Title: THE RELATIONSHIP BETWEEN THE EFFICACY OF PAIN RELIEF AND THE OSCILLATORY NATURE OF PAIN USING PATIENT CONTROLLED ANALGESIA (PCA)

Authors: F. M. Ferrante, M.D., A. G. Rocco, M.D., E. J. Orav, Ph.D., and J. P. Gallo, B.S.

Affiliations: Department of Anesthesia, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115 and Department of Biostatistics, Harvard School of Public Health, Boston, MA 02115

Introduction. The efficacy of patient controlled analgesia (PCA) is based upon the assumption that better pain control is achieved by an individual's self-titration of pain relief with small repetitive doses of narcotics as compared to externally administered bolus injections. Major oscillations in the concentrations of narcotic in blood and tissues, and thereby major oscillations in pain level, would be avoided. Previous studies have demonstrated the efficacy of PCA without thoroughly examining the relationship between pain relief and the oscillatory nature of pain resulting from timing of narcotic administration (Fig. 1). This study examines that relationship.

Methods. Forty patients (12M:28F, mean age 65.1 years) undergoing total knee replacement were randomized into two groups (PCA and I.M.) after informed consent was obtained. On the afternoon before surgery, the PCA group was instructed in the use of the Abbott Life Care PCA infuser. After surgery, both groups were given intravenous morphine in the recovery room until comfortable. On arrival at the ward, I.M. group patients received intramuscular morphine as prescribed by their orthopedic surgeon, and PCA patients had an infuser immediately available. Patients self-administer a 1 mg bolus of morphine sulfate with a 10 minute lockout interval, to a maximum of 10 mg over a four hour period. Visual analog pain scores (VAS) were obtained for 40 consecutive hours after arrival on the ward. Sleep was scored separately.

A mixed-model analysis of variance with repeated measures on individuals was used to analyze the outcome variable of pain. Three main factors were included in the model: treatment (PCA versus I.M.), hour (0600 to 2100) and patients (1 to 40). We also included one interaction term, treatment-by-hour. Treatment and hour were used as fixed effects and the patient was treated as a random effect, thereby allowing correlation between hourly recordings. Only pain measurements between 6:00 a.m. and 9:00 p.m. on the day after surgery were analyzed in order to avoid extreme diurnal variation. In order to align patients upon circadian phase, these same data, averaged by hour within each treatment group, were analyzed as two time series in order to detect and compare oscillations in the pain measurements.

Results. The demographic data, preoperative, intraoperative, postoperative narcotic administration, and type of anesthesia received were not different between PCA and I.M. groups. The mean pain score for the PCA group was 3.75 (total observations = 274) and 3.7752 for the I.M. group (total observations = 260). Tukey's studentized range test showed no difference in means. The mixed model analysis of variance also showed no effect for pain relief between groups. There was a significant effect (p < 0.0001) for hour of day (pain higher in early morning hours) but no group by hour interaction. The total explanatory power of the model was $r^2 = 0.62$. Time series analysis showed a trend of decreasing pain over time for both PCA and I.M. groups (Peak 1, Fig. 2). However, there was also an additional oscillatory period of approximately 5.33 hours (p < 0.07) detected in the I.M. group (Peak 2, Fig. 2). No such oscillation was found in the PCA group.

Discussion. This study presents a statistical model for evaluating the theoretical relationship between dosing interval and pain relief using PCA (Fig. 1). This model demonstrates an oscillation in pain relief in the I.M. group, if an oscillation in pain relief exists with PCA, it is below the limit of sensitivity of the model (2 hours). This is in keeping with the theoretical concept of PCA (on demand pain relief resulting from short dosing intervals). However, PCA is found to be no more effective than I.M. opioid for overall pain relief after total knee replacement. Therefore, as PCA has been shown to be more effective in other populations, the relationship between pain and analgesia in more complex than accounted for by the present theory of PCA. Other factors (age, psyche, placebo-effect) may be involved.

Reference.