

Comparison of preoperative ibuprofen, acetaminophen, and placebo administration on the parental report of postextraction pain in children

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Abstract

Previous investigations demonstrated that administering a preoperative analgesic can reduce postextraction pain in adults. Studies also have shown that ibuprofen was superior in alleviating postextraction pain when compared with acetaminophen. The purpose of this study was to compare the efficacy of the preoperative administration of ibuprofen, acetaminophen, and placebo in reducing postextraction pain in children. Sixty children, aged 2–10 years, requiring primary teeth extractions, were selected to participate in the study. Patients were assigned in a blind, random fashion to one of the three pretreatment drug groups. Parental report of their child's pain and use of analgesics during the immediate 7-hr postoperative period was elicited by telephone the day after the extraction procedure. Thirty-five percent of the patients were reported by their parents to experience postextraction pain. Of those patients, 52% received postoperative analgesics for pain relief (18% of the total). Although there was a trend toward reduced postextraction pain reported by the parents, the preoperative administration of neither analgesic was found to be statistically superior by chi-square analysis to placebo administration. (Pediatr Dent 17:187–91, 1995)

Pain results from the inflammatory response created by tissue damage. Tooth extraction is the most likely pediatric dental procedure to produce inflammation and pain. Previous studies report that some children experienced postextraction pain severe enough to require analgesics for relief.¹⁻² A recent review of the literature suggests that the preoperative administration of an analgesic, rather than the traditional postoperative use when needed, was more effective in reducing postextraction pain because the drug effect preceded — rather than followed — the inflammatory response and subsequent pain.³ Wall⁴ stated that pain was more readily prevented than treated by analgesic administration.

Several investigations in adult populations have evaluated preoperative ibuprofen for postextraction pain following third molar removal.⁵⁻⁷ As early as 1978, Dione and Cooper⁵ suggested that preoperative ibuprofen was effective in reducing the onset and intensity of postextraction pain. Subsequent studies demonstrated that ibuprofen was superior to a placebo,^{3,6,7} acetaminophen,^{3,7} codeine phosphate,⁶ and acetaminophen plus codeine.⁷ These studies concluded that the preoperative administration of acetaminophen was not as effective as ibuprofen in relieving postextraction pain because it lacked anti-inflammatory properties.

Only a few studies have evaluated the analgesic use of ibuprofen in children for postextraction pain. Moore et al.⁸ studied child patients, aged 5–12 years, comparing ibuprofen, acetaminophen, and acetaminophen plus codeine with a placebo. They determined that all three analgesics were effective but ibuprofen was rated superior. McGaw et al.⁹ also found ibuprofen to be more efficacious than acetaminophen or placebo for pain in children undergoing permanent tooth extraction.

The recommended analgesic dosage for ibuprofen is unavailable because it is not approved as an analgesic agent for children. Its approved antipyretic dosage (10 mg/kg), however, was reported to be similar to that of acetaminophen (15 mg/kg),¹⁰ and several studies found that ibuprofen in a dosage of 10mg/kg was significantly superior to acetaminophen in febrile children.^{11,12} Ibuprofen also was found safe and effective as an anti-inflammatory agent in dosages ranging from 10 mg/kg/day to a maximum of 40 mg/kg/day.¹³

Pain assessment is very individual and subjective; it can be only indirectly measured in children through verbal self-report or observation of behaviors that suggest pain.¹⁴ Verbal self-report of pain has been correlated with the observed pain-related behaviors of children, although it depends heavily on communication skills. Behavioral and environmental factors also may influence the child's self-report of pain. Pain assess-

ment in young children also can include physical behaviors such as vocalization, facial expression, and body movement. It has been shown that parents and health care providers can accurately assess pain by these physical behaviors in preschool children.¹⁵⁻¹⁷

Although pain in children is difficult to assess, it clearly occurs in some postextraction patients. The dental literature indicates that preoperative administration of analgesics may lessen postextraction pain. A variety of analgesics has been tested in adults. Only one study evaluated the use of preoperative analgesics in children. Primosch and coworkers² found a nonsignificant positive trend toward reduced postextraction pain with acetaminophen pretreatment in 4- to 10-year-old dental patients when compared with a placebo. This conclusion was based upon telephone interview of parents using both child self-report and parental observation of pain-related behavior over a 7-hr postoperative period. Although ibuprofen is not approved as an analgesic in children, many reports indicate that because of its anti-inflammatory properties, it shows promise as a potentially superior agent. The purpose of this study was to evaluate the efficacy of the preoperative administration of ibuprofen and acetaminophen compared with a placebo for pain relief after primary teeth extractions in pediatric patients.

