Recent advances in post-tonsillectomy analgesia

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Abstract: Although tonsillectomy is a common and relatively safe procedure, postoperative pain after tonsillectomy is so severe that it impairs perioperative recovery disorder. Acute pain can also cause physical discomfort, anxiety, and even behaviour problems, and high-quality acute pain management can promote functional recovery and improve long-term functional outcomes. Despite recent efforts, it is still very difficult to provide sufficient analgesia for most patients due to the special operation site and the limitation of the existing analgesia program. Postoperative pain after tonsillectomy has two components: constant pain and swallow-evoked pain. Surgical intervention in the site of the tonsils might affect local muscles directly or indirectly through circulus tonsillaris nervous plexus. Although numerous drug comparison studies are being performed in this field, its postoperative analgesia programs remain controversial. The GPN is a mixed nerve that contains 3 components including the sensory, motor, and parasympathetic nerve fibres. Theoretically, the GPN block provides us with a direct way to block pain conduction. At present, post-tonsillectomy analgesia in most medical centers is based on analgesic agents, although there have been reports on the use of ultrasound-guided glossopharyngeal nerve (GPN) block. Post-tonsillectomy analgesia has attracted wide attention from multiple disciplines. This article systematically elucidates the various analgesics and methods used in post-tonsillectomy analgesia and explores the feasibility of ultrasound-GPN block, with an attempt to provide new insights for multimodal post-tonsillectomy analgesia.

Keywords: Tonsillectomy; glossopharyngeal nerve block; ultrasound guidance; analgesics; multimodal analgesia

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Introduction

Classic tonsillectomy, the surgical removal of the palatine tonsils, is one of the most commonly performed surgical procedures in the head and neck (1). Postoperative pain is a major problem both in children and adult undergoing tonsillectomy. Safe and effective postoperative analgesia not only reduce pain and associated morbidity but also facilitates the early oral intake and adequate hydration (2,3). In a study by Hultcrantz *et al.*, the median recovery timeline was about 10 days for adults and about 7 days for children, and the pain was most significant about 3–5 days after surgery. According to a Swedish study, there are about 13,000 tonsillectomies performed in Sweden each year, and 26% of these patients contact the hospital due to postoperative pain (4). In the United States, approximately 500,000 patients under the age of 15 receive tonsillectomy each year and postoperative pain will last 1 week in about half of these patients (5). Acute pain can cause physical discomfort, anxiety, and even behavior problems, and high-quality acute pain management can promote functional recovery and improve long-term functional outcomes.

Although a variety of analgesic regimens have been adopted to relieve pain, no consensus on the optimal analgesic regimen has been reached among different centers (6). 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 (7,8). As a result, the post-tonsillectomy analgesia schemes remain controversial. While Sweden has revised its national guidelines for the treatment of pain after tonsil surgery (6,8), 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 (3). Ultrasound-guided glossopharyngeal nerve (GPN) block provides a feasible approach for the perioperative analgesia in patients undergoing tonsillectomy (9). In this article, we will introduce the current medical treatments and the application of GPN block for post-tonsillectomy pain management.

Drugs for post-tonsillectomy analgesia

Post-tonsillectomy pain is caused by the tearing of the mucous membranes and the stimulation of the PGN and vagus nerve. The release of pain-producing substances due to edema and inflammatory exudation in local injured tissue will excite the receptors on nerve endings and thus cause local pain (10,11). 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 (12), and no research has identified a single drug or a combination of multiple drugs that have definite advantages over the other options (11).

Steroids

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% (13). According to Mohamed *et al.*, dexamethasone 0.5 mg/kg before surgery could significantly reduce postoperative pain (14).

NSAIDs

NSAIDs are widely used in clinical practice and can be divided into 2 categories: non-selective NSAIDs and COX-2-selective inhibitors (15). Non-selective NSAIDs are traditional NSAIDs that include ibuprofen, diclofenac sodium, and meloxicam, 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 (8,16). The Swedish national guidelines recommend that administration of celecoxib 2–4 mg/kg daily in children can significantly alleviate pain without increasing the risk of postoperative bleeding (8).

