

# Consequences of Inadequate Analgesia During Painful Procedures in Children

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**Objective:** To explore the effect of inadequate analgesia for painful procedures (bone marrow aspiration, lumbar puncture, or both) on the pain of subsequent procedures.

**Design:** A cohort of patients with cancer who had participated in a placebo-controlled, randomized study that documented the efficacy of oral transmucosal fentanyl citrate for painful procedures rated the pain associated with subsequent procedures performed with open-label oral transmucosal fentanyl.

**Participants:** Twenty-one children undergoing diagnostic procedures who had been participants in a previous study.

**Intervention:** All children were given oral transmucosal fentanyl, 15 to 20 µg/kg, prior to the procedure;

at its conclusion they were asked to rate the associated pain.

**Results:** In children younger than 8 years (n=13), mean pain ratings during each subsequent procedure were consistently higher for those who had received placebo (n=8) in the original study compared with those who had received the active drug (n=5). A repeated-measures analysis of variance suggests that this difference is statistically significant ( $P=.04$ ). Older children (n=8) did not show this pattern.

**Conclusion:** Inadequate analgesia for initial procedures in young children may diminish the effect of adequate analgesia in subsequent procedures.

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**Editor's Note:** This provocative little study should make us stop and think about any painful procedure and the long-lasting effects of inadequate analgesia. Once smitten, twice spurned—or something like that.

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**P**AINFUL PROCEDURES are a major source of distress in children. For many children, the multiple pokes that are necessary for the diagnosis and treatment of chronic disease are often worse than the disease for which they are being treated.<sup>1</sup> For example, in Zeltzer and LeBaron's<sup>2</sup> work on bone marrow aspiration and lumbar puncture pain, the pain is rated as 4.4 of 5 and 3.9 of 5, respectively. Other investigators have reported similar levels of distress associated with these procedures.<sup>3</sup> Unfortunately, however, painful procedures are often essential to adequate diagnosis and treatment. Recent protocols for the treatment of leukemia, for example, require 20 bone

marrow aspirations or lumbar punctures throughout the treatment course.<sup>4</sup>

Despite the frequency and discomfort of these procedures, the pain associated with them historically has received limited attention. Studies in the mid-1980s documented that most pediatric oncology programs had no formal protocols in place to manage procedure pain.<sup>5,6</sup> In addition, when such protocols existed, they tended to rely on inappropriate drugs like chloral hydrate, or painfully administered drug combinations associated with a high incidence of side effects, such as the "Demerol-Phenergan-Thorazine cocktail."<sup>7,8</sup> As a result, many children had to experience these procedures without adequate pain control and with the impression that they would have to endure a seemingly endless series of them in the future.

Pain perception results from a complex intertwining of cognitive, emotional, and social factors that affect how a noxious stimulus is interpreted. If a child has had a procedure that was painful, the memory of that experience may cause

## PATIENTS AND METHODS

The efficacy of oral transmucosal fentanyl for painful diagnostic procedures was demonstrated in a randomized, placebo-controlled clinical trial in 48 children under treatment at the University of Connecticut Division of Pediatric Hematology/Oncology, Farmington. Younger children (ages 3-7 years) rated pain during procedures using the Oucher scale<sup>10</sup> (0-5), while older children (ages 8-18 years) used the visual analog scale (1-10). In both scales, the lowest scores indicate "no pain" and the highest scores indicate "the greatest pain imaginable." Nurses and parents also observed and rated the pain experienced by these children. For each of these measures, children receiving oral transmucosal fentanyl reported and were observed to have significantly less pain than those receiving the placebo.<sup>9</sup>

A compassionate care protocol was instituted for all children enrolled in the previous study whether or not they had initially received the active drug. They were offered oral transmucosal fentanyl for subsequent procedures according to a standard protocol (17.5 µg/kg administered 30 minutes prior to the procedure). Data for the present analysis were collected from the 21 children who required diagnostic procedures during the period studied and elected to receive oral transmucosal fentanyl. As in the original study, self-reports of procedure pain were elicited from younger children using the Oucher scale and from older children using the 10-point visual analog scale. Pain ratings were also collected in a less systematic way from parents and nurses, but the limited amount of data from these observations precluded meaningful analysis.

A Student *t* test (2 tailed) was used to assess the difference between the 2 groups at the first subsequent procedure. A repeated-measures analysis of variance (ANOVA) model was used to explore differences in pain reported between the groups for 4 subsequent procedures.

anxiety about subsequent procedures. This anxiety might influence the degree of pain the child feels during those later procedures. It has been our anecdotal experience and that of others that children who had painful procedures that were adequately managed in the past seem to be less anxious and experience less distress during subsequent procedures.

This article explores data from an opportunistic sample of children in whom this observation could be examined more critically. At this time, ethical constraints preclude any study design in which optimal pain management strategies are not offered to all children. These data, however, were collected before sedation for all children was the standard of care. Children had been randomized to either an active drug group or a placebo control group for a study of the efficacy of oral transmucosal fentanyl citrate for painful procedures.<sup>9</sup> We review the pain experiences of that group of children, some of whom had had inadequate pain man-

## Mean Pain Self-report at First Procedure Following the Original Study

OTFC Study Group*	Children <8 Years	Children ≥8 Years
OTFC	3.4±2.4	5.2±3.4
Placebo	4.7±1.7	5.0±2.5

\*OTFC indicates oral transmucosal fentanyl citrate. Values expressed as mean±SD.

agement in the past and some who had not, during subsequent painful procedures.

