Original Article

Use of Patient-Controlled Analgesia for Pain Control for Children Receiving Bone Marrow Transplant

Peter J. Dunbar, MB, ChB, Peter Buckley, MB, FFARCS, Jonathan R. Gavrin, MD, Jean E. Sanders, MD, and C. Richard Chapman, PhD
Pain and Toxicity Research Program, Division of Clinical Research, Fred Hutchinson Cancer Research Center, and Department of Anesthesiology, University of Washington School of Medicine, Seattle, Washington

Abstract
We report 2 years' experience managing 39 preteen (ages 4–12 years) children with patient-controlled analgesia (PCA) for pain associated with bone marrow transplantation (BMT). We prescribed morphine or hydromorphone PCA (starting bolus 20 μg/kg morphine or 2 μg/kg hydromorphone) with or without continuous infusion (CI), for a period of 6–74 days. The duration of PCA use (median 19 days) depended upon severity of mucositis or other painful conditions. The peak morphine use was on the 11th day after BMT. We prescribed CI opioids in addition to PCA, either at night or around the clock, in 52% of patients. Ninety-five percent of children successfully mastered PCA to control pain associated with BMT. We observed no instances of drug misuse, parental tampering, accidental overdose, or difficulty weaning from opioids. We conclude that opioid PCA, with or without CI, over several days or weeks is safe and effective for preteen children suffering BMT-related pain. J Pain Symptom Manage *1995;10:604–611.*

Key Words
Children, PCA, BMT, pain

Introduction

Patient-controlled analgesia (PCA) is a standard technique for short-term postoperative pain control in adults.[1] PCA is indicated for cancer pain, sickle cell crisis pain, and burn pain in adults.[2–5]

Although care providers often assume that children and adolescents lack sufficient maturity to self-administer opioid drugs, studies indicate that both adolescents and children as young as 5 years of age can safely and effectively use PCA for postoperative pain.[6–11] Other reports show adolescents can safely and effectively use PCA for pain of longer duration, sickle cell crisis,[12] burns,[2] and mucositis following bone marrow transplantation (BMT).[13]

Whether preteen (ages 4–12 years) children can successfully use PCA for pain problems that persist over many days still remains at issue. There are no long term studies in the

Address reprint requests to: Peter J. Dunbar, MB, ChB, Fred Hutchinson Cancer Research Center, 1124 Columbia Street, FB635, Seattle WA 98104, USA.
Accepted for publication: April 10, 1995.

0885-3924/95/$9.50
SSDI 0885-3924(95)00122-F

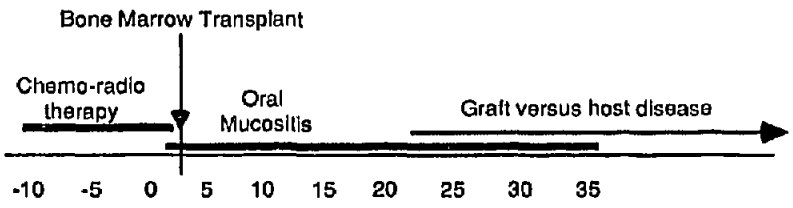


Fig. 1. The time course of bone marrow transplantation (BMT) and its associated pain problems. Day 0 is the day of transplant; the mucositis and graft-versus-host disease (GVHD) are typically of slow onset and variable duration.

literature, although case reports demonstrate its feasibility in this age group.[14] At the Fred Hutchinson Cancer Research Center (FHCRC), we commonly employ PCA for the control of long-term acute pain (mainly oral mucositis) in a BMT setting.[13] We report a retrospective review of the use of PCA in 39 preteen children and describe our methodology for PCA use in this age group.

