Investigating the effects of cuing medication availability on patient-controlled analgesia pump usage in pediatric patients: Results of a randomized controlled trial

NCT02456909

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## Materials and Methods

This single-center, prospective, RCT was conducted at a large children's hospital in the Midwest. The study was approved by the hospital Institutional Review Board, and was registered at www.clinicaltrials.gov (ID: NCT02456909) by the principal investigators prior to study enrollment. Enrollment was April 2015 – August 2017.

### *Participants*

Potential participants between the ages of 7 – 17 years, undergoing an orthopedic, abdominal or thoracic surgery for which PCA is routinely prescribed for post-operative pain management, were identified from the hospital surgery schedule. Eligible patients were opioid naïve, and patients and at least one parent were able to read and speak English. Exclusion criteria included 1) prior experience with PCA, 2) cognitive delay precluding independent use of the PCA button, or 3) pre-operative use of a daily anxiolytic or antidepressant medication.

### *Procedures*

#### *Recruitment and Randomization*

Patients were approached immediately prior to surgery. After informed consent and assent were obtained, participants were randomized into either the control group or the experimental "light" group and were stratified by gender and surgical procedure (orthopedic, abdominal, or thoracic) in blocks of 4. The randomization scheme was created by a statistician on the research team using Windows version 6.0 of "rand.exe" (http://block-stratified-randomization.software.informer.com). Participants were enrolled by the clinical research coordinator, who used the scheme to assign participants to groups after consent. Recruitment continued until each group included 60 completed participants (defined as having completed at least 24 hours of PCA use and completed assessment of the primary outcome). Carefusion

Alaris™ PCA pumps were used for all patients. The PCA profile (i.e. configuration of the light cue operation) for both groups was set up by a nurse in the post-anesthesia care unit (PACU). The starting opioid dose is standardized, and was set up by the PACU nurse. For the control group, the PCA pump was used according to the hospital's standard operating procedures: The PCA emitted a "beep" with every button press, and the status of the green light on the button never changed (i.e., it remained continually lit). For the light group, the PCA pump was configured so that the PCA button only emitted a "beep" when a button press resulted in successful opioid delivery. The green light on the button flashed during opioid delivery, was darkened immediately after delivery and was illuminated at the end of the lockout period, indicating a dose was ready to be delivered. Treatment of side effects was determined by the floor nurse who was not a member of the study team. To ensure consistent messaging, patients and parents in both groups were given scripted instructions regarding PCA use. The patient and guardian were also given a printed copy of the instructions prior to surgery.

***PCA monitoring and Pain assessments***

Either morphine or hydromorphone (converted to morphine equivalents) was administered using PCA for both groups as prescribed by the anesthesia service. Using morphine equivalents, our standardized PCA orders are as follows: 20 mcg/kg for the PCA dose and basal (if used), 8 minute lockout, and a 120 mcg/kg hourly maximum.

Patients had continuous pulse oximetry. Pain and sedation scores were recorded every 2 hours for the first 24 hours, with a minimum of every 4 hours thereafter. PCA use, including injections (i.e. button presses resulting in delivered doses) and attempts (i.e. button presses during the lockout period), were documented hourly by a nurse who was not a member of the study team. If for some reason the nurse was unable to document the hourly number of

injections and attempts (e.g. busy with another patient), the following hour's data would reflect the previous 2 hours' worth of attempts and injections.

Data collection terminated when the PCA was discontinued, or up to 60 hours post-surgery, whichever came first. The study period was defined as beginning when the patient arrived in the Post-Anesthesia Care Unit (PACU) through Post-Operative Day (POD) 2.

**Measures**

All outcomes were collected on post-operative days (PODs) 0-2, with the exception of state anxiety on POD 0, which was collected prior to surgery in the pre-op holding area. The research coordinator administered the STAI once on each POD, and also extracted all other data from the participant's electronic health record (EHR).

***Demographics, anthropometrics, and treatment***

Demographics (age, sex, race and ethnicity) and anthropometrics (height, weight, and BMI percentile) were extracted from the EHR. Benzodiazepine (lorazepam, diazepam), acetaminophen, ibuprofen, and ketorolac use and intraoperative methadone administration were also extracted from the EHR. These data were collapsed across PODs, and reported as presence/absence. Pre-existing chronic pain was also extracted from the EHR and reported as presence/absence.