Centrally acting non-opioid analgesics

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 (17). Schnabel *et al.* found that the use of tramadol immediately after surgery for pediatric patients had good analgesic effect, could alleviate agitation due to pain and discomfort, and did not cause delayed recovery of consciousness (18). In contrast, Sadhasivam *et al.* argued that pediatric patients might develop adverse reactions such as constipation and confusion probably due to the effects of serotonin, and therefore centrally acting non-opioid analgesics should not be recommended for children and teenagers (12).

Opioids

Opioid analgesics include analgesics that stimulate opioid receptors and partial agonists of opioid receptors that have analgesic effects. They mainly act on opioid receptors in the central nervous system and selectively eliminate or alleviate pain. In addition, they can effectively cope with emotional stress due to pain. At present, opioids remain the most widely used drugs for post-operative analgesia in clinical settings (19).

As the first choice for rescue analgesia, opioids are often required when pain relief is not sufficient. The opioids commonly used for analgesia after tonsillectomy are mainly morphine, oxycodone, sufentanil, and fentanyl, although pentazocine, butorphanol, and dizocine are also often used.

However, there are large individual differences in the responses and a risk of respiratory depression after the use of opioids. Both the U.S. Food and Drug Administration and European medical authorities have issued warnings that deaths have occurred postoperatively in children with obstructive sleep apnea (OSA) who received opioids for pain relief following tonsillectomy (20). Children with OSA symptoms or a nocturnal blood oxygen saturation of less than 85% are more sensitive to morphine and other opioids and have a higher risk of developing severe opioid-related respiratory depression (12).

α2 agonists

α2-adrenoreceptor agonists possess multifaceted attributes of sedation, anxiolysis, hypnosis, analgesia, and sympatholysis (5). 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 (21). The typical α2 agonists are dexmedetomidine and clonidine, of which clonidine is usually studied as an adjuvant for local anesthetics (22).

For patients with OSA or other respiratory obstruction conditions who cannot use opioids, α2 agonists can be a good alternative. Tesoro *et al.* found that preoperative or intraoperative use of clonidine or dexmedetomidine decreased the incidence of agitation after surgery (23); Zhang *et al.* demonstrated that intravenous dexmedetomidine infusion at ED_{50} (0.13 μg/kg) or ED_{95} (0.30 μg/kg) during induction for 10 min could prevent half or almost all EA after sevoflurane and remifentanil anesthesia during pediatric tonsillectomy and adenoidectomy (24).

Pregabalin

Pregabalin is an antiepileptic drug. Møiniche *et al.* have demonstrated that pregabalin may prevent or weaken the excitement of the central nervous system that leads to intensified postoperative pain (25). Jokela *et al.* reported that perioperative use of pregabalin 600 mg was superior to diazepam 10 mg in reducing the dose of oxycodone (26). Park *et al.* found that administration of pregabalin 300 mg prior to tonsillectomy decreases fentanyl consumption compared with that after diazepam 4 mg, without an increased incidence of adverse effects (27).

Techniques of GPN block

The GPN originates from the posterolateral groove located between the olives of the medulla oblongata and the pontine angle. It initially has 3 or 4 roots, which then merge into the neural stem. The stem passes through the jugular foramen and is surrounded by a separate nerve sheath before it leaves the skull. The GPN then runs in front of the internal jugular vein and internal carotid artery and is distributed in the mucosa of the pharynx, palatine tonsil, and posterior 1/3 of the tongue (28,29). The GPN is a mixed nerve that contains 3 components including the sensory, motor, and parasympathetic nerve fibers. The sensory fibers innervate the entire sensation of the pharynx, soft palate, dorsal side of the tongue, palatine tonsil, auditory tube, and tympanic cavity. The motor fibers target the pharyngeal muscle. The parasympathetic fibers are distributed in the carotid sinus and carotid body (30). Theoretically, GPN block can effectively stop the pain conduction caused by tonsillectomy but may also lead to breathing and/or circulation problems.