Methods and materials

The subjects consisted of 60 healthy children, aged 2-10 years, requiring one or more uncomplicated extractions of primary teeth. All patients were treated in the University of Florida Pediatric Dental Clinic for planned procedures or emergency care. The study was approved by the University of Florida Institutional Review Board, and an informed consent was obtained from the parents. Patients without a home telephone and without parental supervision for 7-hr postoperatively were excluded from the study. Patients taking analgesics within 4 hr prior to the dental extraction, and patients with a history of prolonged bleeding, platelet disorders, or allergic reactions to aspirin or any of the drugs tested also were excluded from the study.

Those subjects meeting the selection criteria were given one of three solutions:

1. Ibuprofen suspension (Children's Advil®, Whitehall Labs, New York, NY)
2. Acetaminophen elixir (Children's Tylenol®, McNeil Labs, Fort Washington, PA)
3. A cherry-flavored placebo solution.

Twenty containers of each solution were prepared, coded, and randomized at the beginning of the investigation and the subjects were assigned the containers in order of the randomized sequence. Each patient received an age-dosed volume (Table 1) of the assigned solution from a number-coded plastic container containing a premeasured volume (20 ml). Both operator and child/parent were blinded to the content of the

TABLE 1. AGE-DOSED VOLUME OF STUDY SOLUTIONS

Age	Ibuprofen*		Acetaminophen†		Placebo	
	mg	tsp	mg	tsp	mg	tsp
2-3 yrs	150	1½	240	1½	-	1½
4-5 yrs	200	2	320	2	-	2
6-8 yrs	250	2½	400	2½	-	2½
9-10 yrs	300	3	480	3	-	3

* Children's Advil Suspension, (100 mg/5 ml, fruit flavored, red), Whitehall Labs, New York, NY.

† Children's Tylenol Elixir, (160 mg/5 ml, cherry flavored, red), McNeil Labs, Fort Washington, PA.

container. The assigned solution was taken by the patient 15 min before administering the local anesthetic agent. The time of the preoperative solution administration was recorded on the data sheet.

All children were given 2% lidocaine with 1:100,000 epinephrine injection for local anesthesia sufficient enough to obtain adequate anesthesia but not exceeding 4.4 mg/kg. All primary teeth were extracted intact with a minimum of surgical trauma in an uncomplicated fashion. Parents were instructed to look for pain-related behaviors (crying, agitation, withdrawal, etc.) that were unique for their child and to note any verbal report of pain by the child for a 7-hr period following the extraction. The parents agreed to be contacted by telephone the following morning and were given an appropriate amount of Children's Tylenol® (McNeil Labs, Fort Washington, PA) chewable tablets with instructions to give them to the child only if postoperative pain occurred. A pamphlet containing written home care instructions also was provided to the parents.

All parents were called by the same investigator on the morning following the dental extractions to collect information regarding the report of postextraction pain during the 7-hr period following the surgery and whether analgesics were given to relieve the reported pain. The telephone conversation followed a standardized format in that the parent was first asked if the child experienced pain. The vast majority of parents answered without hesitation and appeared comfortable in their assessment. The parents were asked to explain the basis of their assessment (observed behavior, self-report, or both). In those rare cases where further clarification was necessary, additional inquiry was made to validate the response until both parties were satisfied. No attempt was made to establish rank relative or severity of the pain experience.

