

Pediatric Pain Letter

Abstracts and Commentaries on Pain in Infants, Children, and Adolescents

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Introduction

The proof is in the practice...

As clinicians, it is our goal to give the best possible care to our patients. We work hard, we care, and we are determined. Yet most of us fail completely in keeping up with the literature. It is unethical to practice any health profession without up-to-date knowledge, yet most practitioners read the research literature for less than three minutes per day. Many professions have no requirements for meaningful continuing education. Further, quality assurance methods to guarantee the calibre of continuing education programs are seldom used. Most employers neither require nor make available opportunities for consultation with the clinical research literature. Most clinicians do not know how to use the literature to guide clinical practice. Many of us rely on information from word of mouth, the media, or from those who are trying to sell something.

As researchers in pediatric pain, our goal is to discover new knowledge and to improve the lot of children. We are usually focussed on the first and believe the second goal will occur automatically. But it doesn't. New knowledge in medical research is diffused very slowly. This may be particularly true in psychosocial areas because usually no profit is made from psychosocial advances. Has a researcher really done his or her job if no effort is made to disseminate knowledge to practitioners?

There are many good excuses for the lack of diffusion, but they are excuses, nonetheless. What more can you do to help bridge the gap between research and your practice? Is your practice sufficiently up-to-date? Is it sufficiently evidenced-based? Have you lobbied your employer to be sure all health professionals where you work are up-to-date? Have you made yourself knowledgeable about using research evidence to make clinical decisions? Is your practice ethical? Each of us has an obligation to ensure that we are comfortable with our own answers to these questions.

Abstracts

Pain Management at the End-of-Life

Collins, J. J., Grier, H. E., Kinney, H. C., & Berde, C. (1995). Control of severe pain in children with terminal malignancy. *Journal of Pediatrics*, 126, 653-657.

Objective. To determine characteristics of children with malignancy who require massive opioid infusions during the terminal stage.

Design. Retrospective chart review.

Setting. Children's Hospital and Dana-Farber Cancer Institute, Boston, USA.

Participants. 199 children (range = 5 months-20 ½ years at time of death) who died from malignancy between March, 1989 and July, 1993 and who were < 18 years of age at time of diagnosis. Diagnoses: leukemia-lymphoma (44%), solid tumors (33%), and CNS tumors (23%).

Main Outcome Measures. Opioid administration characteristics and autopsy data were recorded. Perceived adequacy of analgesia was determined from opinions of patients, parents, nurses, and physicians. Children older than 6-7 years gave self-report ratings of pain severity on a 0-10 numeric scale; the Objective Pain Scale (Broadman et al., 1988) was used for children <6 years or for those who could not provide a self-report.

Results. A subgroup of 12 children (6%; 7 female) required massive opioid infusions, defined as more than 3 mg/kg/hour of morphine dose equivalents. An additional 6 children required epidural or spinal infusion or celiac plexus blockade, in addition to the morphine infusion, to reduce side effects. Initially, opioids to manage pain were given orally, but if not tolerated, other forms of administration were used (e.g., intravenous, subcutaneous, transdermal). Children in the massive opioid infusion subgroup received high doses only

through intravenous administration. Alternative analgesics (e.g., corticosteroids) were given to 8 patients in the subgroup before massive infusion was attempted. Notable increases in opioid infusion doses for the subgroup occurred during the last 2 weeks of life. Four children in this subgroup received adequate analgesia with opioids alone. Extraordinary measures (e.g., epidural or subarachnoid infusions, or sedation) were required to achieve adequate analgesia in the remaining 8 children. High opioid doses were frequent in cases where solid tumors spread to the spinal nerve roots, nerve plexus, large peripheral nerve, or caused spinal cord compression.

Conclusions. Although the standard WHO procedures of opioid administration in the control of terminal malignancy pain are usually adequate, there is a subgroup of children who require more aggressive measures (e.g., high opioid doses and sedation) to achieve the desired analgesic effects. Guidelines were presented to aid in the management of opioid resistance in children and infants with terminal malignancy.

Collins, J. J., Grier, H. E., Sethna, N. F., Wilder, R. T., & Berde, C. B. (1996). Regional anesthesia for pain associated with terminal pediatric malignancy. *Pain*, 65, 63-69.

Objective. To describe the characteristics of children with terminal malignancy who require regional anesthesia and to describe the safety, tolerability, and effectiveness of regional anesthesia in terminal childhood malignancy.

Design. Retrospective chart review.

Setting. Dana-Farber Cancer Institute and Children's Hospital, Boston, USA.

Patients or Participants. Eleven children (range= 5 months-16.3 years at time of death; 7 female) identified as having died of malignancy during June, 1986 and April, 1994, who required regional anesthesia (epidural or subarachnoid infusions, or neurolytic blockade) to manage pain during the end-of-life stage of the disease. Patients had to be <17 years old at the time of regional anesthesia administration to be included in the review. Nine patients had solid tumors and 2 had hematological malignancy.

Main Outcome Measures. Records were reviewed for characteristics of malignancy, opioid analgesia administration, and epidural or subarachnoid infusions. Pain was assessed with a self-report numerical rating scale (0-10) for children >6 years, and by the Objective Pain Scale (Broadman et al., 1988) for younger children and for those unable to provide a self-report. Judgements from patients, parents, nurses, and physicians were combined to determine the adequacy of

analgesia.

Results. Across patients, epidural or subarachnoid infusions were required for a duration of 3 days to 7 weeks. Children who experienced dose limiting side effects (e.g., respiratory depression) of opioids, neuropathic pain that was unresponsive to massive opioid infusions, and those who received analgesia for procedural pain (e.g., thoracocentesis) required epidural or subarachnoid infusions. In all patients, pain was reported as localized to one area. Analgesia was judged as satisfactory in all cases after regional anesthesia was administered, and remained so throughout the treatment course. Some complications associated with regional anesthesia included dural puncture headache, mild respiratory depression, and loss of bladder, bowel, and motor function.

