Research Article

Effect of Cryotherapy plus Flurbiprofen Axetil for Pain Management in Children Undergoing Tonsillectomy

Ping Gao,1 Wenyun Wang,2 Wenhui Yang,2 Tingting Yan,2 and Biaoxin Zhang3

1School of Nursing, Anhui Medical University, Department of Emergency Medical, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei 230032, China
2Department of Anesthesiology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei 230001, China
3Department of Otolaryngology Head and Neck Surgery, The First Affiliated Hospital of Anhui Medical University, Hefei 230032, China

Correspondence should be addressed to Biaoxin Zhang; sibiaoggom@163.com

Received 11 May 2022; Revised 28 May 2022; Accepted 2 June 2022; Published 14 July 2022

Objective. To investigate the effect of cryotherapy using ice pops for physical analgesia and preventive analgesia using flurbiprofen axetil for pain management in children undergoing tonsillectomy.

Methods. A total of 120 children scheduled for tonsillectomy were recruited after assessment for eligibility and assigned to a control group (group C), flurbiprofen axetil group (group F), cryotherapy group (group I), and cryotherapy plus flurbiprofen axetil group (Group FI) via the random number table method. Groups F and FI were given 1 mg/kg of flurbiprofen axetil through intravenous injection 30 min before surgery, while group C received an equal amount of saline at the same time point. Groups I and FI received sweet ice pops for pain relief after recovery from anesthesia. The modified Children’s Hospital of Eastern Ontario Pain Scale (mCHEOPS) scores and pediatric anesthesia emergence delirium (PAED) scores at 5 minutes (T1), 30 minutes (T2), 60 minutes (T3), 4 hours (T4), and 24 hours (T5) postoperatively, and the incidence of postoperative complications in the children were recorded by investigators who were masked to the grouping results.

Results. From T1 to T4, significantly lower mCHEOPS scores and PAED scores were observed in group F, group I, and group FI versus those in group C (P < 0.05). At T2, group FI showed significantly lower mCHEOPS scores and PAED scores versus groups F and I (P < 0.05). There were no significant differences in the mCHEOPS scores and PAED scores between the four groups at 24 h postoperatively (P > 0.05). The differences in the documented postoperative complications between the four groups did not come up to the statistical standard (P > 0.05). Conclusion. Cryotherapy plus flurbiprofen axetil for pain management significantly mitigates post-tonsillectomy pain and delirium in children and facilitates recovery, with no significant adverse events.

1. Introduction

Tonsillectomy is a widely performed surgical procedure worldwide and is the second most common surgery performed on children [1]. Removal of the tonsils is possible in cases of recurrent acute tonsillitis, peritonsillar abscesses, and in young children, where the tonsils have become enlarged and hypertrophied, resulting in poor circulation of the upper respiratory tract and even difficulty in breathing and swallowing [2]. Other conditions, such as tonsillar keratosis and tonsillar tumours, can also be treated by this procedure [3]. Pain, bleeding, agitation, and dysphagia after tonsillectomy are the main factors affecting postoperative recovery [4]. The pain, mainly at the throat and the ears, builds up for the first few days and is usually at its worst around the fifth day after surgery. Intense pain is one of the most important postoperative complaints after tonsillectomy, and inadequate postoperative pain management is associated with negative consequences such as the development of chronic postoperative pain, impaired throat function, and negative psychological states.
Currently, pain management after tonsillectomy consists of physical analgesics, such as ice packs, and pharmacological management. Nonsteroidal anti-inflammatory drugs (NSAIDs) are privileged for pharmacological analgesia [5], and other drugs include preemptive dexmedetomidine nasal drip or local anesthetic application [6, 7]. Flurbiprofen axetil reduces prostaglandin synthesis by inhibiting cyclooxygenase (COX) in the spinal cord and periphery, reducing the nociceptive hypersensitivity state caused by surgical trauma [8]. Lipid microsphere formulations are more potent, have a more rapid onset of action, last longer, and are less likely to cause adverse effects such as gastric mucosal damage [9]. Its use in postoperative analgesia has the advantage that it has no central depressant effect, does not interfere with the awakening of patients under anaesthesia, and can be used immediately after surgery [10]. However, relatively little knowledge is available related to the joint use of physical and pharmacological analgesia in children undergoing tonsillectomy. To this end, this study was undertaken to evaluate the clinical effects and safety of cryotherapy using ice pops for physical analgesia and preventive analgesia using flurbiprofen axetil for pain management in children undergoing tonsillectomy, so as to provide a reference for clinical application.

