implantation. (i.e. postauricular incision). Qian et al. showed that patients undergoing a postauricular incision were prescribed, but also used significantly more opioids for a longer time than patients undergoing transcanal procedures.[5] Opioids may be necessary in patients with contraindications to nonsteroidal anti-inflammatory drugs (NSAIDs) or those taking daily opioid medications due to chronic pain. Mavrommatis et al. conducted a retrospective study and concluded that the main difference between patients needing opioids and those not needing them was chronic pain conditions.[14] The two main reasons for surgeons not wanting to prescribe NSAIDs is the fear of kidney damage and postoperative bleeding.[15] A Cochrane review analyzing 23 trials concluded that in patients with normal preoperative renal function, NSAIDs should not be withheld because of concerns about postoperative renal impairment.[16] Multiple studies have shown that NSAIDs are not associated with increased postoperative bleeding.[17–19] An additional reason for not prescribing NSAIDs might be fear of gastrointestinal side effects, such as heart burn or ulcers. Ibuprofen has been shown to have a lower risk of gastrointestinal (GI) side effects compared to diclofenac for example.[20] Further, studies have shown that many GI concerns can be avoided with the addition of proton pump inhibitors.[21]

Commonly seen as a less harmful analgesic option given its categorization as "weak" opioid according to the WHO grading system, codeine may have unpredictable outcomes on patients.[22] Some patients are CYP2D6 poor metabolizers and some are rapid or ultrarapid metabolizers.[23] Although the first group does not benefit from this medication, the latter have a substantially increased risk of toxicities, especially in young users.[23]

Codeine is mainly prescribed in premixed combinations with ibuprofen or acetaminophen; patients are often unaware that such a premixed combination contains an opioid which may be the basis of misuse, overuse, and toxicities.[24] Studies have shown that codeine is associated with dependence and overdose-related mortality.[24] Misuse of premixed combinations can further lead to an overdose of the nonopioid drug and lead to severe toxicities.[24] The onus is clearly on the prescribing physicians to limit the use of codeine for postoperative pain, while avoiding premixed combinations to improve awareness.

Limitations of the presented study include the nonrandomized preference allocation and the small sample size. The lack of inclusion of intra- and perioperative analgesic and steroid therapy prior to discharge could have had a material effect on pain management in the first 24 hours postoperatively. A further important limitation is the inclusion of two different surgical procedures. This adds a confounding factor into the study results as well as the inclusion of the use of long-lasting local anesthetics at the end of 43% of the cochlear implantations. Recall bias and the subjectivity of pain grading via a numerical scale are inherent limitations in a qualitative study. Additionally, patients were not queried on any supplements, which might have been used for pain therapy such as cannabidiol or herbal supplements. Lastly, although NRSs have been validated as measurement tool for postoperative pain,[10] there is an inherent bias. Studies have shown that patients tend to be influenced by pain peaks and last experienced pain.[25] Further there is a neglect for the duration of pain.[25] Consequently, to evaluate accurate pain experiences patients would probably have to report pain scores on an hourly or even more frequent basis.

CONCLUSION

Postoperative pain following routine otologic surgery can be effectively managed with combination of acetaminophen and NSAID for most surgical candidates. When opioids, such as codeine are prescribed, the amount should be limited.