Conclusions. For pediatric patients with terminal malignancy who experience refractory pain unresponsive to the traditional WHO analgesic model for pain control, regional analgesia may serve as an alternative approach to pain management. The authors emphasized that the choice of analgesic agents and routes of administration must be individualized, carefully monitored, and frequently adjusted with changes in the child's clinical condition.

Partridge, J. C. & Wall, S. N. (1997). Analgesia for dying infants whose life support is withdrawn or withheld. *Pediatrics*, 99, 76-79.

Objective. To examine the frequency of opioid administration to infants whose life sustaining therapy has been discontinued or withheld. Factors related to the use of opioid analgesia and discontinuation of life support were also examined.

Design. Retrospective chart review.

Setting. University-based tertiary care centre-level III intensive care nursery, San Francisco, California.

Participants. Health records of 121 infants who died after life support was withdrawn (n=108) or withheld (n=13) were reviewed. Complete records were available for 120 cases. Demographic characteristics were not reported.

Main Outcome Measures. Neonatologists' daily notes were reviewed to determine the reason for discontinuing or withholding life support: (1) futility, when death was expected regardless of treatment; (2) severe impairment, if concerns were raised about long term disability; and (3) suffering, if treatment was thought to cause suffering for the infant. Records were reviewed to determine whether opioid analgesia was given when life support was withheld or withdrawn. The specific opioid dosage was noted.

Results. The majority (84%) of infants received opioids after life sustaining treatment was discontinued or withheld. Infants

were more likely to receive opioids if diagnosed with necrotizing enterocolitis (100%), or congenital anomalies (93%), relative to infants diagnosed with other disorders (e.g., respiratory failure, hypoxic ischemic encephalopathy). For cases in which futility or severe impairment were cited as reasons to discontinue or withhold life support, 84% and 85% respectively, received opioids. All cases received opioids when suffering was cited as the reason to discontinue or withhold life support. Birth weight did not appear to influence analgesic administration decisions. Sixty-four percent of infants were administered morphine doses within the usual pharmacologic range, but 36% received higher doses.

Conclusions. These findings suggest that neonatologists administer opioid analgesics to terminal infants whose life support has been withdrawn or withheld, particularly for conditions known to be painful. Opioid administration may represent "rational and humane care" geared towards the minimization of unnecessary pain and suffering in dying infants, despite the potential consequence of respiratory depression and hypotension.

Robinson, W. M., Ravilly, S., Berde, C., & Wohl, M. E. (1997). End-of-life care in cystic fibrosis. *Pediatrics*, 100, 205-209.

Objective. To document the use of preventative, therapeutic, and palliative care in patients with cystic fibrosis (CF) during the last month of life, relative to traditional "comfort only" approach developed for childhood cancer.

Design. Retrospective chart review.

Setting. Cystic Fibrosis Center, Children's Hospital, Boston, USA.

Participants. Patients >5 years who died from CF-related chronic respiratory disease between 1984-1993. 71 cases were reviewed, of which 15 were excluded because either terminal care information was unavailable, death followed lung transplantation, they were <5 years at the time of death, or death was due to suicide. Of the remaining cases, 44 records were available for review (mean age at time of death = 27 years; range=6-46 years).

Main Outcome Measures. Use of oral vitamin preparations was considered preventative care; use of intravenous antibiotics, chest physical therapy, assisted ventilation, or phlebotomy for serum electrolytes were considered therapeutic care; and administration of oral or intravenous opiates for pain and dyspnea was considered palliative care.

Results. During the last 12 hours of life, therapeutic care in the form of intravenous antibiotics was used in 75% of cases, while 36% received chest physiotherapy, and during the last

24 hours of life phlebotomy was performed in 50% of the cases. Also during the last 12 hours of life, 72% received preventative care in the form of oral vitamin preparations. A majority of patients (86%) received palliative care in the form of opioids at the time of death. Daily opioid administration for more than 3 months was used in 25% of cases. Duration of opioid use to manage dyspnea ranged from <1 hour to >30 days, and the majority of patients were treated with maximum opioid doses of <5mg/hour (range = 5-30mg/hour). At the time of death, all patients had a do not resuscitate order and all but one died in the hospital.

Conclusions. A combination of preventative, therapeutic, and palliative care was provided at the end-of-life phase for CF patients and may serve as an alternative approach to the traditional "comfort only" terminal care model developed for childhood cancer.

Commentary

The amount of information available about pediatric pain management in the terminally ill lags considerably behind that available for the adult population. These articles serve to clarify several important issues in this difficult area. The very important point that the overwhelming majority of pediatric pain in the terminal phase is able to be managed with conservative measures is highlighted through three articles describing notable exceptions. The small subpopulation of terminally ill children who require extraordinary measures such as regional anesthesia, massive opioid administration, or the provision of terminal sedation are the focus of discussion in the articles by Collins et al. (1995, 1996) and Kenny and Frager (1996). Such difficult cases can cause conflict and confusion with regards to ethical principles and appropriateness of care that must be anticipated and formally addressed.

Partridge et al. (1997) describes the analgesic management for 120 dying infants over a 3 year period who were having life support withdrawn or withheld. The doses of opioids used for 64% of the infants who received opioids were described as being within the usual pharmacologic range of 0.1-0.2mg/kg/dose of parenteral morphine equivalents. Although this dose is within the usual range for children outside the neonatal period, the standard recommendation for infants is the administration of ¼ to ½ of the usual pharmacologic range of 0.1-0.2 mg/kg, followed by careful titration to effect. Other than this detail, and an inappropriate reference to "addiction" when referring to opioid tolerance, this article should be very helpful for centring a discussion among neonatologists as to how end-of-life distress or

potential distress should best be anticipated and managed. The ethical principles supporting management of presumed distress are briefly sketched in this paper. A more elaborate discussion to help with resolution of the potential ethical conflict and confusion is found in Kenny and Frager (1996) and Siever (1996).