2. Materials and Methods

2.1. Baseline Patient Profile. 120 children scheduled for tonsillectomy and/or adenoidectomy were recruited for prospective analysis and assigned by random number table to the control group (group C), flurbiprofen axetil group (group F), cryotherapy group (group f), and cryotherapy plus flurbiprofen axetil group (group Fl). The experiments were approved by the ethics committee of The First Affiliated Hospital of USTC (no. FAHUStC753). All participants’ families were informed, and they signed the consent form.

Inclusion criteria were (1) patients aged 3–11 years; (2) patients with an American Society of Anesthesiologists (ASA) physical status classification of I-II [11] and normal cardiopulmonary, hepatic, and renal function; (3) no preoperative chronic pain.

Exclusion criteria were (1) history of NSAID drug allergy, recent peptic ulcer, neuromuscular sensory abnormalities, hepatic, renal, and haematological dysfunction; (2) patients who have used analgesics within the last 24 hours; (3) patients who have undergone another procedure for the above reasons.

2.2. Treatment Methods. The blood pressure, oxygen saturation, and electrocardiogram of the children were monitored before surgery. All children received 0.1 mg/kg of tropisetron intravenously before surgery. 1 mg/kg of flurbiprofen axetil was administered to groups Fl and F 30 min before surgery, and an equal amount of saline was given to group C at the same time point. The general anesthesia was established using 0.05 mg/kg of midazolam, 0.4 ug/kg of sufentanil, 0.2 mg/kg of etomidate, and cisatracurium besylate. After tracheal intubation, the breathing machine was connected for respiratory control, and the tidal volume was maintained at 8–10 ml/kg. Combined intravenous-inhalation anesthesia was used for anesthesia maintenance, with continuous infusion of propofol and remifentanil, intermittent inhalation of 0.5% to 1% sevoflurane, and additional cisatracurium besylate as needed. The heart rate and blood pressure of the children were maintained within 30% of the preoperative baseline values, the anesthesia was terminated at the completion of the operation, and the children were immediately sent to the postanesthesia care unit (PACU). The tracheal tube was removed when the children could breathe freely and were hemodynamically stable, and the patients of the children were asked to accompany the children to PACU. Children in groups I and FI were given a sweet ice pop for physical analgesia for 5 minutes after extubation under the instruction of the medical staff. Children with postoperative modified Children’s Hospital of Eastern Ontario Pain Scale (mCHEOPS) scores greater than 4 points were given flurbiprofen axetil at a dose of 1 mg/kg.

2.3. Outcome Measures

(1) The operating time and volume of intraoperative bleeding in the children were recorded.

(2) Postoperative pain in the children was assessed using mCHEOPS scores and postextubation agitation of the children was assessed using the pediatric anaesthesia emergence delirium (PAED) scale [12]. Scoring criteria are shown in Tables 1 and 2. The mCHEOPS scores and PAED scores at 5 minutes (T1), 30 minutes (T2), 60 minutes (T3), 4 hours (T4), and 24 hours (T5) postoperatively were recorded by investigators who were blinded to the grouping results. The mCHEOPS scores consisted of 5 domains, each with a score of 0–10 points, and the score was proportional to the severity of pain. The PAED scores also consisted of 5 domains, each with a score of 0–20 points, and the score was proportional to the severity of agitation.

(3) The occurrence of traumatic bleeding, nausea and vomiting, postoperative diarrhea, and fever was recorded 3 days after surgery. Traumatic bleeding was defined as bleeding that requires surgical intervention for hemostasis. Postoperative diarrhea was defined as the number of bowel movements ≥3 times/day with loose stools. A postoperative temperature >38.0°C was defined as a febrile case.