***Primary Outcome: Patient satisfaction with pain management***

The primary outcome was the patient's response to a single question, focused specifically on satisfaction with pain management: "*How satisfied were you with your pain management (was your pain well controlled)?,"* with 0 = "very dissatisfied" and 10 = "very satisfied". Participants answered additional questions to rule out factors that could potentially explain between-group similarities or differences in opioid consumption (e.g. Did you

understand how to use the pain pump?). These questions were completed independently by the patient within 24 hours of the end of the study period. Questions were developed by experts in pediatric pain management and were based on the study by Patak et al.[1]

### *Secondary Outcomes*

#### *Opioid consumption and opioid-related side-effects*

Data on opioid consumption and treatment of related side effects were extracted from the EHR. Total opioid consumed via PCA was calculated from all opioid delivered via the basal rate and via injections, and is reported in mg/kg/hr. Hydromorphone was converted to morphine equivalents by multiplying the total amount of hydromorphone consumed (mg) by 5.[2]

Data on side effects requiring treatment included nausea/vomiting, pruritus, over sedation (using the Children's Hospital of Wisconsin Sedation Scale,[3] and respiratory depression. Treatment was coded as yes/no for each POD.

#### *Pain intensity*

*Pain scores*: Pain scores were recorded from the time patients left the PACU until discontinuation of the PCA or through POD 2 (whichever came first) and were extracted from the EHR. Pain was assessed using the age appropriate, hospital approved pain scale. Children either used a 0-10 (0 = no pain, 10 = worst pain possible) numeric rating scale, or the 0-10 Faces Pain Scale-Revised [10].

#### *PCA usage*

The total number of hourly injections and attempts were extracted from the EHR.

#### *State Anxiety*

The Spielberger State-Trait Anxiety Inventory for Children (STAI-C), state version, is a well-validated 20 item questionnaire used to assess anxiety about a current situation or impending event [4]. Each question begins with the stem "I feel…" and ends with 3 choices (e.g., "very calm," "calm," "not calm"). Respondents are instructed to consider "*how you feel right now*." A total score is computed from a sum of the items, with scores ranging from 0 – 60. The STAI-C was administered by the research coordinator once before surgery (POD 0) and once per day on POD 1 and POD 2. Elevated state anxiety was based on T-scores and was defined as ≥ 1 standard deviation above the mean.[5]

**Power Analysis**:

An *a priori* sample size calculation was based on the primary outcome. Rahman et al. examined patient satisfaction with pain relief for those randomized to pain management with PCA vs. intravenous boluses of analgesia titrated to patient comfort levels.[6] Based on a 1-5 scale (1 = excellent, 5 = disappointing), the average pain relief rating for patients in the PCA group was significantly better at 2.0 (± 0.37) than the rating for patients in the control group at 3.0 (± 0.24). With a power of 80%, a type I error rate (alpha) of 0.05, and a two-tailed t test, 60 patients would have been needed in each group to detect a difference of at least 0.16 SD between the light and control groups.

**Statistical Analysis**

Modified intent-to-treat analyses included all randomized participants, with the exception of those who did not receive the allocated intervention, as shown in Figure 1. Means and standard deviations or median and interquartile range (IQR) when data were skewed, were used for continuous data, and categorical items were described using frequency statistics. A Chi-square test or a Fisher's exact test was used to explore the relations between categorical variables, and bivariate correlations (Pearson correlation test) were used to explore correlations

between continuous variables. Comparisons between intervention and control groups and between age groups [children (≤12 years) and adolescents (13-17 years)] were conducted using a Mann-Whitney test. Missing data were treated using listwise deletion, and assumed to be missing completely at random. A two-sided p-value<0.05 was used to define what was considered significant.

Multivariable analyses using a mixed model with random time were used to examine the effect of the intervention group and age group on two dependent variables (DV): 1) opioid consumption over time and, 2) injections:attempts ratio over time. The independent covariates (IV) considered were pain scores, methadone use and the interaction between methadone use and intervention group, age group, intervention group, and the interaction between age group and intervention group. A backward model selection procedure was used, with a p-value <0.05 as a criterion to keep the variable in the multivariable model. Based on this criterion, the interaction between intraoperative methadone and intervention group was dropped from the model. The DV opioid consumption was transformed using square root to satisfy model assumptions. The parameters were estimated using Maximum likelihood, and unstructured covariance structure was used for repeated measurements. The mixed model with random effects allows for missing data, under the assumption that data were missing at random. Statistical analyses were calculated using SPSS 24 (IBM SPSS Inc., Chicago, IL) and SAS 9.4 software (SAS Institute Inc., Cary, NC).