Methods

The Pain and Toxicity Service provides pain and symptom management service for three 20-bed wards at the FHCRC. BMT is a rescue therapy for refractory or relapsed hematological malignancies and certain other fatal diseases, including some cancers, aplastic anemia and a few inborn metabolic or immune disorders. The medical team prepares patients for BMT by delivering normally supralethal doses of chemotherapy and total body irradiation. Reinfusion of bone marrow occurs after this preparative regimen. During the next 10–18 days, until engraftment occurs, 80%–90% of patients experience severe oral mucositis or other complications sufficiently painful to require opioid analgesics. The mucositis resolves quickly with engraftment of the donated marrow. The time course of BMT related toxicities is illustrated in Figure 1. Opioids are delivered intravenously because patients cannot take medication orally due to mucositis, and thrombocytopenia precludes intramuscular or subcutaneous delivery.

After mucositis, the most common cause of pain is graft-versus-host disease (GVHD). This complication, unique to BMT cases involving nonnative marrow, is a multisystem disorder characterized by cell-mediated rejection of the host (patient) tissues by the graft. GVHD commonly causes abdominal pain. Some patients with GVHD require PCA opioids during the acute phase until immunosuppressive agents work to quiet the syndrome and thus eliminate pain.

We offer opioid PCA, with or without supplemental continuous infusion (CI), to all children who appear to be mature enough to understand our instructions. We emphasize issues of self-care and control and encourage activity. Patients, regardless of age, are instructed to push the button when they hurt, perform oral hygiene once an hour, and get out of bed often. We encourage patients to experiment with balancing analgesic protection for the activities of daily life, hygiene, mouth care, and mobility, against negative opioid side effects such as sedation, nausea, and dysphoria.

Demographics

The FHCRC performed 856 BMTs during the study period, calendar years 1992 and 1993. For this report, we retrospectively reviewed records for all patients who used PCA and were aged 12 years or under. (A few patients younger than 6 years were managed with CI, but insufficient data were collected for reporting.) The Pain and Toxicity Service managed PCA in 39 patients between the ages of 4 and 12 years inclusive (21 male, 18 female) (Figure 2.) Three children had two discrete episodes of PCA use (defined as greater than 7 days off opioids between episodes). All used PCA initially for mucositis and again, later for GVHD, varicella zoster, and relapse of leukemia, respectively.

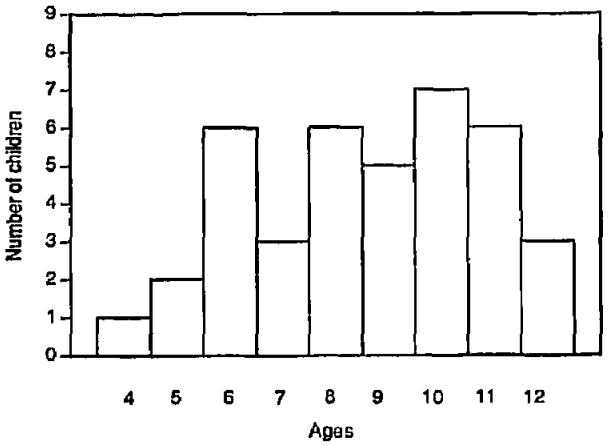


Fig. 2. A histogram of the children's ages in years.