BIBLIOGRAPHY

1. Dang S, Duffy A, Li JC, et al. Postoperative opioid-prescribing practices in otolaryngology: a multiphasic study. *Laryngoscope* 2020;130:659–665. https://doi.org/10.1002/lary.28101.
2. Justicz N, Gadkaree SK, Yamasaki A, Lindsay RW. Defining typical acetaminophen and narcotic usage in the postoperative rhinoplasty patient. *Laryngoscope* 2021;131:48–53. https://doi.org/10.1002/lary.28531.
3. Ngombu S, Hooks A, Rock AN, et al. Comparison of opioid prescription patterns and consumption following Otologic surgery. *Otol Neurotol* 2020;41:229–234. https://doi.org/10.1097/MAO.0000000000002490.
4. Boyd C, Shew M, Penn J, et al. Postoperative opioid use and pain management following otologic and neurotologic surgery. *Ann Otol Rhinol Laryngol* 2020;129:175–180. https://doi.org/10.1177/0003489419883296.
5. Qian ZJ, Alyono JC, Woods OD, Ali N, Blevins NH. A prospective evaluation of postoperative opioid use in otologic surgery. *Otol Neurotol* 2019;40:1194–1198. https://doi.org/10.1097/MAO.0000000000002364.
6. Hill MV, Stucke RS, Billmeier SE, Kelly JL, Barth RJ Jr. Guideline for discharge opioid prescriptions after inpatient general surgical procedures. *J Am Coll Surg* 2018;226:996–1003. https://doi.org/10.1016/j.jamcollsurg.2017.10.012.
7. Manchikanti L, Helm S II, Fellows B, et al. Opioid epidemic in the United States. *Pain Physician* 2012;15:ES9–ES38.
8. Substance Abuse and Mental Health Services Administration. Results from the 2010 National Survey on Drug Use and Health: summary of national findings. NSDUH series H-41, HHS publication no. (SMA) 11-4658. Substance Abuse and Mental Health Services Administration, Rockville, MD, 2011.
9. Dahm V, Lui JT, Liepins R, et al. Is otologic surgery contributing to the opioid epidemic? *J Otolaryngol Head Neck Surg* 2021;50:38. https://doi.org/10.1186/s40463-021-00521-1.
10. Hjermstad MJ, Fayers PM, Haugen DF, et al. Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: a systematic literature review. *J Pain Symptom Manage* 2011;41:1073–1093. https://doi.org/10.1016/j.jpainsymman.2010.08.016.
11. Heilbronn C, Lin H, Bhattacharyya N. Adult ambulatory otologic surgery: unplanned revisits and complications. *Laryngoscope* 2020;130:1788–1791. https://doi.org/10.1002/lary.28346.
12. Walrave Y, Maschi C, Bailleux S, et al. Pain after tonsillectomy: effectiveness of current guidelines? *Eur Arch Otorhinolaryngol* 2018;275:281–286. https://doi.org/10.1007/s00405-017-4788-0.
13. Campbell HT, Yuhan BT, Smith B, et al. Perioperative analgesia for patients undergoing otologic surgery: an evidence-based review. *Laryngoscope* 2020;130:190–199. https://doi.org/10.1002/lary.27872.
14. Mavrommatis MA, Fan CJ, Villavisanis DF, et al. Opioids are infrequently required following ambulatory otologic surgery. *Otol Neurotol* 2021. https://doi.org/10.1097/MAO.0000000000003264.
15. Nguyen BN, Barta RJ, Stewart CE, Heinrich CA. Toradol following breast surgery: is there an increased risk of hematoma? *Plast Reconstr Surg* 2018;141:814e–817e. https://doi.org/10.1097/PRS.0000000000004361.
16. Lee A, Cooper MG, Craig JC, Knight JF, Keneally JP. Effects of nonsteroidal anti-inflammatory drugs on postoperative renal function in adults with normal renal function. *Cochrane Database Syst Rev* 2007;2:CD002765. https://doi.org/10.1002/14651858.CD002765.pub3.

17. Gobble RM, Hoang HLT, Kachniarz B, Orgill DP. Ketorolac does not increase perioperative bleeding: a meta-analysis of randomized controlled trials. *Plast Reconstr Surg* 2014;133:741–755. https://doi.org/10.1097/01.prs.0000438459.60474.b5.
18. Strom BL, Berlin JA, Kinman JL, et al. Parenteral ketorolac and risk of gastrointestinal and operative site bleeding. A postmarketing surveillance study. *JAMA* 1996;275:376–382.
19. Wick EC, Grant MC, Wu CL. Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques: a review. *JAMA Surg* 2017;152:691–697. https://doi.org/10.1001/jamasurg.2017.0898.
20. Hernandez-Diaz S, Rodriguez LA. Association between nonsteroidal anti-inflammatory drugs and upper gastrointestinal tract bleeding/perforation: an overview of epidemiologic studies published in the 1990s. *Arch Intern Med* 2000;160:2093–2099. https://doi.org/10.1001/archinte.160.14.2093.
21. Lazzaroni M, Porro GB. Management of NSAID-induced gastrointestinal toxicity: focus on proton pump inhibitors. *Drugs* 2009;69:51–69. https://doi.org/10.2165/00003495-200969010-00004.
22. World Health Organization. *Cancer Pain Relief: With a Guide to Opioid Availability*. 2nd ed. Geneva, Switzerland: World Health Organization; 1996. http://apps.who.int/iris/bitstream/10665/37896/1/9241544821.pdf. Accessed April 28, 2021.
23. Owusu Obeng A, Hamadeh I, Smith M. Review of opioid pharmacogenetics and considerations for pain management. *Pharmacotherapy* 2017;37:1105–1121. https://doi.org/10.1002/phar.1986.
24. Frei MY, Nielsen S, Dobbin MD, Tobin CL. Serious morbidity associated with misuse of over-the-counter codeine-ibuprofen analgesics: a series of 27 cases. *Med J Aust* 2010;193:294–296. https://doi.org/10.5694/j.1326-5377.2010.tb03911.x.
25. Redelmeier DA, Kahneman D. Patients' memories of painful medical treatments: real-time and retrospective evaluations of two minimally invasive procedures. *Pain* 1996;66:3–8. https://doi.org/10.1016/0304-3959(96)02994-6.