Both of Collins' papers describe the infrequent requirements for what would be considered "extraordinary" pain interventions for children who are terminally ill from a malignancy. The use of regional anesthesia for this patient population was assessed over an eight year period. Approximately 3% of the children dying with a malignancy over the study period were treated with regional techniques. A similarly small number of children, 6% of the children who died of pediatric malignancies over four years, required "massive" opioid infusions for pain relief. These case reviews set the background for how and when to identify a symptom as "refractory" and what can generally be expected as part of the more usual course of managing pain at the end-of-life in childhood. A more detailed approach to the assessment of refractory symptoms in the terminal phase, including pain, may be found in Kenny and Frager (1996).

Another significant paper about end-of-life symptom management is that of Robinson et al. (1997). This article addresses the care related to end-stage cystic fibrosis. Although pediatric patients are included in the study population, as the age ranged from 6-46 years, it does not describe how many of the 44 patients were in the pediatric age group. Despite this lack of information, the points raised in the article are important ones. Although inevitable, there is a remarkable lack of information about the mode of premature deaths of individuals living with cystic fibrosis, nor are there published guidelines for practitioners on how to best support these patients through the difficult and prominent symptoms of pain and breathlessness. In an illness where respiratory compromise is feared, this article affirms the ethical imperative of providing adequate symptom management. Eighty-six percent of patients with cystic fibrosis who died from related respiratory failure over the 7-year study period received opioid therapy for the symptoms of dyspnea and pain. This article would have been substantially improved through the incorporation of measurements of dyspnea or pain and the degree of relief achieved. The reader is afforded virtually no information as to whether the doses of opioids administered were effective in treating the target symptom. However, in the relatively young field of evaluating symptoms and their management at the end-of-life, it is an excellent start.

Although a relatively infrequent occurrence, the death of a child has long lasting repercussions on family and staff. Due to a paucity of information and guidelines about end-of-life

care, practitioners are often left to their own devices in managing these patients through an inconsistent pattern of trial and error and prayer. These articles can help to serve as a catalyst for discussion among the various team members in intensive care units, neonatal nurseries, pediatric wards, and community health practices. Together, a comprehensive approach to the dying child can be planned to help best support not only the child but also those who bear witness to this most difficult of times in life.

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References

- Kenny, N. P. & Frager, G. (1996). Refractory symptoms and terminal sedation of children: Ethical issues and practical management. *Journal of Palliative Care*, 12(3), 40-45.
- Siever, B. A. (1994). Pain management and potentially life-shortening analgesia in the terminally ill child: The ethical implications for pediatric nurses. *Journal of Pediatric Nursing*, 9, 307-312.

Acetaminophen... Use as Directed?

Ragg, P. & Davidson, A. (1997). Comparison of the efficacy of paracetamol versus paracetamol, codeine and promethazine (Painstop®) for premedication and analgesia for myringotomy in children. *Anaesthesia and Intensive Care*, 25, 29-32.

Objective. To determine and compare the effectiveness and rate of side-effects of paracetamol and paracetamol combined with other analgesics used following ear surgery:

Design. Double-blind, randomized controlled trial.

Setting. Royal Children's Hospital, Melbourne, Australia.

Participants. Children undergoing scheduled day myringotomy with or without middle ear drain tube insertion (n=95; 35 female; age range=1-12 years). The majority of surgeries were bilateral.

Interventions. Children received either 1 mL/kg of Painstop® (n=50; paracetamol 12 mg/kg, codeine 0.5 mg/kg and promethazine 0.65 mg/kg in 5% alcohol v/v) or 1 mL/kg of paracetamol 20 mg/kg (n=45) 30 to 60 minutes prior to anaesthesia induction.

Main Outcome Measures. Pain was assessed by a blinded observer upon arrival to the post-anaesthesia care unit, and

30, 60, and 120 minutes following surgery using a 0 (nil) to 3 (severe) rating scale. Children older than 3 years used a 4-item faces scale to rate their pain. Sedation was assessed as awake, drowsy, or asleep. Side-effects were noted.

Results. No difference was observed between groups on rate of complications. The time to first eye-opening and oral intake was significantly longer in the Painstop® group. No differences were found between groups on either observer ratings or self-report ratings of pain.

Conclusions. Excellent analgesia was obtained in both groups and both provided safe premedication for this type of surgery.

Penna, A. C., Davidson, K. P., & Penna, C. M. (1993). Is prescribing paracetamol 'pro re nata' acceptable? *Journal of Paediatrics and Child Health*, 29, 104-106.

Objective. To determine the prescribing pattern of paracetamol in a children's department in a general hospital.

Design. Chart review.

Setting. Westmead Hospital, Sydney, Australia (general urban hospital)

Participants. All children (n=299) admitted to the hospital during a one month period.

Main Outcome Measures. Rate of paracetamol use, reasons for use, the specific regimen prescribed, and maximum cumulative dose administered was determined from the health records of participants.

Results. 190 children (63.5%) were prescribed paracetamol during their hospital stay, and 152 were given this treatment. They ranged in age from 1-145 months (1 month - 12.1 years). The majority of these children had surgical and medical (e.g., asthma) admissions. The dosage in 77.9% of cases was 4 hourly p.r.n., which was more likely to result in administration of paracetamol of 120 mg/kg/day. Twenty-six children were given a dose greater than 90 mg/kg/day; 9 of these children were less than 1 year of age. The most frequent indication for paracetamol use was fever and pain.

Conclusions. The potential for hepatotoxicity in very young infants exists; caution needs to be used when prescribing paracetamol p.r.n. or on a regular basis.

Anderson, B., Anderson, M., & Hastie, B. (1996). Paracetamol prescribing habits in a children's hospital. *New Zealand Medical Journal*, 109, 376-378.

Objective. To determine current prescribing habits in a children's hospital to assess safety of current practice.