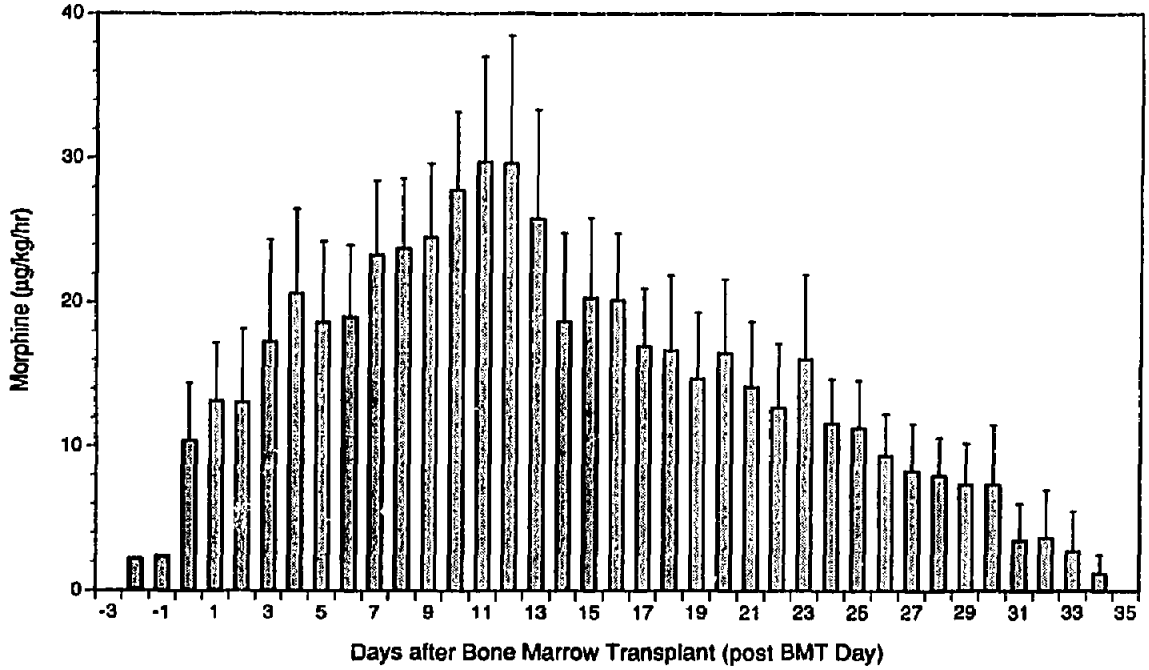
PCA Delivery

We used Abbott 4100 series PCA machines, which permit PCA, CI, and combined PCA + CI modes. This model has a memory that records opioid demands and deliveries. To reduce the risk of medication error, we used only two concentrations of each medication (morphine 1 or 5 mg/mL, hydromorphone 0.2 or 1 mg/mLl).

We prescribed initial bolus settings of approximately 20 μg/kg for morphine and 3 μg/kg for hydromorphone. The lock-out was 8 minutes, and the initial dose range was approximately 15–40 μg/kg. We prescribed morphine for all our patients unless they were allergic to morphine, had renal dysfunction, or had used hydromorphone in the past and preferred it.

Experienced pediatric nurses (staffing ratio 1:2) observed the children closely, taught them how to use the PCA, and adjusted the bolus sizes within the limits prescribed by the Pain and Toxicity Service. The team aimed to titrate medication to patient satisfaction rather than to a predefined pain score. Mucositis pain comes on gradually and loading doses are not generally required (Figure 3).[15] We occasionally started a continuous infusion (CI), approximating 40% of previous 24-hr use to deliver better analgesia or reduce side effects. In response to persistent reports of night pain, and especially if the patient reported being awakened by mucositis pain, we added a nocturnal CI adjusted empirically to provide

Fig. 3. This figure illustrates opioid use over days post-bone marrow transplantation (BMT) for mucositis (the closest analogy to postoperative day), and their mean daily dose (μg/kg/hr) with 95% confidence limits. The pattern of opioid use tended to wax and wane with the severity of oral mucositis and other complications. Overall the patients' opioid demand peaked about day 11. We observed marked patient-to-patient variability.