2.4. Statistical Analysis. All statistical analyses were performed with the use of SPSS 17.0. Normally distributed measurement data are expressed as the mean ± standard deviation; a t-test was used to determine the statistical significance of differences between the groups, and an ANOVA with repeated measure design was used for intragroup comparisons. Count data are expressed as the
number of cases and percentages (%) and analyzed using the chi-square test. The rank-sum test was used for the comparison of rank data. Statistically significant results were defined as \( P < 0.05 \).

### 3. Results

#### 3.1. Baseline Patient Characteristics and Intraoperative Indices

There were no significant differences in the baseline characteristics such as age, weight, and gender ratios, the operation time, and the intraoperative bleeding volume between the four groups of children \( (P > 0.05) \) (Table 3).

#### 3.2. Postoperative Pain and Agitation

From T1 to T4, significantly lower mCHEOPS scores and PAED scores were observed in group \( F \), group \( I \), and group \( FI \) versus those in group \( C \) \( (P < 0.05) \). At T2, group \( FI \) showed significantly lower mCHEOPS scores and PAED scores versus groups \( F \) and \( I \) \( (P < 0.05) \) (Table 4).

#### 3.3. Postoperative Complications

The differences in the occurrence of traumatic bleeding, nausea and vomiting, postoperative diarrhea, and fever between the four groups of children did not come up to the statistical standard \( (P > 0.05) \) (Table 5).

### 4. Discussion

Most children complain of severe pain after tonsillectomy, which compromises the quality of life and leads to reduced diet, dysphagia, dehydration, and possibly long-term behavioral and/or psychological alterations [13]. Postoperative pain also predisposes children to agitation during the recovery period, especially in the early stages of tracheal tube removal in the PACU. Therefore, the significance of the control of mitigation of postoperative pain in pediatric tonsillectomy has been established definitively.

The aim of this study was to evaluate the clinical effectiveness and safety of physical analgesia using ice lolly cryotherapy and prophylactic analgesia using flurbiprofen.

---

**Table 1**: Modified children’s hospital of eastern Ontario pain scale scores.

| Scores                  | 0 points | 1 point     | 2 points |
|-------------------------|----------|-------------|----------|
| Crying                  | None     | Moaning     | Screaming|
| Facial expressions      | Smiling  | Calm        | Painful  |
| Language                | No pain  | No complaint of pain | Complaint of pain |
| Body reaction           | Normal   | Relaxed     | Nervous and quivering |
| Legs                    | Normal   | Kicking     | Need for constraints |

**Table 2**: Pediatric anesthesia emergence delirium scores.

| Items                                      | 4 points | 3 points     | 2 points   | 1 point     | 0 points    |
|--------------------------------------------|----------|--------------|------------|-------------|-------------|
| Eye contact with their guardians           | None     | Infrequent   | Moderate   | Frequent    | Extremelyfrequent |
| Behavioral purposefulness                  | None     | Infrequent   | Moderate   | Frequent    | Extremelyfrequent |
| Recognize the environment                  | None     | Infrequent   | Moderate   | Frequent    | Extremelyfrequent |
| Restlessness and agitation                 | None     | Infrequent   | Moderate   | Inrequent   | None        |
| Unmitigated crying                         | None     | Frequent     | Moderate   | Inrequent   | None        |

**Table 3**: Baseline characteristics and intraoperative indices \( (\bar{x} \pm s, \ n=30) \).

| Groups | \( n \) | Male/female | Age (year) | Height (cm) | Weight (kg) | Operation time (min) | Intraoperative bleeding volume (ml) |
|--------|------|-------------|------------|-------------|-------------|----------------------|-----------------------------------|
| \( C \) | 30   | 21/9        | 6.87 ± 2.73| 121.28 ± 15.78| 22.30 ± 8.15| 78.37 ± 14.76         | 26.40 ± 8.17                      |
| \( F \) | 30   | 19/11       | 6.70 ± 2.07| 116.60 ± 11.78| 23.28 ± 7.91| 73.10 ± 16.43         | 23.37 ± 6.80                      |
| \( I \) | 30   | 21/9        | 7.07 ± 2.38| 116.42 ± 12.65| 22.78 ± 8.64| 78.65 ± 17.33         | 22.76 ± 6.76                      |
| \( FI \)| 30   | 22/8        | 7.20 ± 2.57| 120.00 ± 14.06| 22.94 ± 8.89| 75.53 ± 15.17         | 22.17 ± 7.03                      |