Design. Retrospective survey.

Setting. Children's hospital.

Participants. All medical staff (administrators, radiotherapists, and research fellows excluded) involved in patient care at a children's hospital. Eighty questionnaires were sent out and 53 were (66%) returned.

Main Outcome Measures. Staff were asked about safe daily doses of paracetamol for children > 4 months, ≤ 3 months, and neonates in the first 2 weeks of life. Hospital pharmacists then noted prescription charts and recorded doses in excess of 95 mg/kg/day.

Results. Thirteen practitioners recommended a dose greater than 90 mg/kg/day for the oldest age group and 4 recommended this dose as safe for children ≤ 3 months. Between 5 and 11 practitioners reported that they did not know what a safe dose of paracetamol was, depending on the age group in question. Based on the pharmacy audit, between 2% and 3% of children in the two oldest age groups were administered paracetamol which exceed 95 mg/kg/day.

Conclusions. Although the incidence of paracetamol over-prescribing and over-administration is relatively low, more attention should be directed to the total daily dose of this drug. Further research on paracetamol toxicity should be conducted.

Anderson, B., Kanagasundaram, S., & Woollard, G. (1996). Analgesic efficacy of paracetamol in children using tonsillectomy as a pain model. *Anaesthesia and Intensive Care*, 24, 669-673.

Objective. To compare the analgesic efficacy of paracetamol given orally compared to rectally in children for pain from tonsillectomy.

Design. Randomized, double-blind, controlled trial.

Setting. Children's hospital.

Participants. Children (n=100; mean age = 7 years; 47 males) scheduled to have tonsillectomy with or without adenoidectomy.

Interventions. Children were randomly assigned to receive either 40 mg/kg of paracetamol elixir 40 minutes prior to surgery or 40 mg/kg of paracetamol in a suppository following anaesthetic induction.

Main Outcome Measures. A nurse, blinded to method of drug delivery, assessed pain 30 minutes following surgery using an objective pain scale. Children provided self-reports using a "smiley face" scale. Postoperative morphine usage was also noted.

Results. Children given oral paracetamol had higher peak plasma concentrations of paracetamol than children given rectal paracetamol. Children given oral paracetamol had lower median pain scores than children given rectal paracetamol.

Only 10 children receiving oral paracetamol required morphine following surgery compared to 23 in the rectal paracetamol group. There was no difference observed in the number of children who vomited in each group.

Conclusions. A clear relation was observed between plasma concentration of paracetamol and analgesia. The authors concluded that paracetamol provides adequate analgesia following tonsillectomy provided that plasma concentrations are in the antipyretic range.

Anderson, B. J., Woolard, G. A. & Holford, N. H. G. (1995). Pharmacokinetics of rectal paracetamol after major surgery in children. *Paediatric Anaesthesia*, 5, 237-242.

Objective. To determine the pharmacokinetics of rectally administered paracetamol given to children following orthopaedic surgery.

Design. Before-after trial; duration of follow-up=18 hours.

Setting. Not stated.

Participants. 21 children enrolled but 1 child was removed because she was given an additional dose of paracetamol (10 males; median age= 8 years; range=12 mo - 17 years). Five children had lower limb surgery and 15 children had spinal surgery. All children required overnight monitoring in a postoperative observation area.

Intervention. 40 mg/kg of rectal paracetamol was given postoperatively.

Main Outcome Measures. Blood samples were taken at the time of drug administration and every hour for first 4 hours, every 2 hours for next 6 hours, and every 4 hours for following 8 hours. Volume of distribution (Vd/F), clearance (Cl/F), first-order absorption rate constant (KA), lag time (Tlag), maximum concentration (C_{max}), time to C_{max} (T_{max}), fraction of drug absorbed (F), and elimination half life (T_{1/2}), of serum paracetamol were determined using appropriate analytical methods.

Results. The mean plasma concentration of paracetamol at 6 hours following administration was 0.07 mmol/L, within the antipyretic range. The mean C_{max} was 0.115 mmol/L, which is well below levels associated with liver toxicity. The mean T_{max} was 137 minutes. However, there was considerable variability across children in values for all variables, thus mean values should be interpreted with caution.

Conclusions. The authors suggested that due to the coefficients of variance of 40%, some children may not achieve a C_{max} which is therapeutic.

Rivera-Penera, T., Gugig, R., Davis, J., McDiarmid, S., Vargas, J., Rosenthal, P., Berquist, W., Heyman, M. B., & Ament, M. E. (1997). Outcome of acetaminophen overdose in pediatric patients and factors contributing to hepatotoxicity. *Journal of Pediatrics*, 130, 300-304.

Objective. To determine the outcome of acetaminophen overdose in a pediatric population and to assess factors related to toxic effects in the liver.

Design. Retrospective chart review.

Setting. Several tertiary care hospitals in California, USA.

Participants. Seventy-three children 19 years old or younger who were diagnosed with acetaminophen overdose with no previous history of liver disease. Children were divided into study groups based on results of pretreatment liver tests: the abnormal liver test group consisted on children whose aspartate or alanine transaminase values were ≤ 100 U/L; the normal liver test group consisted of children whose liver tests were normal.

Main Outcome Measures. The effect of the following variables on outcome was examined: amount of acetaminophen ingested (mg/kg); demographic information; time between drug ingestion and onset of symptoms; time between drug ingestion and hospital admission; time between drug ingestion and N-Acetylcysteine administration; number of overdoses; and use of other medications that alter hepatic metabolism.

Results. All children who had abnormal liver tests ($n=28$; 38%) developed severe hepatotoxicity. Six of these children required liver transplantation; 5 were successful and 1 child died immediately following surgery. All of these 6 children were less than 10 years old and all had late-stage encephalopathy. The remaining 22 children were managed medically. Of these, 18 were given N-Acetylcysteine; 17 children responded well and 1 died. The remaining five children did not qualify for N-Acetylcysteine therapy and their liver function returned to normal within 3-5 days following acetaminophen ingestion. Of the 45 children with normal liver test results, 30 (66%) had toxic serum levels and were given N-Acetylcysteine. No child in this group developed liver failure.

