DMR DIGESTIVE MEDICINE RESEARCH
A JOURNAL FOCUSING ON BASIC AND CLINICAL RESEARCH ON DIGESTIVE MEDICINE

Peer Review File

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Comment 1: Page 1, lines 15-18: this part describes epidemiology of tonsillectomy and could be removed since is out of the scope of the paper. The introduction must focus on post tonsillectomy pain and its effect on quality of life.

Reply 1: We have removed this part which describes epidemiology of tonsillectomy out of the paper and access to some other documents. We added some words concerning post tonsillectomy pain and its effect on the quality of life.

Comment 2: Page 1, lines 29-33: the following sentences require references: “Clinically, the commonly used drugs for post-tonsillectomy analgesia include analgesics, non-steroidal anti-inflammatories (NSAIDs), local anesthetics, and hormones. However, NSAIDs may cause postoperative bleeding, opioids can induce respiratory depression and drug dependence, and local anesthetics are associated with life-threatening adverse events.”

Reply 2: We added some references.
11. Elinder K, Soderman AC, Stalfors J, et al. Factors influencing morbidity after paediatric tonsillectomy: a study of 18,712 patients in the National Tonsil Surgery Register in Sweden. Eur Arch Otorhinolaryngol. 2016;273(8):2249-56.
12. Ericsson E, Brattwall M, Lundeberg S. Swedish guidelines for the treatment of pain in tonsil surgery in pediatric patients up to 18 years. Int J Pediatr Otorhinolaryngol. 2015;79(4):443-50.

Comment 3: Page 1, lines 35-40: the following sentences require references: “no definite guideline on post-tonsillectomy analgesia has been available in China and many other countries. As the concept of Enhanced Recovery After Surgery (ERAS) has been widely recognized, perioperative pain management is expected to be conducted throughout patient care. Many studies have urged the adoption of multimodal analgesia to reduce the side effects of a single analgesic drug and improve the efficacy. Ultrasound-guided glossopharyngeal nerve (GPN) block provides a feasible approach for the perioperative analgesia in patients undergoing tonsillectomy.”

Reply 3: We added some references.
4.Inanoglu K, Akkurt BCO, Turhanoglu S, et al. Intravenous ketamine and local

bupivacaine infiltration are effective as part of a multimodal regime for reducing post-tonsillectomy pain. Med Sci Monitor. 2009;15(10):Cr539-Cr43.
13. Liu Q, Zhong Q, Tang G, et al. Ultrasound-guided glossopharyngeal nerve block via the styloid process for glossopharyngeal neuralgia: a retrospective study. J Pain Res. 2019;12:2503-10.

Comment 4: 1- Page 2, lines 47-51: the sentences require references: "Therefore, the current drug treatments for post-tonsillectomy pain mainly include steroids, NSAIDs, centrally acting non-opioid analgesics, opioids, α-2 receptor agonists, and pregabalin. These drugs have their unique characteristics and side effects, and no research has identified a single drug or a combination of multiple drugs that have definite advantages over the other options". Reference 7 could be used.

Reply 4: We added some references

15. Kim DH, Jang K, Lee S, et al. Update review of pain control methods of tonsil surgery. Auris Nasus Larynx. 2020;47(1):42-7.
16. Sadhasivam S, Myer CM, 3rd. Preventing opioid-related deaths in children undergoing surgery. Pain Med. 2012;13(7):982-3; author reply 4.

Comment 5: Page 2, lines 53-58: the sentences require references: "Inflammatory mediators (e.g. bradykinin and serotonin) around local tissues are released with the progression of inflammation. These substances have been shown to directly activate peripheral nociceptors, whereas inflammatory mediators such as prostaglandins can increase the sensitivity of peripheral nociceptors. Steroids are used to prevent postoperative nausea and vomiting (PONV) and pain. A meta-study has shown that steroids can reduce the frequency of postoperative nausea by 50%."

Reply 5: We added some references as advised.

17. Naja Z, Kanawati S, Al Khatib R, et al. The effect of IV dexamethasone versus local anesthetic infiltration technique in postoperative nausea and vomiting after tonsillectomy in children: A randomized double-blind clinical trial. Int J Pediatr Otorhinolaryngol. 2017;92:21-6.

Comment 6: Page 2, line 63: it is preferable not to include paracetamol with nonsteroidal anti-inflammatory drugs (NSAIDs) since paracetamol (acetaminophen) could be considered an atypical NSAID due to its weak inhibitory actions for both COX-1 and COX-2 [Miranda HF, Puig MM, Prieto JC, Pinardi G. Synergism between paracetamol and nonsteroidal anti-inflammatory drugs in experimental acute pain. Pain 2006;121:22-88.]

