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LETTERS TO THE EDITOR

Controlled Trial of Morphine vs Hydromorphone for Patient-Controlled Analgesia in Children with Postoperative Pain

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Dear Editor,

Patient-controlled analgesia (PCA) is standard care of postoperative children aged roughly 8 years and over (depending on maturity) [1], allowing patients to choose their preferred balance of analgesia and side effects [2]. Morphine sulfate is generally considered the drug of choice. Expected toxicities include a 30–70% incidence of nausea and/or vomiting [3,4], a 10–80% incidence of itching [3–5], and rarer cases of urinary retention [2,4]. Respiratory depression is serious although unusual [2]. While the spectrum of anticipated toxicities is similar, anecdotal reports indicate a lower incidence of side effects with hydromorphone when compared with morphine [6]. We performed a double-blind, randomized, controlled trial comparing the toxicity of morphine with that of equianalgesic doses of hydromorphone used for PCA in children.

A sample of 96 healthy children (aged 8–21 years) hospitalized after surgery was randomized to receive either morphine or hydromorphone PCA. A morphine : hydromorphone potency ratio of 1:5 was assumed, and the opioids were administered as an 0.015 mg/kg morphine equivalents demand dose (0.015 mg of morphine or 0.003 mg of hydromorphone), with an 8-minute lock out interval and a 0.375 mg/kg morphine equivalents 4-hour maximum dose. Opioid use, pain, respiratory depression (hypopnea and/or hypercapnea sufficient to warrant intervention), nausea, emesis, itching, and urinary retention were recorded every 8 hours and treated as needed. PCA use continued until pain declined sufficiently to allow transition to oral analgesics, or toxicity of sufficient severity to discontinue the study was encountered. Pain assessments were performed every 4 hours while the patient was awake. Patient demographic characteristics, hours of PCA exposure, total opioid dose, and highest pain scores were summarized with descriptive statistics and compared with independent samples *t*-tests or chi-square tests. Toxicities of the two treatments were compared by computing the frequency of each toxicity within each treatment group.

Ninety-six patients were evaluated; 11 of those (three morphine, eight hydromorphone) were withdrawn before completion of the study for unacceptable opioid side effects, leaving 85 patients for complete analysis. There was no difference between treatment groups in demographic characteristics, the presence of a urinary catheter, opioid use, pain scores, treated side effects, or the presence of an oxygen requirement (Table 1). No patient developed clinically significant bradycardia or hypotension during the treatment period. Overall, 74% reported nausea, 43% emesis (maximum in first 24 hours), 50% itching (maximum at 48 hours), and 8% urinary retention.

Table 1 Clinical characteristics of each patient group

	Hours	ME (mcg/kg/h)	VAS	% Need O_2	% Need Antiemetic	% Treat Pruritus	% Treat UR
M (N = 45)	47 ± 24	35 ± 19	6 ± 2	29	67	36	7
H (N = 51)	36 ± 24	37 ± 30	6 ± 3	22	65	33	10
P-value	0.03	0.76	0.69	0.41	0.84	0.82	0.79

M = Morphine; H = Hydromorphone; ME = morphine equivalents; UR = urinary retention; VAS = visual analog scale.
Correction made after online publication September 26, 2012: the "% Treat UR" column has been updated in Table 1.

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Most patients unable to complete the study (73%) had received hydromorphone ($P = 0.17$). All five patients withdrawn for respiratory depression had received potentially sedative drugs either during the recent anesthetic [4] or diphenhydramine administered to treat pruritus [1]. When two patients were withdrawn from the study at a time of day when pharmacy staff were not available to provide information as to treatment group, patients were "changed" to hydromorphone even though they had been assigned to the hydromorphone group.

Although many [6,7] believe that hydromorphone has a more favorable side-effect profile, delivery of equianalgesic doses of morphine or hydromorphone by PCA results in the same side effects in children and adolescents with postoperative pain. In our practice, the opinion that morphine is more likely to cause side effects is shown by the fact that in the absence of information as to the drug's identity, uncomfortable patients were "changed" to hydromorphone PCA even though they were already receiving it.

The children in our study used amounts of opioid similar to those in other studies, achieved comparable pain control [2,3,8], and had nausea [3] and itching [3] well within reported ranges. The time course of side effects, with nausea and vomiting developing early and itching more slowly, can be useful in assessment of the reasons for the variation in incidence of these side effects between studies.

Hydromorphone provides an acceptable alternative to morphine PCA but does not have a more favorable overall side-effect profile in children with postoperative pain. While there are no population-based differences between the drugs, interindividual differences do exist. The choice for any single patient depends primarily on their history; perhaps, genetic testing will be able to decrease the trial and error associated with this method of selection. Coadministration of potentially sedative drugs should intensify monitoring for respiratory depression.

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