**Table 4**: Postoperative pain and agitation \( (\bar{x} \pm s, \ n=30) \).

| Indices       | Groups | \( n \) | \( T_1 \) | \( T_2 \) | \( T_3 \) | \( T_4 \) |
|---------------|--------|--------|----------|----------|----------|----------|
| MCHEOPS scores| \( C \) | 30     | 3.4 ± 0.8| 3.4 ± 0.7| 3.2 ± 0.7| 2.2 ± 0.8|
|               | \( F \) | 30     | 2.5 ± 0.6\( a \)| 2.6 ± 0.8\( a \)| 2.1 ± 0.9\( a \)| 1.2 ± 0.5\( a \)| 0.8 ± 0.5|
|               | \( I \) | 30     | 2.5 ± 0.7\( a \)| 2.8 ± 0.9\( a \)| 2.1 ± 0.8\( a \)| 1.2 ± 0.5\( a \)| 0.8 ± 0.4|
|               | \( FI \)| 30     | 2.2 ± 0.6\( a \)| 1.8 ± 0.8\( ab \)| 1.8 ± 0.8\( a \)| 1.2 ± 0.4\( a \)| 0.7 ± 0.5|
| PAED scores   | \( C \) | 30     | 6.7 ± 1.6| 8.2 ± 2.4| 7.8 ± 1.8| 3.5 ± 1.8|
|               | \( F \) | 30     | 5.8 ± 1.2\( a \)| 6.3 ± 1.5\( a \)| 6.2 ± 2.0\( a \)| 2.4 ± 1.3\( a \)| 1.6 ± 1.4|
|               | \( I \) | 30     | 5.4 ± 1.5\( a \)| 5.2 ± 1.4\( a \)| 6.4 ± 2.2\( a \)| 2.6 ± 1.3\( a \)| 1.2 ± 0.8|
|               | \( FI \)| 30     | 5.3 ± 1.6\( a \)| 4.2 ± 1.3\( ab \)| 6.4 ± 1.5\( a \)| 2.2 ± 1.6\( a \)| 1.2 ± 0.7|

Note: \( a \) indicates a significant difference \( (P < 0.05) \) in comparison with group \( C \); \( ab \) indicates a significant difference \( (P < 0.05) \) in comparison with groups \( F \) and \( I \).
axetil children undergoing tonsillectomy. Prophylactic analgesia refers to the reduction of postoperative pain by reducing the transmission of surgically induced pain stimuli to the centre and preventing central sensitisation by preemptive analgesic drugs. Flurbiprofen axetil is a nonsteroidal anti-inflammatory drug that is commonly used clinically for prophylactic analgesia [14]. It can be used for postoperative pain relief in children, has a rapid onset of action, lasts for a long time, and has no significant side effects, which is relatively safe. The dosage of this drug should be strictly followed to avoid overdosing, which may affect the normal growth and development of the child [15]. In this study, children who received flurbiprofen axetil combination with cryotherapy achieved the lowest pain scores and agitation scores, suggesting a synergistic effect of cryotherapy and prophylactic analgesia in post-tonsillectomy pain management.

There is considerable evidence to support the impact of cryotherapy on post-tonsillectomy pain management. Vieira et al. [16] reported that the use of 500 ml of saline at 5°C to 10°C for 3 and 6 days postoperatively reduced pain. Similar results were obtained by Shin et al. [17], who used 300 ml of saline at 5°C to relieve postoperative pain. The current data confirm that cryotherapy has a significant effect on pain relief and agitation in the early posttracheal extubation period. The mechanism of action of cryotherapy is that low temperatures reduce tissue congestion and swelling and lower the activation threshold of tissue damage receptors and the conduction rate of pain nerve signals [18]. In this study, children in Groups I and FI received sweet ice lollies, which would create localised hypothermia in the mouth and a sweet taste to soothe the child.

Flurbiprofen axetil is a nonsteroidal anti-inflammatory drug with stable pharmacokinetics and no significant adverse complications when used in pediatric patients over 6 months of age [19], but it may impair platelet function and lead to increased surgical bleeding. Postoperative follow-up in this study showed that flurbiprofen axetil used 30 minutes before surgery as prophylactic analgesia did not increase trauma bleeding. Furthermore, the lack of difference in postoperative complications among the four groups of children also suggests that the combination of cryotherapy plus flurbiprofen axetil has a high safety profile.