Reply 6: We have read the reference carefully and removed paracetamol out of the NSAIDS as advised.

Comment 7: Page 2, lines 61-66: the sentences require references: “NSAIDs are widely used in clinical practice and can be divided into 2 categories: non-selective NSAIDs and COX-2-selective inhibitors. Non-selective NSAIDs are traditional NSAIDs that include ibuprofen, diclofenac sodium, meloxicam, and paracetamol, which have inhibitory effects on both COX-1 and COX-2 in a non-selective manner; in contrast, the COX-2-selective inhibitors (e.g. celecoxib and parecoxib) are highly selective, which dramatically decreases gastrointestinal toxicities when alleviating inflammation and pain.”

Reply 7: We added three references.
12. Ericsson E, Brattwall M, Lundeberg S. Swedish guidelines for the treatment of pain in tonsil surgery in pediatric patients up to 18 years. Int J Pediatr Otorhinolaryngol. 2015;79(4):443-50.
19. Kuritzky L, Samraj GP. Nonsteroidal anti-inflammatory drugs in the treatment of low back pain. J Pain Res. 2012;5:579-90.
20. Eccleston C, Cooper TE, Fisher E, et al. Non-steroidal anti-inflammatory drugs (NSAIDs) for chronic non-cancer pain in children and adolescents. Cochrane Database Syst Rev. 2017;8:CD012537.

Comment 8: Page 2, lines 70-74: the sentences require references: “Tramadol is a typical centrally acting non-opioid analgesic with a variety of mechanisms of action including weak to negligible opioid effects. Its effect is equivalent when orally or intramuscularly administered. Its analgesic effect is weaker than that of morphine and roughly half of that of codeine. It has no adverse effects such as respiratory depression or constipation. Long-term use of tramadol can also lead to drug dependence.”

Reply 8: We added one reference.
21. Bravo L, Mico JA, Berrocoso E. Discovery and development of tramadol for the treatment of pain. Expert Opin Drug Discov. 2017;12(12):1281-91.

Comment 9: Page 2, line 74: Wang et al is not mentioned in the references list

Reply 9: We rechecked the references and corrected the mistakes. We replace wang with the correct name of the author, Schnabel A, and add the reference.
22. Schnabel A, Reichl SU, Meyer-Friessem C, et al. Tramadol for postoperative pain

treatment in children. Cochrane Database Syst Rev. 2015(3):CD009574.

Comment 10: Page 2, line 77: the sentence citing Sadhasivam et al needs to end with reference [11]

Reply 10: We have found the reference.
16. Sadhasivam S, Myer CM, 3rd. Preventing opioid-related deaths in children undergoing surgery. Pain Med. 2012;13(7):982-3; author reply 4.

Comment 11: Page 3, lines 99-102: the sentences require references: "As analgesics, they have been used for more than 40 years. They can simulate normal sleep without inducing respiratory depression. Also, they can lower the doses of other analgesics. The typical α2 agonists are dexmedetomidine and clonidine, of which clonidine is usually studied as an adjuvant for local anesthetics."

Reply 11: We added two references.
25. Schmidt AP, Valinetti EA, Bandeira D, et al. Effects of preanesthetic administration of midazolam, clonidine, or dexmedetomidine on postoperative pain and anxiety in children. Paediatr Anaesth. 2007;17(7):667-74.
26. Moss JR, Cofer S, Hersey S, et al. Comparison of clonidine, local anesthetics, and placebo for pain reduction in pediatric tonsillectomy. Arch Otolaryngol Head Neck Surg. 2011;137(6):591-7.

Comment 12: Page 4, line 137: Sotaro et al is not mentioned in the references list

Reply 12: We added the reference in the references list.
39. Funasaka S, Kodera K. Intraoral nerve block for glossopharyngeal neuralgia. Arch Otorhinolaryngol. 1997;215(3-4):311-5

Comment 13: Page 4, line 155: Azman et al is not mentioned in the references list

Reply 13: We added the reference in the references list.
37. Azman J, Stopar Pintaric T, Cvetko E, et al. Ultrasound-Guided Glossopharyngeal Nerve Block: A Cadaver and a Volunteer Sonoanatomy Study. Reg Anesth Pain Med. 2017;42(2):252-8.

Comment 14: The style must follow the journal's requirement. Names of journals should be abbreviated as used in Pubmed

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Reply 14: We used EndNote to manage all the references and changed the style into Vancouver.

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