Conclusions. In this study, parental dosing errors in children younger than 10 years and suicidal gestures in children older than 11 years of age were the most frequent causes of acetaminophen overdosing. Contributing factors to toxic liver effects included delayed treatment, ingestion of other medications with hepatotoxic effects, and undetected multiple overdosing

Commentary

The perioperative analgesic efficacy of single oral doses of at least 15 mg/kg of acetaminophen has been proven in adults (Moore et al., 1997) and in children using pain models such as myringotomy tube insertion (Tobias, 1995; Ragg & Davidson, 1997).

What dose?

The recommended maximum daily dose for short term use (< 48 hours) of acetaminophen is now 90 mg/kg/day (Temple, 1983; Nahata, 1984). The best dosing regimen and plasma levels required for optimum perioperative analgesia are unknown.

Penna et al. (1993), in a retrospective audit of acetaminophen usage for pyrexia and analgesia, showed that up to 60% of pediatric inpatients received acetaminophen and that the dose received was most likely to exceed 90 mg/kg/day (74% of patients) when a q4h PRN dosage regimen was used. One can infer from these data that the individual doses prescribed were greater than 15 mg/kg and that patients received every possible dose. Anderson et al. (1996a) described a 17% incidence of overprescribing.

Current evidence supports a preoperative dose of at least 20mg/kg po for the management of mild postoperative pain in children. This dose was as effective as a mixture of acetaminophen, codeine, and promethazine in preventing postoperative pain after myringotomy (Ragg & Davidson, 1997).

Plasma levels at 24 hours after a scheduled dosing regimen of 20 mg/kg q6h po (80 mg/kg/day) resulted in peak levels of 106 $\mu\text{mol/L}$ (range=45-139 $\mu\text{mol/L}$) and low trough levels of 50 $\mu\text{mol/L}$ (range=21-83 $\mu\text{mol/L}$; Sanderson, 1997). The low trough levels may be subtherapeutic in more severe pain models.

In children undergoing tonsillectomy, with or without adenoidectomy, a preoperative dose of 40mg/kg po of acetaminophen elixir resulted in postoperative plasma levels of 150 $\mu\text{mol/L}$ (SD=60 $\mu\text{mol/L}$). Lower pain scores in the recovery room were associated with plasma acetaminophen concentrations greater than 70 $\mu\text{mol/L}$ (Anderson et al., 1996b).

The optimum short term (< 48 hours) oral dose in healthy children may be 30 mg/kg q8h (Nahata, 1984) or involve a higher loading dose and subsequent smaller scheduled doses.

What route?

The rectal route of administration of acetaminophen results in delayed (T_{max} 2.3h) and variable plasma levels. It is not recommended when a rapid onset of analgesia effect is

required (Anderson et al., 1995). Pre- or intraoperative rectal administration may be useful for providing analgesia in the later postoperative period (e.g., 2-4 hours postoperative) and in cases when oral intake is not tolerated. An initial dose of 40-45 mg/kg is recommended. Determination of the optimum dose interval when this higher dose is used requires further investigation but it is likely to be q8h or longer.

Is toxicity a problem?

Hepatic and renal toxicity are associated with plasma levels of > 800 µmol/L and these may occur after a single dose of > 150 mg/kg. Unintentional toxicity occurs at the hands of caregivers who administer the wrong dose due to failure to follow directions, use of improper formulation, or use multiple acetaminophen-containing analgesics (Rivera-Penera, 1997). Scheduled acetaminophen discharge orders with attention to the specific formulation may be safer for the family management of pain after discharge.

The routine perioperative use of acetaminophen should be short term in patients without significant coexisting hepatic and renal disease. Other risk factors include malnutrition and dehydration. Patients on medications which induce the hepatic P450 system (e.g., phenobarbital, phenytoin, rifampin) or other hepatotoxins are at higher risk for toxicity.

In conclusion, the use of oral acetaminophen for perioperative analgesia should not be "as directed" (i.e., 10-15 mg/kg q4-6 h PRN up to 65 mg/kg/day). The optimum 24 hour dose regimen for perioperative analgesia requires further investigation.

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References

- Moore, A., Collins, S., Carroll, D., & McQuay, H. (1997). Paracetamol with and without codeine in acute pain: A quantitative systematic review. *Pain*, 70, 193-201
- Nahata, M. C., Powell, D. A., Durrell, D. E., & Miller, M. A. (1984). Acetaminophen accumulation in pediatric patients after repeated therapeutic doses. *European Journal of Clinical Pharmacology*, 27, 57-59.
- Sanderson, P. M., Montgomery, C. J., & Betts, R. (1997). Plasma levels of acetaminophen at 24 h after a perioperative oral dose regimen of 20 mg/kg q6h in paediatrics. *Canadian Journal of Anaesthesia*, 44, A55A.
- Temple, A. R. (1983). Pediatric dosing of acetaminophen. *Pediatric Pharmacology*, 3, 321-327.
- Tobias, J. D., Lowe, S., Hersey, S., Rasmussen, G. E., & Werkhaven, J. (1995). Analgesia after bilateral myringotomy and placement of

pressure equalization tubes in children: acetaminophen versus acetaminophen with codeine. *Anaesthesia and Analgesia*, 81, 496-500.

Presence of Parents During Painful Procedures

Kain, Z. N., Mayes, L. C., Caramico, L. A., Silver, D., Spieker, M., Nygren, M. M., Anderson, G., & Rimar, S. (1996). Parental presence during induction of anesthesia: A randomized controlled trial. *Anesthesiology*, 84, 1060-1067.

Objective. To examine the usefulness of parental presence as a behavioral intervention during anesthesia induction for children undergoing outpatient surgery.