However, at any time during treatment with all (NSAIDs), adverse reactions of gastrointestinal bleeding, ulceration, and perforation can occur, and the risk can be fatal [20]. When gastrointestinal bleeding or ulceration occurs in patients taking the drug, it should be discontinued. Clinical trials have shown that this product may cause an increased risk of serious cardiovascular thrombotic adverse events, myocardial infarction and stroke, the risk of which may also be fatal [21]. Patients with cardiovascular disease or risk factors for cardiovascular disease are at greater risk [22]. In Chinese medicine, the main ingredients of Du Liang soft capsules are Angelica dahurica and Rhizoma Chuanxiong, which is an orally administered proprietary Chinese medicine preparation [23]. The clinical effects are mainly to dispel wind and cold, invigorate blood, and promote blood circulation. The clinical effects are mainly for the treatment of headaches, and the TCM symptoms need to be of the type of wind-cold and blood stasis blocking the arteries and channels [24]. A study has demonstrated the efficacy of Du Liang soft capsule in relieving pain after hand tonsillectomy with no significant adverse effects, which provides another basis for the combined treatment of Chinese and Western medicine [25].

However, there are a number of limitations to this study. The number of popsicles consumed by children was not standardised, there were subjective judgements on postoperative pain and agitation scores, and the limited duration of postoperative follow-up did not allow for an objective evaluation of long-term outcomes. More scientific and precise indicators are needed for evaluation in follow-up trials.

5. Conclusion

Flurbiprofen axetil preventive analgesia is available for postoperative analgesia in children undergoing tonsillectomy, and ice pops offer an economical and safe alternative for short-term postoperative analgesia. Cryotherapy plus flurbiprofen axetil for pain management significantly mitigates post-tonsillectomy pain and delirium in children and facilitates recovery, with no significant adverse events.

Data Availability

No data were used to support this study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] R. Subramanyam, A. Varughese, J. P. Willging, and S. Sadhasivam, “Future of pediatric tonsillectomy and perioperative outcomes,” International Journal of Pediatric Otorhinolaryngology, vol. 77, no. 2, pp. 194–199, 2013.
[2] D. H. Darrow and C. Siemens, “Indications for tonsillectomy and adenoidectomy,” The Laryngoscope, vol. 112, no. S100, pp. 6–10, 2002.
Evidence-Based Complementary and Alternative Medicine

[3] L. Licitra, J. Bernier, C. Grandi, M. Merlano, P. Bruzzi, and J. L. Lefebvre, “Cancer of the oropharynx,” Critical Reviews In Oncology-Hematology, vol. 41, no. 1, pp. 107–122, 2002.

[4] J. C. Sowder, C. M. Gale, J. L. Henriksen et al., “Primary caregiver perception of pain control following pediatric adenotonsillectomy: a cross-sectional survey,” Otolar-nygology—Head and Neck Surgery, vol. 155, no. 5, pp. 869–875, 2016.

[5] M. I. Tawalbeh, O. O. Nawasreh, and A. M. Husban, “Comparative study of diclofenac sodium and paracetamol for treatment of pain after adenotonsillectomy in children,” Saudi Medical Journal, vol. 22, no. 2, pp. 121–123, 2001.

[6] X. Long, Y. Gong, and P. Chen, “Application of dacronin hydrochloride gum plasma in tonsillectomy in children,” Journal of Clinical Anesthesiology, vol. 35, no. 7, pp. 671–675, 2019.

[7] H. Zhang, T. Ma, and L. Zhao, “Effect of dexmedetomidine nasal drops on recovery after tonsil adenoidectomy in children,” Journal of Clinical Anesthesiology, vol. 35, no. 6, pp. 556–559, 2019.

[8] X. Zhao and L. Ji, “Flurbiprofen axetil: analgesic effect and adverse reaction,” Pakistan Journal of Pharmaceutical Sciences, vol. 31, pp. 1163–1167, 2018.