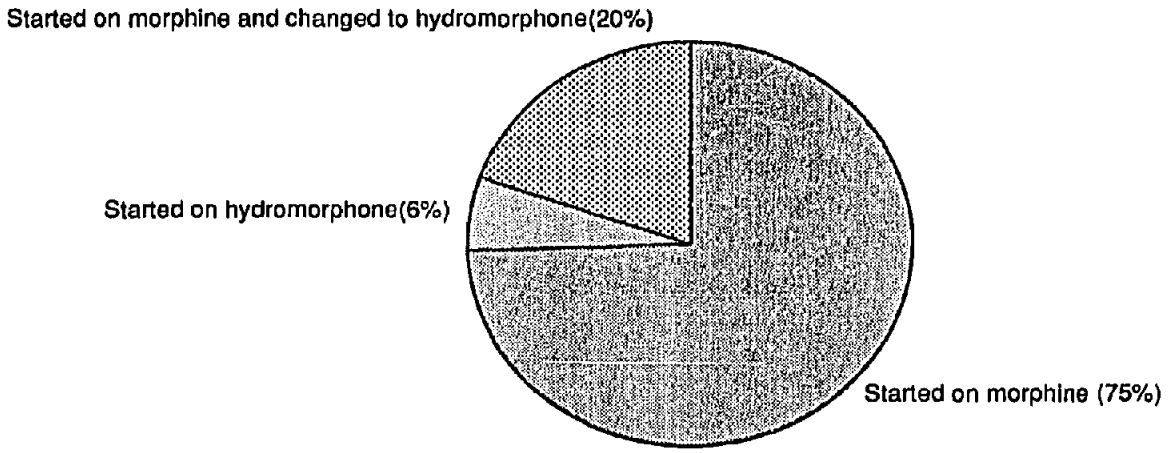


Fig. 4. Opioid used for PCA.

approximately one-half of the child's anticipated need based on the previous night's use. With diminishing pain and mucositis, we did not actively wean the children from the PCA but adjusted the bolus size downward as daily use decreased.

Data Recording

The Pain and Toxicity service (attending or fellow) visited each patient daily and recorded analgesic use by shift from the memory of the PCA machine into our service records. We also recorded pain and symptom evaluations including side effects of opioid and other medications, satisfaction with pain control, and mental status into the patient's chart as clinically indicated.

Results

PCA proved safe and effective for 37 of the 39 children (95%). Only two children failed to benefit from PCA. One boy aged 10 years, had an XYY polysomy, a history of sociopathic behavior, and attention deficit disorder. The other, a girl aged 6 years, had a severely dysfunctional single parent, who was unable to provide normal parental support. The child regressed behaviorally under the stress to a greater degree than similar children with good parental support. Subsequently, we managed pain in these children with a continuous infusion of morphine.

Two children who used PCA successfully died of BMT complications. In both cases a long period of slowly progressive multi-organ failure preceded death. Opioid requirements characteristically declined with deterioration of mental status but increased if respiratory failure requiring intubation interceded and the opioids were used for sedation.

Mean duration of PCA use was 19 days but varied widely: 8 children <10 days, 18 children 10–20 days, 9 children for 20–30 days, and 6 children >30 days. We started the PCA with hydromorphone on three occasions and with morphine on 38 occasions. In ten patients, we changed from morphine to hydromorphone in an attempt to remedy side effects (Figure 4).

The children who successfully used PCA became adept at its use within 2 or 3 days. We did not observe any instance of the following potential problems: respiratory depression, overdose, psychological dependence on PCA, the development of opioid tolerance, or attempted misuse of opioid drugs by a family member. CI, either at night or around the clock, was used in 52% of PCA episodes. We often observed daytime sedation, which was usually corrected by reducing use of antiemetics and other CNS depressants. We changed opioids only after adjusting the antiemetic regime. We did not use stimulants or opioid antgonists during the period studied.

Figure 5 shows the breakdown of the data according to indications for PCA. The majority used it for oral mucositis pain. For those with GVHD, abdominal pain was the most common complaint.