## RESULTS

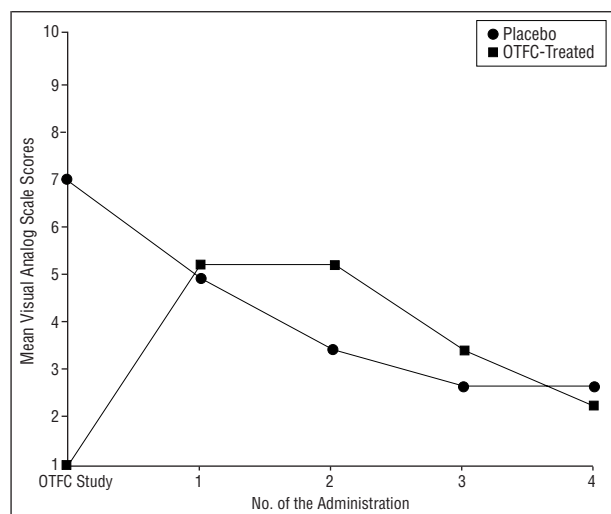
The sample included 13 younger children (8 who received placebo and 5 who received oral transmucosal fentanyl) and 8 older children (4 who received placebo and 4 who received oral transmucosal fentanyl). Due to variation in the requirement for procedures and adequacy of data collection, the number of subsequent procedures analyzed per child ranged from 1 to 12. Thirteen children had 4 or fewer procedures, however, while only 7 had 5 procedures and 3 had more than 5 procedures. Thus data from 4 procedures were used for the repeated-measures ANOVA.

Mean pain scores reported for the first procedure following the original study are provided in the **Table**. Pain ratings for older children were similar for both groups. The younger children who originally received placebo reported more pain than the original group who received oral transmucosal fentanyl, although this difference is not statistically significant with the sample size.

The mean pain ratings for the 4 subsequent procedures are plotted in **Figure 1** for older children and in **Figure 2** for younger children. The results for older children suggest that there was no difference between pain experienced during the initial procedure and that experienced during subsequent procedures, whether or not the children had received oral transmucosal fentanyl originally. For younger children, however, reported pain is consistently higher on average for those children who received placebo initially compared with those who received oral transmucosal fentanyl initially. In the ANOVA analysis, the effect for this group is significant at  $P=.05$  ( $F_{1,19} = 4.42$ ).

## COMMENT

These data suggest that inadequate analgesia for initial procedures in young children may diminish the effect of adequate analgesia in subsequent procedures. This conclusion is congruent with clinical experience and developmental theory. Young children who have had a negative experience resulting from inadequate analgesia might anticipate that their next experience will be similarly negative. Given their developmental level and cognitive capabilities, they are less likely to be influenced by preparation and discussion. In comparison, older children who function at a different cognitive level can understand that the medication they will be given the next time may be



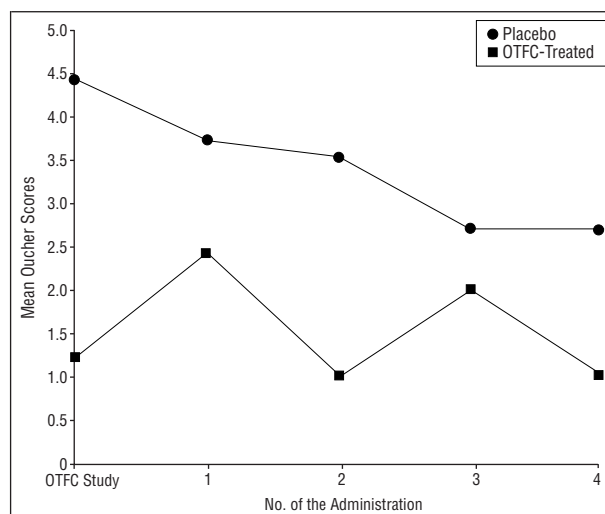
**Figure 1.** Visual analog scale scores for children older than 8 years. OTFC indicates oral transmucosal fentanyl citrate was administered for pain.

more effective and that recurrent painful experiences are not inevitable.

One can surmise, therefore, that once a child has a negative initial experience there is a change in the mental "set point" of his or her interpretation of that noxious stimulus. It is possible that this set point can only be reset with adequate preparation and information. The conceptual abilities of children younger than 8 years are typically inadequate to process this information. We believe our data argue for the importance of aggressive pain control during the initial procedures performed on children who will require multiple procedures. The data also suggest that, if analgesics are used, it is critically important that they be effective the first time, especially for younger children. This argues against the traditional strategy of selecting a lower dose and titrating upward.

This study is limited by small sample size and by the variability in the number and timing of procedure for each child. Because of the small sample size, Figure 1, for example, seems to suggest an increase in pain during the subsequent procedures on older children who received oral transmucosal fentanyl in the original study. However, this finding is an artifact of the few children in this group and the difference is not statistically significant. The small sample size makes statistical analysis relatively speculative. Nevertheless, it is evident that the average report of pain for younger children who have had adequate initial analgesia is lower than that for children who have had inadequate initial analgesia.

While we recognize the limitations of this study, the findings are congruent with both clinical experience and our initial hypothesis. Therefore, we believe that unless there are data to the contrary, it is the obligation of individuals caring for children requiring multiple procedures to aggressively manage the pain associated with those procedures from the start. During subsequent procedures, the treatment plan can be individualized for each child depending on the child's temperament, specific



**Figure 2.** Mean Oucher scale scores for children 8 years old or younger. OTFC indicates oral transmucosal fentanyl citrate was administered for pain.

disease, family and social variables, and other characteristics. However, we believe that appropriate and adequate analgesia should be given at the outset, so that the parents and child who are already grappling with this enormous change in their lives do not have to bear the additional burden of unnecessary pain.

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