[9] F. Huang, X. Cao, J. Li, and Y. Han, “Analogic effect of flurbiprofen axetil in treatment of single hole thoracoscopic surgery for pneumothorax,” Pakistan journal of pharma-cological sciences, vol. 30, pp. 1875–1882, 2017.

[10] K. Yamashita, M. Fukuksui, Y. Ando et al., “Preoperative administration of intravenous flurbiprofen axetil reduces postoperative pain for spinal fusion surgery,” Journal of Anesthesia, vol. 20, no. 2, pp. 92–95, 2006.

[11] S. R. Haynes and P. G. P. Lawler, “An assessment of the consistency of ASA physical status classification allocation,” Anaesthesia, vol. 50, no. 3, pp. 195–199, 1995.

[12] N. Sikich and J. Lerman, “Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale,” Anesthesiology, vol. 100, no. 5, pp. 1138–1145, 2004.

[13] S. R. Robinson and G. L. Purdie, “Reducing post-tonsillectomy pain with cryoanalgesia: a randomized controlled trial,” The Laryngoscope, vol. 110, no. 7, pp. 1128–1131, 2000.

[14] K. Wang, J. Luo, L. Zheng, and T. Luo, “Preoperative flur-biprofen axetil administration for acute postoperative pain: a meta-analysis of randomized controlled trials,” Journal of Anesthesia, vol. 31, no. 6, pp. 852–860, 2017.

[15] X. Xiao, Q. Zhang, Z. Ouyang, and X. Guo, “Comparison of perioperative flurbiprofen axetil or celecoxib administration for pain management after total-knee arthroplasty: a retrospective study,” Medicine (Baltimore), vol. 97, no. 37, Article ID e12391, 2018.

[16] L. Vieira, L. Nissen, Y. Amara, G. Sela, V. Fonseca, and L. Vieira, “Reducing postoperative pain from tonsillectomy using monopolar electrocautery by cooling the oropharynx,” International Archives of Otorhinolaryngology, vol. 18, no. 2, pp. 155–158, 2014.

[17] J. M. Shin, J. Y. Byun, B. J. Baek, and J. Y. Lee, “Effect of cold-water cooling of tonsillar fossa and pharyngeal mucosa on post-tonsillectomy pain,” American Journal of Otolaryngology, vol. 35, no. 3, pp. 353–356, 2014.

[18] S. F. Nadler, “Nonpharmacologic management of pain,” Journal of the American Osteopathic Association, vol. 104, no. 11 Suppl 8, pp. S6–S12, 2004.

[19] E. Kumpulainen, P. Välikalto, M. Kokki et al., “Plasma and cerebrospinal fluid pharmacokinetics of flurbiprofen in children,” British Journal of Clinical Pharmacology, vol. 70, no. 4, pp. 557–566, 2010.

[20] M. R. Tramer, A. R. Moore, J. M. D. Reynolds, and H. J. McQuay, “Quantitative estimation of rare adverse events which follow a biological progression: a new model applied to chronic NSAID use,” Pain, vol. 85, no. 1, pp. 169–182, 2000.

[21] W. B. White, G. Faich, A. Whelton et al., “Comparison of thromboembolic events in patients treated with celecoxib, a cyclooxynegase-2 specific inhibitor, versus ibuprofen or diclofenac,” The American Journal of Cardiology, vol. 89, no. 4, pp. 425–430, 2002.

[22] R. S. Bresalier, R. S. Sandler, H. Quan et al., “Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial,” New England Journal of Medicine, vol. 352, no. 11, pp. 1092–1102, 2005.

[23] S. Yu, Y. Hu, Q. Wan et al., “A multicenter, double-blind, randomized, placebo-controlled trial to evaluate the efficacy and safety of duliang soft capsule in patients with chronic daily headache,” Evidence Based Complementary and Alternative Medicine, vol. 2015, Article ID 694061, 8 pages, 2015.

[24] Y. A. Guohan and S. Z. Xiaobo, “Duliang soft capsule for wind-cold headache: clinical trial,” China Pharmacy, 2007.

[25] Y. Zhu, C. Lu, and L. Zhi, “Observation on the analogic effect of traditional Chinese medicine duliang soft capsules after tonsillectomy,” Chinese Journal of Health Medicine, vol. 20, 2018.