We report these results using days post-BMT, as we believe that it is the standard chronologi-

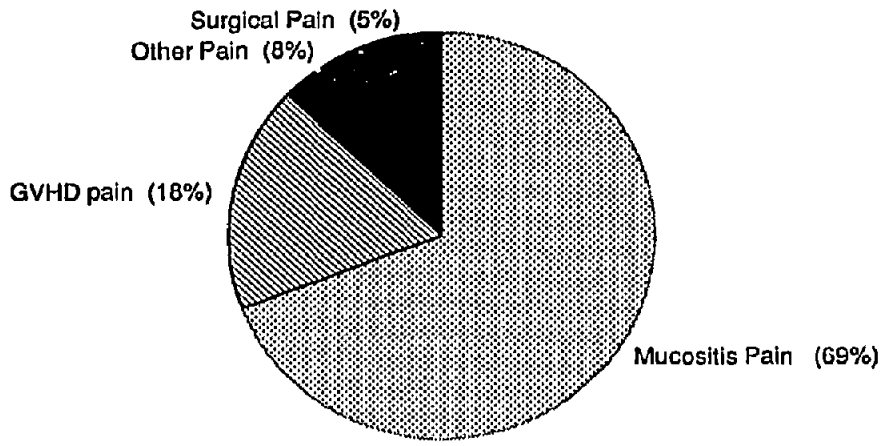


Fig. 5. Shows the breakdown of the episodes according to indications for patient-controlled analgesia (PCA). The majority used it for oral mucositis pain. For those with graft-versus-host disease (GVHD), abdominal pain was the most common complaint.

cal measure for this clinical setting. Figure 3 illustrates opioid use over days post-BMT for mucositis, the number of patients using PCA, and their mean daily dose (μg/kg/hr) with 95% confidence limits. The pattern of opioid use tends to wax and wane with the severity of oral mucositis and other complications. Overall, the patients' opioid demand peaked about day 11.

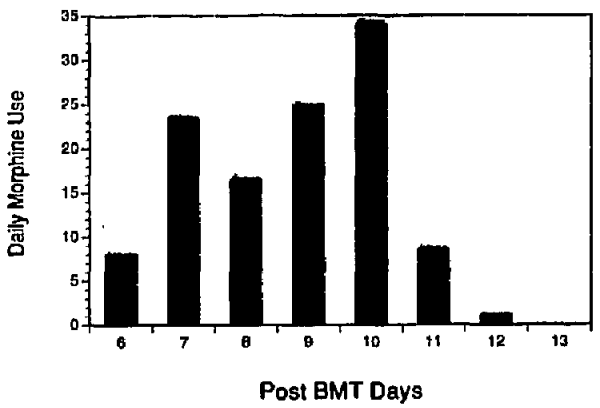
There were wide variations of opioid use in this population, which did not correlate with the patients' ages. We highlight this in the following figures. Figure 6 illustrates the PCA use pattern for a child whose pain started on day 6 and resolved by day 12. Figure 7 shows the opioid use for a child whose mucositis pain decreased till day 16 then flared up again. Figure 8 shows data from a patient who decreased his opioid use until day 28 but, as he developed GVHD, increased it again until control of GVHD at day 46.

Discussion

This study featured a relatively long duration of PCA use. The median duration was 19 days, but six PCA episodes (15%) lasted for more than a month. Postoperative studies describe the short-term problems of opioid use in detail, but longer duration studies may reveal latent problems, such as the development of tolerance to opioids, conflicts between patient family and caregivers, patient frustration, sleep disturbances, and psychological dependence on medication.

In our setting, children undergoing BMT used PCA to control their pain and to facilitate their activities of daily life (mouth care and personal hygiene), rather than to eliminate pain altogether. We believe that active self-care of this sort promotes a quicker recovery from BMT, and we titrated PCA dosage to activity. We did not ask the children to formally rate pain with one of the standard scales, but carefully assessed patient satisfaction with pain control and found this to be a satisfactory way of adjusting the PCA. This may be an area for further investigation as pain scaling can be impracticable in this population.

Fig. 6. Illustrates the patient-controlled analgesia (PCA) use pattern for a child whose pain started on day 6 and resolved by day 12.