Results

The study was designed so that 20 subjects were assigned randomly to each of the three solution groups. The distribution of subject characteristics among the groups was remarkably similar even though no attempt was made to balance the characteristics of the individual groups. The groups were analyzed statistically using

TABLE 2. COMPARISON OF VARIABLES AMONG THE THREE SOLUTION GROUPS

	<i>Ibuprofen</i> [*]	<i>Acetaminophen</i> [†]	<i>Placebo</i>	<i>Significance</i>
Age – Months (mean ± se)	80.3 ± 5.1	78.9 ± 4.8	79.7 ± 4.6	<i>P</i> > 0.05*
Weight – kg (mean ± se)	24.5 ± 2.3	24.4 ± 2.5	23.6 ± 1.9	<i>P</i> > 0.05*
Race -White	14	14	14	<i>P</i> > 0.05†
-Black	6	6	6	
Sex -Male	13	12	13	<i>P</i> > 0.05†
-Female	7	8	7	
Postextraction pain reported	6/20 (30%)	7/20 (35%)	8/20 (40%)	<i>P</i> > 0.05†
Postoperative analgesics taken	4/20 (20%)	3/20 (15%)	4/20 (20%)	<i>P</i> > 0.05†

* ANOVA.

† Chi Square.

ANOVA, which revealed no significant differences in age and weight among the groups. The mean age was 79 months (range: 27–128 months) and mean weight was 24 kg. Chi-square analysis also showed no significant differences in race and sex among the groups.

Table 2 exhibits the prevalence of postextraction pain for each group as reported by the parents. Thirty-five percent of the patients were reported by their parents to experience postextraction pain. Of those patients, 52% received postoperative analgesics for pain relief (18% of the total group). The prevalence of postextraction pain according to test solution group was reported as: ibuprofen (30%), acetaminophen (35%), and placebo (40%), but the difference among the groups was not statistically significant by chi-square analysis. The prevalence of postoperative analgesic usage according to test solution group was reported as ibuprofen (20%), acetaminophen (15%), and placebo (20%). No attempt was made to establish rank relativity or severity of the pain, but 52% of the parents perceived that the reported pain was significant enough to warrant postoperative analgesic administration. Although the use of ibuprofen can cause platelet dysfunction, no increased perioperative bleeding was observed or reported for any of the subjects.

Discussion

Although a weight-based dosage schedule may be the preferred method of prescribing pediatric medications, manufacturer's instructions use age-based schedules of dosage calculation. Because of this common practice, the age-dosed volumes (Table 1) were selected in this study. (The recommended analgesic dosage for ibuprofen is unavailable because it is not approved as an analgesic agent for children.)

Several studies have evaluated ibuprofen as an anti-inflammatory, antipyretic agent in children. The anti-

inflammatory property of ibuprofen tested by Steans et al.¹³ in children with juvenile chronic arthritis and was found safe and effective. Bertin et al.¹⁸ also showed ibuprofen safe and effective in treating tonsillitis and pharyngitis. Its efficacy was related to its antipyretic, anti-inflammatory, and analgesic properties. Ibuprofen also has been proven safe and effective in the relief of postoperative dental pain in adults.¹⁹

In our study, it is difficult to explain why ibuprofen was not more effective in reducing postextraction pain in children when ibuprofen consistently has been proven an effective pre-extraction modality in adults.^{3,5-7} One possible explanation is that the adult studies involved third molar extraction procedures, which were more traumatic to the tissue than simple extraction of primary teeth.

For example, 96% of adults receiving preoperative analgesics for third molar extraction reported postoperative pain⁵ compared with 30–40% of children in our study and previous studies using only postoperative analgesics.^{1,8} In addition, adult subjects were able to use reliable objective pain scales to report their pain experience. A reliable and practical pain scoring system with children has yet to be perfected. Previous attempts to use child self-report scales administered by parents in a design similar to our study was judged potentially unreliable due to problems with children's compliance, communication, and cooperation.² Quantifiable pain scales do exist that can be administered by trained personnel to children but are best given, for practical reasons, in close proximity to the pain stimulus.^{17,20} In a postextraction pain study design, one must wait until the effects of local anesthesia have diminished to test for postoperative pain, and it would be impractical to sequester the children for several hours postoperatively in the clinic. Although relying on parental observation for reporting pain in their children had its limitations, the pain literature indicates that parents can accurately assess pain in their children by their displayed behavior.^{15,16} In this study, the child's verbal self-report of pain was considered a valid indicator of pain, but one could argue circumstances where differentiating real from perceived pain would pose a significant challenge.