Design. Randomized controlled trial.

Setting. Children's Hospital at Yale-New Haven, USA.

Participants. Eighty-four children (range=1-6 years) undergoing elective outpatient surgery and general anesthesia. Children who had previous surgery or hospitalization, or a developmental delay were excluded. Control and intervention groups did not significantly differ on demographic characteristics or baseline measures of parent and child anxiety and child temperament.

Intervention. Participants were randomly assigned to remain with or be absent from their child during induction of general anesthesia; no description of parents' behavior during induction was provided.

Main Outcome Measures. Child anxiety was assessed from serum cortisol. A number of behavioral measures based on parent and observer report assessed child temperament, and parent and child anxiety. Measures were taken in the preoperative holding area, during induction, and at 2 weeks and 6 months post-surgery. Ratings of perceived helpfulness to the child during induction were also used.

Results. The parental presence group did not significantly differ from the parental absence group on measures of anxiety. Predictors of the child's anxiety during anesthesia induction, as measured by cortisol concentration, included parental presence, child's age, baseline temperament of the child, and parent trait anxiety. Children had lower cortisol concentrations when their parent was present, if they were > 4 years of age, the parents' trait anxiety was low, and the child had a low baseline score on the activity subscore of the measure of temperament. A majority of parents rated themselves as helpful to their child (90%) and the anesthesiologist (68%) by being present during the induction, but only a minority of the anesthesiologist's ratings viewed parental presence as helpful

(12%).

Conclusions. Parental presence may be an effective behavioral intervention for some children undergoing anesthesia induction for outpatient surgery, particularly if the child is older than 4 years or has a low baseline activity level as determined by an assessment of the child's temperament, and if the parent has low trait anxiety.

Fenlon, W. L., Dobbs, A. R., & Curzon, M. E. J. (1993). Parental presence during treatment of the child patient: a study with British parents. *British Dental Journal*, 174 (23), 23-28.

Objective. To examine the effect of parental presence on child behavior while at the dentist and to determine parents' preferences and reasons for being present/absent.

Design. Randomized controlled trial.

Setting. Paedodontic Clinic of the Central Hospital at Leeds.

Participants. 32 children (range=4-12 years; mean=8 years; 14 girls) attending the dentist with a parent (23 mothers) for a routine check-up .

Interventions. Parents were randomly assigned to either remain or not remain with their child during the visit.

Main Outcome Measures. Before treatment, parents reported frequency of attendance and separation of the child, the parent's feelings about separation, and reasons that they would like to be present or absent during treatment. Parents also filled out a dental anxiety scale. Children's behavior was videotaped during treatment and was assessed using the Frankl Scale which describes a child's behavior during a dental situation as either "definitely negative", "negative", "positive", or "definitely positive". After treatment, parents reported their feelings about their position, preference for future positioning, and the parent's perception of the child's enjoyment of the visit.

Results. There were no significant differences in the behavior of children whose parents were present compared to those whose parents were absent during treatment. There was a trend suggesting that younger children behaved more negatively than older children when separated from their parents, $p < 0.084$; further, all the negative behavior was displayed by the 3 youngest participants. All parents indicated that they preferred to be present for their child's dental visit, and only 5 parents out of 32 noted occasions when they would prefer to be absent (e.g., during an extraction).

Conclusions. Children's behavior did not appear to be related to whether parents were present or absent during a dental visit. The most common reasons that parents indicated for remaining with their child were: 1) it was also the child's

preference; and 2) the parent wanted to observe the check-up. Findings suggest that age may be an important factor in determining whether a parent should remain with their child during a dental procedure.

Bauchner, H., Vinci, R., Bak, S., Pearson, C., & Corwin, M. J. (1996). Parents and procedures: A randomized controlled trial. *Pediatrics*, 98, 861-867.

Objective. To examine the influence of parental presence during common invasive procedures performed on children on pain, procedure, parent and clinician anxiety, and parental satisfaction with care.

Design. Randomized controlled trial.

Setting. Boston City Hospital pediatric emergency department, Boston, USA.

Participants. Children < 3 years old undergoing venipuncture, intravenous cannulation, or urethral catheterization and their parents participated. A total of 431 parents participated (75% of eligible 572 parents; n=153 in the intervention group; n=147 in the present group; and n=131 in the not present group). Groups had similar demographic characteristics, prior pediatric emergency room experience, similar distributions of procedures, and frequency of hospitalizations.

Intervention. Parents were randomly assigned to one of three groups: (1) parent was present and given instructions on how to calm and relax their child; (2) parent was present but not given instructions; (3) no parent was present. Parents were given instructions to touch, talk to, and maintain eye contact with their child during the procedure, and refrain from restraining their child.

Main Outcome Measures. Parents and clinicians rated the child's pain on a 3-point categorical scale (1=severe/great; 2=moderate; 3=some/little). Cry analysis was also used to measure pain. Parents rated their overall satisfaction with their child's care.

Results. There were no significant differences between groups on pain ratings or on parent ratings of satisfaction. Procedures performed in the presence of parents with instructions, those without, as well as those with parents absent, were similar in the performance of procedures. Groups did not differ on ratings of clinician anxiety or parental satisfaction with the child's care. Clinicians and parents present during procedures demonstrated poor agreement in ratings of the child's pain. Clinicians were less likely to rate the child's pain as extreme or severe (15%) than the parent who was present (52%). Parents present during procedures reported less anxiety than those absent.

Conclusions. Parental presence is not an effective

intervention for reducing pain during common invasive procedures, but it did not interfere with the clinicians' performance of the procedure nor did it increase the clinicians' anxiety. Further, parental anxiety was lower when present. Parents who wish to be present during these common procedures should be encouraged to do so.

O'Laughlin, E. & Ridley-Johnson, R. (1995). Maternal presence during children's routine immunizations: The effect of mother as observer reducing child distress. *Children's Health Care, 24*(3), 175-191.