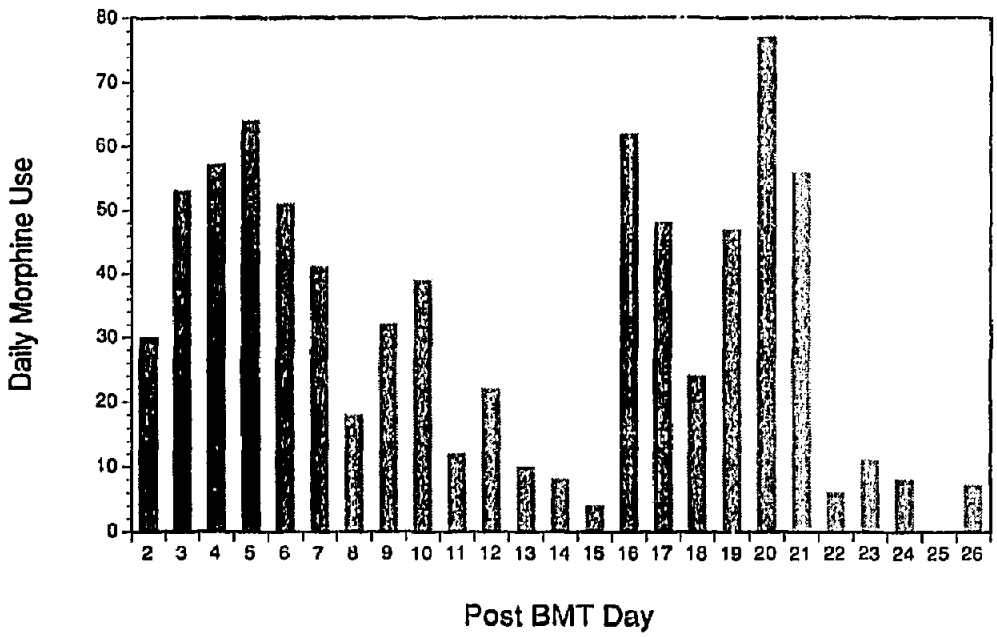


Fig. 7. Shows the opioid use for a child whose mucositis pain decreased till day 16 then flared up again. He stopped his patient-controlled analgesia (PCA) on day 26.

Children, like adults, have widely variable opioid requirements. No child in the study overdosed (requiring treatment with an opioid antagonist). We believe the use of PCA enables the child and the caregivers to tailor opioid delivery to the patient's requirements. In contrast, during the study period at least one medication error occurred in younger children treated with "traditional" continuous infusion, with nurse-administered boluses, on the same wards. We surmise the small bolus of drug which has peak effect after 5 or 10 min, may help the patients and caregivers notice a tendency toward overdose earlier than with CI, which produces blood levels that peak many hours after the infusion starts.

A discussion of parent, child, and caregiver relationships are outside the scope of this article, but the importance of a functional relationship for PCA use is supported by our observed failures. Hospital staff and physicians treat adults and children differently in most settings. Whereas adults are generally independent, children are part of the parent-child unit, and a three-way relationship between child, parent, and care providers develops. We routinely gave detailed explanations and reassurances to adult patients, but we simply told the children in this study to push the button for pain. We omitted detailed instructions on PCA use because we preferred to teach the children, and their parents, over several days, in concert with their nurse. At our daily visits, we reassured the child and the parents, explained side effects that they or the nurses had observed, and adjusted the bolus size for optimal effect.

Publications suggest that the nurses and parents sometimes push the PCA button.[16] In our experience, if the button was easily accessible to the child, he or she almost always wanted to control it. We occasionally observed children who became too sick to use the PCA, and we prescribed a CI with or without "nurse administered" PCA. We supported the parents and the child with extensive education and counseling. On our daily clinical rounds, we asked not only about the welfare of the patient but also about how the family was coping. This often led to the discussion of concerns tangential to the patient's pain and gave us a better understanding of how to look after the patient. The two PCA failures mentioned in the results both had severely dysfunctional families with whom such counseling was impossible.