Another possible explanation may reside in the subtle differences found in the inflammatory response between children and adults. Children have been characterized as having a retarded gingival inflammatory response to plaque pathogens.²¹ This retarded inflammatory response may be due to the decreased leukocyte chemotaxis at the site. A site of tissue damage resulting from a dental extraction may likely respond in a similar manner in children. Thus, the decreased leukocyte

chemotaxis in children affords less of an opportunity for a potential anti-inflammatory agent like ibuprofen to exert much influence upon the inflammatory process and subsequent pain response. An additional explanation may be that the 15-min waiting period prior to local anesthesia administration was insufficient to provide adequate blood levels before the initiation of tissue trauma. A longer waiting period may prove to be more beneficial but less operationally practical.

Several studies have investigated the prevalence of postextraction pain in children. Moore et al.⁸ found that 33% of children, aged 5 to 12 years, reported moderate to severe pain following the extraction of primary or permanent teeth. In another survey, the prevalence of postextraction pain in children, 37.6%, increased with age.¹ These findings were comparable to our study where 40% of the control group reported postextraction pain, as well as 35% in the acetaminophen group and 30% in the ibuprofen group. Our study used a parental interview, rather than a returned mail survey, which could have entered selection bias into the sampling method.

Previous studies also have indicated that children reporting pain following dental extractions often expressed the need for analgesics. The percentage of children experiencing postextraction pain requiring administration of analgesics has been reported to range from 59¹ to 67%.² In our study, analgesic use among patients with reported pain was comparative at 52% and was not influenced by the use of pretreatment analgesics.

Young children undergoing similar surgical procedures may vary in their pain response due to individual differences in temperament.²² Hospitalized 3- to 7-year-old children classified as high intensity received a significantly greater amount of postoperative analgesics following elective urologic surgery than children classified as low intensity.²³ In addition, the temperament variables, rhythmicity and approach, were directly associated with a child's ability to cope with the pain produced by obtaining a blood sample.²⁴ Following dental extractions under general anesthesia, young children were reported to be more likely to complain of pain if accompanied by their mothers.²⁵ These factors further contribute to the complexity of pain assessment in children. Clearly, the multifactorial, subjective nature of pain perception renders any objective measurement tool less valid and reliable in a pediatric population.

There continues to be concern expressed in the literature about the reported underestimation of children's need for postoperative analgesics.²⁶⁻²⁸ Adults tend to underestimate a child's pain reaction, having the misconception that children do not experience pain with the same intensity or duration as adults.²⁹ A recent survey of Seattle dentists revealed that 36% never provided pain medication to children following dental extractions.³⁰ There are no data, however, to support the view that a child's pain threshold is higher than an adult or that the pain experience is less intense.³¹ Because of these

misconceptions, the common practice to disregard the need for postoperative pediatric pain management, and the uncertainty that adult supervision will dispense analgesics — and then only if available to them — strongly supports considering routine preoperative analgesic administration to ensure a uniform, practical approach to postoperative pain management.

Pediatric pain management is a complex and controversial subject. In children, pain assessment is difficult to measure due to their limited language skills, developmental factors, previous experience, and the parental attitude toward the child's pain.^{14,32} It is, therefore, possible to conclude that any pain assessment based upon verbal self-report and parental observation of pain-related behaviors must be interpreted carefully and with caution. In the future, a greater sample size with a narrower age range and the development of more reliable pain assessment methods may help to better elucidate the efficacy of routine presurgical analgesic administration in children. Because of the positive trend in the reported data, a more discrete study of the influence of preoperative analgesics for postextraction pain management may have positive implications for reducing pediatric dental patients' pain. In addition, understanding the risk factors contributing to the creation of postoperative dental pain in children would help to identify potential candidates who would most benefit from the use of preoperative analgesics as a rational pain management strategy. Although ibuprofen has not received approval for analgesic use in children, clinical investigations must continue to evaluate its efficacy for the relief of pediatric dental pain.

Conclusions

Based upon the results of this study the following conclusions were drawn:

1. The prevalence of postextraction pain in children as reported by their parents was 35%
2. Approximately 52% of the parents reporting postextraction pain in their children administered analgesics to them
3. When compared with a placebo, neither acetaminophen nor ibuprofen given preoperatively had a statistically significant ($P > 0.05$) effect upon the prevalence of reported postextraction pain.

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The authors thank Ms. Rhonda Cooper, coordinator, Investigative Drug Services, Pharmacy Administration, Shands Hospital, University of Florida, Gainesville, for her advice and assistance.

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