Objective. To examine the impact of maternal involvement on child distress during a routine immunization.

Design. Randomized controlled trial.

Setting. Private pediatric practice.

Participants. 36 children (mean age=5.1 years; range=4.8-5.7 years; 19 boys) and their mothers undergoing 5-year "well-child" examinations and immunizations.

Intervention. Participants were randomly assigned to 1 of 4 groups: mother absent during injection; mother present but asked to watch only; mother present as usual (noninstructed, high maternal involvement, routine control group); and mother present and trained as coping coach with a choice of one of five methods of distraction.

Main Outcome Measures. The Pleasure scale of the Self-assessment mannequin (Lang, 1978) was used as a self-report measure of pre- and post-injection emotional response. Observations of child expressive and disruptive behavior were made before, during, and following the injection using seven distress behaviors grouped into three categories: expressive behaviors (cry/scream, fuss/whine, verbal pain, and request for emotional support); resistant behaviors (verbal resistance and physical resistance); and nonverbal distress (muscular rigidity). Nurses and observers made global ratings of the child's distress using a Likert scale from 1 (least) to 9 (most).

Results. Following the injection, significantly higher levels of pleasure were associated with the watch condition versus the routine condition; no differences were observed between the remaining two groups. Children in the routine condition displayed significantly more expressive behavior than in the watch condition; again, no differences were observed between the remaining groups. No differences were observed between groups on global ratings of child distress.

Conclusions. Maternal use of distraction did not appear to influence self-reported or observed child distress. Children who showed the least amount of distress following the immunization were those in the watch condition. The authors suggested that this condition facilitated the best outcome

because it minimized the cueing or disinhibition of protest behavior typical of the routine condition. Future research should assess effectiveness of this intervention with more stressful medical procedures and a more anxious population.

Blount, R. L., Powers, S. W., Cotter, M. W., Swan, S. & Free, K. (1994). Making the system work. Training pediatric oncology patients to cope and their parents to coach them during BMA/LP procedures. *Behavior Modification, 18*(1), 6-31.

Objective. To determine the effectiveness of training young pediatric oncology patients to use coping behaviors prior to and during painful medical procedures, and to evaluate the effectiveness of training their parents to coach them to use these behaviors at appropriate times.

Design. Before-after trial.

Setting. Children's Hospital, Birmingham, USA.

Participants. Three children, aged 4-7 years, diagnosed with acute lymphocytic leukaemia and their parents, referred by the medical staff because they displayed more distress than other patients during bone marrow aspirations (BMA) and lumbar puncture (LP) procedures. Two additional children were recommended for this intervention; one parent declined and the other moved.

Interventions. Parents were trained to distract their child by interacting with toys, coloring, reading books, or other topics of conversation. Party blowers were used as an age-appropriate method of deep breathing during the painful phase of the procedure. Training took place the morning prior to the painful procedure.

Main Outcome Measures. Child distress, child coping, and adult coping promoting was measured using the CAMPIS and CAMPIS-R; Blount, et al. (1989, 1990).

Results. All of the parents increased their rate of coping. Each child responded with increased coping and decreased observable distress after the first treatment session. One child returned to baseline levels of coping and distress on the next two sessions. The other two children maintained their high rates of coping and low rates of observable distress during the remaining treatment and maintenance sessions. Parents' coaching of their children to use coping behaviors also remained high during maintenance sessions.

Conclusions. Two of the 3 child-parent pairs benefitted significantly from the intervention aimed at increasing a child's coping behaviors during painful procedures. Future research should examine additional psychosocial factors (e.g., anxiety, depression) which may impact on promoting coping in a medical setting.

Commentary

Should parents stay with their children during painful procedures? This question has been studied in the contexts of venepuncture and immunization, dental procedures, induction of anaesthesia, burn care, lumbar puncture, bone marrow aspiration, and minor emergency procedures such as suturing.

It is well established that most parents and children prefer to stay together, and children report that the presence of a parent is one of their most important aids in coping (Bauchner et al., 1989; Gonzalez et al., 1989; Ross & Ross, 1988). Parental presence is assumed to reassure the child, prevent the added stress of panic at separation, and distract attention from frightening aspects of the situation. On the other hand, policies excluding parents have traditionally been justified by the supposition that their presence can increase acting out and pain expression by children (thereby perhaps increasing their subjective pain), and that parental presence makes staff members nervous and wastes their time (Brown & Ritchie, 1990; Kain et al., 1996).

We identified nine controlled trials in which a parent (usually the mother) was randomly assigned to remain or not to remain with the child during a painful or stressful procedure. It is difficult to collate the results of these studies because of major differences in their procedures and dependent variables. For example, in one study the "absent" parent was known by the child to be watching through a one-way mirror (Fenlon et al., 1993). Moreover, diverse measures of outcome, such as self-rated and parent-rated distress, observer-rated negative behaviour such as crying and muscular rigidity, and physiological measures such as blood cortisol, tend to have low correlations with each other. However, based on overt distress alone, the results can be summarized as follows. In four studies, parent presence *per se* had no significant effect (Bauchner et al., 1996; Doctor, 1994; Fenlon et al., 1993; Kain et al., 1996). In two studies, children in the parent-absent condition showed more distress (Frankl et al., 1962; Vernon et al., 1967). In three studies, children in the parent-present condition showed more distress (Gonzalez et al., 1989; O'Laughlin & Ridley-Johnson, 1995; Shaw & Routh, 1982).

Research interest is shifting towards a greater emphasis on what parents actually do in the treatment room, rather than simply on their presence. Some parent behaviours, such as criticism, excessive reassurance, and commands, are associated with greater distress (Dahlquist et al., 1995). Parents are not often instructed as to how they can help (Watt-Watson et al., 1990). On the other hand, parents who are taught to be active in distracting their children through conversation and reading, or in reassuring them through touch

and eye contact, are able to reduce the children's distress (Blount et al., 1992, 1994). Many appropriate ways for parents to help have also been outlined by Kuttner (1996).