We encountered no difficulty weaning the children from the PCA. As a child's opioid

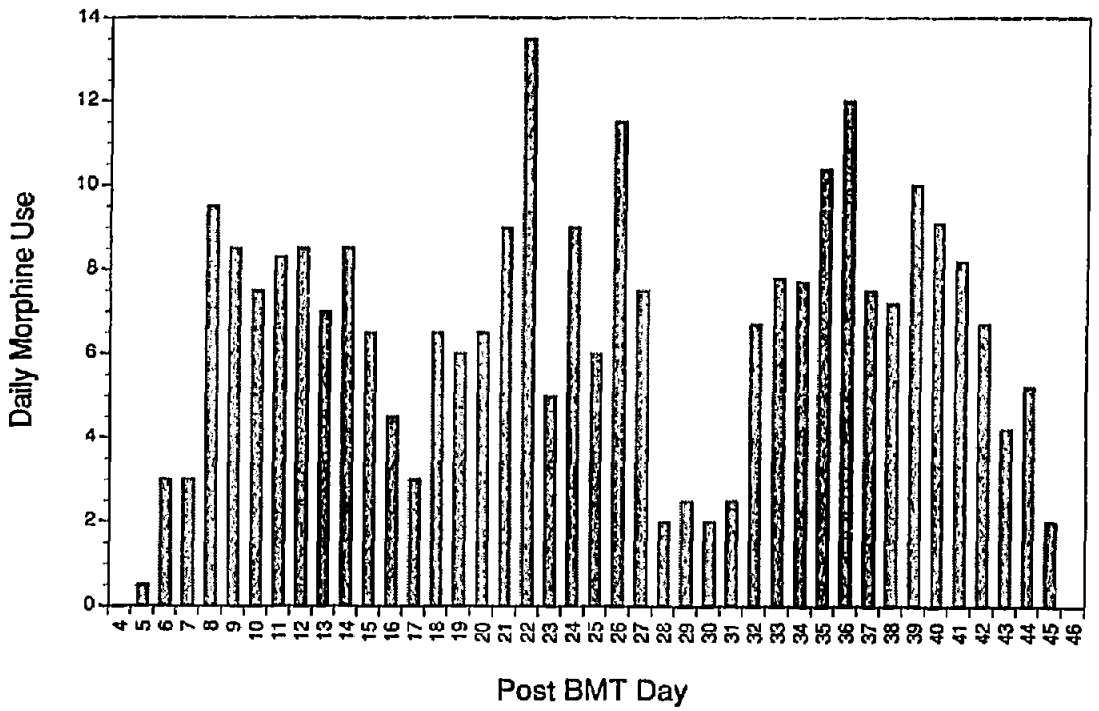


Fig. 8 Shows data from a patient who decreased his opioid use until day 28 but, as he developed GVHD, increased it again until control of graft-versus-host disease (GVHD) at day 46.

consumption fell, we decreased the bolus size, reducing the opioid side effects while maintaining a comfortable level of analgesia. When PCA use appeared minimal, we discussed transition to oral analgesics. We also noted that deteriorating mental status associated with multi-organ failure was accompanied by reduced opioid requirements. Opioid requirements seemed to remain minimal even after the acute phase of organ failure.

The role of CI in postoperative studies in adults is controversial. Recent studies[17] show the beneficial effect on analgesia of adding CI to PCA. Our clinical impression that the use of nighttime CI improves sleep finds support in recent postoperative studies.[18] In BMT, where sleep deprivation is a major concern, improved sleep may partially account for the beneficial effect. Unfortunately, the data in this retrospective review of our patients is not sufficiently rigorous to confirm our clear clinical impression of the benefits of adding CI to PCA in selected patients.

One-quarter of our patients who started PCA with morphine changed to hydromorphone to control side effects or to enhance pain control. This interesting observation requires further investigation.