There are 2 approaches to the GPN block: the intraoral approach, mainly performed by the operator (31-33), and the extraoral approach, mainly performed by an anesthesiologist (34).

Intraoral approach

The intraoral technique is typically performed for analgesia by the operator upon the completion of tonsillectomy. Generally, it can be further divided into 2 approaches: the palatoglossal fold approach and the palatopharyngeal fold approach (35). The palatoglossal fold approach uses the palatoglossal arch as a positioning mark, during which a blade is introduced into the lateral wall of the oropharynx. The palatopharyngeal fold approach uses the palatopharyngeal arch as the positioning mark, and the agent is delivered into the base of the palatoglossal arch. In the study performed by Funasaka *et al.*, the palatopharyngeal fold was closer to the root of the GPN, and the palatopharyngeal fold approach was more effective in blocking the sensory fibers of the GPN (36).

Mohamed *et al.* found that the preoperative injection of 3 mL of local anesthetic agent into bilateral tonsils, along with intravenous injection of dexamethasone 0.5 mg/kg, could effectively reduce pain after tonsillectomy (14). In the study conducted by Hong *et al.*, topical ropivacaine with ketamine lowered the pain score within 1 hour after surgery, but the pain score showed no significant difference 1 hour later (31). Junaid *et al.* found that the use of bupivacaine infiltration or packing immediately following the tonsillectomy achieved adequate postoperative analgesia (37).

Extraoral approach

The extraoral approach initially used the styloid process as the positioning mark, with low accuracy and severe side effects. Nowadays, a variety of imaging techniques including X-ray, ultrasound, and computed tomography (CT) are used for positioning. In particular, ultrasound is a simple and highly efficient positioning technique during perioperative analgesia (9).

At present, there are 3 main methods for ultrasound-guided GPN block: (I) blocking the parapharyngeal space at the distal branch of the GPN; (II) blocking the jugular arteriovenous space along the longitudinal axis (34); and (III) blocking the nerve transversely under the guidance of transstyloid ultrasound. Ažman *et al.* demonstrated that the parapharyngeal space at the distal branch of the GPN is far away from the jugular artery and vein, and thus the puncture is safer, but the effectiveness of the block was slightly worse than the other 2 methods in their study (34).

In his book, Narouze explained in detail the ultrasound-guided transstyloid approach: (I) linear probes are placed between the ipsilateral mastoid and mandibular angle, and below the ear lobule; (II) after an increase of echoes, which represent the styloid, is found between the internal jugular vein and internal carotid artery, the puncture needle is inserted by using the out-of-plane approach; (III) when the tip of the needle meets the styloid, 2–3 mL of local anesthetic is injected near the styloid, which can offer good analgesia at the tonsils (38).

Complications of GPN block

The complications of GPN block are strongly related to the block approach selected. The intraoral approach and the ultrasound-guided jugular arteriovenous space longitudinal axis approach may be more likely to cause hematoma or require intravascular local anesthetic injection (39). Due to its relatively high block site, the ultrasound-guided transstyloid approach is more prone to swallowing difficulties; even worse, vagus nerve block may lead to bradycardia, reflex tachycardia, syncope, and vocal cord paralysis (38). In addition, the carotid sinus nerve is another important branch of the GPN, and accidental blockage of this nerve will cause drastic hemodynamic fluctuations (33,40).

Post-tonsillectomy analgesia has attracted wide attention from multiple disciplines. Although there have been many studies on a variety of combinations of different drugs for analgesia, the overall analgesic effects remain poor due to limitations in side effects such as bleeding, respiratory depression, nausea, and vomiting, and no relevant consensus has been reached as to which combination is superior. Studies on the ultrasound-guided GPN block will shed new light on multimodal analgesia. Although this technology has its limitations, it is still worthy of further investigation.

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