It should be routine practice in pediatric settings to encourage parents to remain present during most health-care procedures, and to support their use of touch and distracting verbal interaction to facilitate their children's efforts to cope. Future research should focus on finding effective methods of training for parents who are highly anxious or who have children under four years of age.

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References

- Bauchner, H., Vinci, R., & Waring, C. (1989). Pediatric procedures: Do parents want to watch? *Pediatrics*, *84*, 907-909.
- Blount, R., Bachanas, P., & Powers, S. (1992). Training children to cope and parents to coach them during routine immunizations: Effects on child, parent, and staff behaviors. *Behavior Therapy*, *23*, 689-705.
- Brown, J., & Ritchie, J. (1990). Nurses' perceptions of parent and nurse roles in caring for hospitalized children. *Children's Health Care*, *19*, 28-36.
- Dahlquist, L., Power, T., & Carlson, L. (1995). Physician and parent behavior during invasive pediatric cancer procedures: relationships to child behavioral distress. *Journal of Pediatric Psychology*, *20*, 477-490.
- Doctor, M. (1994). Parent participation during painful wound care procedures. *Journal of Burn Care and Rehabilitation*, *15*, 288-292.
- Frankl, S., Shiere, R., & Fogels, H. (1962). Should the parent remain with the child in the dental operator? *Journal of Dentistry in Children*, *34*, 212-218.
- Gonzalez, J., Routh, D., Saab, P., Armstrong, F., Shifman, L., Guerra, E., & Fawcett, N. (1989). Effects of parent presence on children's reactions to injections: behavioral, physiological, and subjective aspects. *Journal of Pediatric Psychology*, *14*, 449-462.
- Kuttner, L. (1996). *A Child in Pain: How to Help, What to Do*. Vancouver: Hartley & Marks.
- Ross, D., & Ross, S. (1988). *Childhood Pain: Current Issues, Research, and Management*. Urban & Schwarzenberg, Baltimore.
- Shaw, E., & Routh, D. (1982). Effect of mother presence on children's reaction to aversive procedures. *Journal of Pediatric Psychology*, *7*, 33-42.
- Vernon, D., Foley, J., & Shulman, J. (1967). Effect of mother-child separation and birth order on young children's responses to two potentially stressful experiences. *Journal of Personality and Social Psychology*, *5*, 162-174.
- Watt-Watson, J., Evernden, C., & Lawson, C. (1990). Parents' perceptions of their child's acute pain experience. *Journal of Pediatric Nursing*, *5*, 344-349.

Announcements

Meetings

September 24 -27, 1998: *2nd Biennial International Forum on Pediatric Pain*, White Point Beach Resort, White Point, Nova Scotia, Canada. The topic for the meeting will be chronic and recurrent pain, and it will again be a focussed, research-based conference, with many distinguished international faculty including Tony Dickenson (UK), Sunny Anand (USA), Anna Taddio (Canada), Gunnar Olsson (Sweden), Bo Larsson (Sweden), Neil Schechter (USA), Navil Sethna (USA), and Patrick McGrath (Canada). Registration is limited to 120 participants. Further information is available at our website <<http://is.dal.ca/~pedpain/pedpain.html>>. Contact: Conventional Wisdom via email at <katefin@chebucto.ns.ca>; fax (902) 423-5232; or telephone (902) 453-4664. Mailing address: CONVENTIONAL WISDOM, 6496 Liverpool St., Halifax, NS, B3L 1Y4, Canada.

Other

Teaching Module: The Network Project Teaching Module on the Management of Cancer Pain in Children. Prepared by John J. Collins, Charles B. Berde, and Maura E. Byrnes, these educational materials contain a comprehensive lecture with references and over 50 colour slides. Cost: \$225.00 (US dollars, make cheque payable to "The Network Project, CC5112/F7062"). For further information contact the Network Project, Memorial Sloan-Kettering Cancer Center, Box 421, 1275 New York Ave, New York, NY, 10021, USA. Tel: (212) 583-3042; Fax: (212) 230-1953.

Treatment for Fibromyalgia: An exercise videotape designed specifically for children and adolescents with fibromyalgia is now available. This videotape includes warm up, aerobic, and cool down sections, with intermittent heart rate checks. The video can be purchased for individual use (\$19.99 per copy (US dollars), includes shipping) and institutional use (Preview #604001 \$45.00; Purchase #294001 \$89.00 first copy, then \$15.00 for each additional copy). Contact: Dr. Lynn Rusy, Pediatric Pain Clinic, Children's Hospital of Wisconsin, 9000 W. Wisconsin Ave., PO Box 1997, Mulwaukee, WI, 53201, USA. (Tel) 414-266-2507 or 1-800-444-7747 or email: maxishare@chw.org.

Special Article: Schechter, N. L., Blankson, V., & Pachter, L. M. (1997). The ouchless place: No pain, children's gain, *Pediatrics*, 99(6), 890-894. This paper details a multidisciplinary program developed to promote adequate pain management on a pediatric inpatient unit of a large, urban, teaching hospital. The authors discuss issues surrounding program development, quality assurance, and family-centred care.

Website: Visit us on the World Wide Web (<http://is.dal.ca/~pedpain/pedpain.html>).

If you would like to participate

Your participation in abstracting and writing commentaries for the Pediatric Pain Letter is welcomed. Please send submissions according to the specifications outlined in our Author's Kit. An Author's Kit can be obtained from Julie Goodman, Managing Editor, Pediatric Pain Letter, Psychology Department, Dalhousie University, Halifax, Nova Scotia, B3H 4J1; email jgoodman@is2.dal.ca; requests can be made in writing or by email. Abstracts and commentaries on any aspect of pain in infants, children, and/or adolescents are appropriate. We will attempt to use abstracts and commentaries but the editors reserve the right to edit or reject contributions.

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