We have shown that opioid PCA in preteen children, with or without CI, is safe and effective in the BMT setting. Promising areas for future investigation include (a) the role of continuous infusion with PCA and its affect on sleep patterns, (b) the differences between side effects of long-term opioids in children versus adults, and (c) the reasons patients request and doctors change opioids during long duration painful episodes.

Acknowledgment

Supported in part by NIH/NCI grants CA 58552-08, AA-CA 36444, ALC-CA18029, and AMT-CA47748.

References

1. Acute Pain Management Guideline Panel. *Acute Pain Management: Operative or Medical Procedures and Trauma. Clinical Practice Guideline.* AHCPR Pub. No. 92-0032. Rockville, MD: Agency for Health Care Policy and Research, Public Health Service, U.S. Depart-

ment of Health and Human Services, Feb. 1992.

2. Gaukroger PB, Chapman MJ, Davey RB. Pain control in pediatric burns—the use of patient-controlled analgesia. Burns 1991;17:396–399.

3. Jacox A, Carr DB, Payne R, et al. *Management of Cancer Pain. Clinical Practice Guideline* No. 9. AHCPR Publication No. 94-0592. Rockville, MD. Agency for Health Care Policy and Research, U.S. Department of Health and Human Services, Public Health Service, March 1994. .

4. Schechter NL, Berrien FB, Katz SM. PCA for adolescents in sickle-cell crisis. Am J Nurs 1988;88:719.

5. Shapiro BS, Cohen DE, Howe CJ. Patient-controlled analgesia for sickle-cell-related pain. J Pain Symptom Manage 1993;8:22–28.

6. Broadman IM, Brown RE, Rice IJ, Higgins T, Vaughan M. Patient controlled analgesia in children and adolescents: a report of postoperative pain management in 150 patients. Anesthesiology 1989;V71:A1170.

7. Gillespie JA, Morton NS. Patient-controlled analgesia for children: a review. Paediatr Anaesth 1992;2:51–59.

8. Tyler DC. Patient-controlled analgesia in adolescents. J Adolesc Health Care 1990;11:154–158.

9. Vetter TR. Pediatric patient-controlled analgesia with morphine versus meperidine. J Pain Symptom Manage 1992;7:204–208.

10. Walson PD, Graves PS, Mortensen ME, Kern RA, Torch MA. Patient-controlled versus conventional analgesia for postsurgical pain relief in adolescents. Dev Pharmacol Ther 1992;19:32–39.

11. Weldon BC, Connor M, White PF. Pediatric PCA: the role of concurrent opioid infusions and nurse-controlled analgesia. Clin J Pain 1993;9:26–33.

12. Schechter NL, Berrien FB, Katz SM. The use of patient-controlled analgesia in adolescents with sickle cell pain crisis: a preliminary report. J Pain Symptom Manage 1988;3:109–113.

13. Mackie AM, Coda BC, Hill HF. Adolescents use patient-controlled analgesia effectively for relief from prolonged oropharyngeal mucositis pain. Pain 1991;46:265–269.

14. Mowbray MJ, Gaukroger PB. Long-term patient-controlled analgesia in children. Anaesthesia 1990;45:941–943.

15. Dunbar PJ, Buckley FP, Gavrin JR. Longer duration PCA opioids in children (6–12) for bone marrow transplant related pain. Paper presented at American Pain Society (APS) 12th Annual Scientific Meeting in Orlando, FL; 1993.

16. Broadman LM, Rice LJ, Vaughan M, Ruttimann UE, Pollack MM. Parent assisted "PCA" for postoperative pain control in young children. Anesth Analg 1990;70:S34.

17. Doyle E, Harper I, Morton NS. Patient-controlled analgesia with low dose background infusions after lower abdominal surgery in children. Br J Anaesth 1993;71:818–822.

18. Doyle E, Robinson D, Morton NS. Comparison of patient-controlled analgesia with and without a background infusion after lower abdominal surgery in children. Br J Anaesth 1993;71:670–673.