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Case Report Open Access

Opioid Resistant Pain Successfully Managed with Magnesium, Lidocaine and Ketorolac in the Post-Anesthesia Care Unit: A Case Series

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Abstract

Opioid resistant pain in the Post-Anesthesia Care Unit is challenging and often poorly controlled. Post-operative pain greater than 7/10 pain despite 8 mg of IV morphine or equivalent was defined as opioid resistant pain. This case series reports five consecutive patients with opiate resistant pain who were successfully managed with a one-time concomitant IV bolus of 1 gm magnesium, 100 mg lidocaine, and 15 mg ketorolac. The patients were continuously monitored in the PACU. This novel combination produced greater than 50 percent mean pain score reduction with no adverse effects.

Introduction

We present a case series in which a combination of 1 gm magnesium (500 mg/ml, American Reagent), 100 mg lidocaine (20 mg/ml, Hospira), and 15 mg ketorolac (30 mg/ml, Hospira) successfully managed opioid resistant pain in the Post-Anesthesia Care Unit (PACU). The medicines were combined in the same syringe and diluted to 10 ml with saline. To avoid injecting magnesium and lidocaine too rapidly, the medicines were administered as a two ml bolus immediately and then one ml every 30 seconds by the clock (4.5 minutes total). Post-operative analgesia typically involves as needed IV opioids; unresponsive patients can present a demanding therapeutic challenge. Anecdotally, the magnesium, lidocaine, and ketorolac (MLK) combination has proven efficacious with minimal side effects at our home institution.

Five consecutive patients with opioid resistant, post-operative pain that were administered MLK in the PACU are presented. Opioid resistant pain, defined as greater than 7/10 pain despite 8 mg of morphine or equivalent, is consistent with prior studies [1]. At our home institution, typical post-operative analgesic orderes are 0.2 mg hydromorphone every 10 minutes as need for pain with a maximum of 2 mg to be administered. Pain scores were recorded 30 minutes after MLK administration. Patient heart rate, respiratory rate, blood pressure, and sedation were continuously monitored.

Case Series

A 23 year-old male presented for wound vacuum change and fasciotomy closure eight days following Superficial Femoral Artery graft, Common Femoral Vein ligation, and left leg fasciotomies secondary to multiple gunshot wounds. In the 24 hours preceding surgery, he required 36 mg morphine IV and six vicodin tablets. Surgery was performed under spinal anesthesia (10 mg tetracaine, 12.5 mcg fentanyl, and 100 mcg epinephrine). After spinal resolution, despite 100 mcg fentanyl, 2 mg hydromophone and 25 mg meperidine, he reported 8/10 pain in the PACU. Thirty minutes following MLK administration, pain improved to 3/10.

A 43 year-old male with no past medical history (PMH) underwent open ventral hernia repair under general anesthesia (GA). He received 350 mcg of fentanyl during the surgery. Pain was uncontrolled in the PACU despite 3.2 mg hydromorphone. MLK administration improved pain from 7/10 to 3/10 and facilitated the patient's discharge home.

A 20 year-old male underwent GA for Open Reduction Internal Fixation (ORIF) of a left distal radius fracture. During the procedure, the patient received 350 mcg of fentanyl and 2 mg of hydromorphone. In the PACU, despite 8 mg of morphine, the patient reported 9/10 pain. Following MLK administration, pain improved to 6/10. He was subsequently discharged home.

A 63 year-old female with PMH of colon cancer, proctocolectomy, and diverting ileostomy presented for colostomy take down. Medication history included prior FOLFOX chemotherapy, bupropion for depression, and vicodin and gabapentin for chronic pain. She received 150 mcg of fentanyl during GA. Despite 2 mg of hydromorphone in the PACU, she reported 10/10 pain. MLK administration decreased pain to 5/10.

A 26 year-old male underwent GA for right tibia/fibula ORIF for injuries sustained during a motor vehicle accident. PMH was significant for newly diagnosed HIV and panic attacks. Intra-operatively, the patient received 350 mcg of fentanyl and 1.4 mg of hydromorphone. In the PACU, 3.2 mg hydromorphone did not control pain. Initially, 30 minutes following MLK administration, pain improved from 10/10 to 4/10. However, the effect was transient. Pain regressed to 8/10 in an additional 30 minutes. He was discharged from the PACU to the floor without receiving additional opioids.

Aggregate patient data is presented in Table 1. Mean intra-operative and PACU morphine doses were 30 mg and 16.8 mg. Following MLK administration, the mean pain score decreased from 8.8 to 4.2. The mean pain score reduction was 52.6 percent; the median was 57.1 percent.

Discussion

Magnesium, lidocaine, and ketorolac are approved medications that are used safely in daily, clinical practice. Since magnesium, lidocaine, and ketorolac all work by different mechanisms, they should

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Patient	1	2	3	4	5	Mean	Median
Age	23	43	20	63	26	35	26
Weight (kg)	80	89.8	68	80.2	95.3	82.7	80.2
Intra-op morphine (mg)*	10**	35	46.9	15	43.4	30.1	35
PACU morphine (mg)*	25.5	19.2	8	12	19.2	16.8	19.2
Pre-MLK pain score	8	7	9	10	10	8.8	9
Post-MLK pain score	3	3	6	5	4	4.2	4
Percent reduction	62.5	57.1	33.3	50	60	52.6	57.1

* 0.01 mg fentanyl, 0.167 mg hydromorphone, and 10 mg meperidine were used as 1 mg morphine equivalents (Pocket Anesthesia).
** Pt also received 12.5 mcg intrathecal fentanyl

Table 1: PACU Opioid Administration and Post-MLK Pain Score Reduction.

logically exhibit synergistic instead of additive effects; analagous to the interaction between opioid and non-steroidal anti-inflammatory drugs [2]. While ketorolac is a common opioid-sparing analgesic, magnesium and lidocaine are more investigational.

Magnesium antagonizes prejunctional calcium, inhibits acetylcholine release at the neuromuscular junction, stabilizes the membrane, decreases catecholamine release, and antagonizes the NMDA receptor [3]. Nerve injury creates a burst of glutamate-mediated activity at N-Methyl-D-Aspartate (NMDA) receptors that is excitotoxic to inhibitory interneurons in the dorsal horn of the spinal cord, leads to pain disinhibition, and contributes to persistent pain [4]. Magnesium exerts its effects on the NMDA receptor by physically occluding the receptor pore and allosterically modulating the NR2B subunit, a subtype that contributes preferentially to pathological processes linked to glutamate over-excitation [5]. Previously, a randomized prospective trial demonstrated that a 8 mg/kg IV magnesium infusion during surgery significantly lowered post-operative pain scores for the first 12 hours and decreased post-operative morphine requirements for the first 24 hours compared with placebo following lower extremity orthopedic surgery [6].

Lidocaine is an amide local anesthetic that blocks voltage-gated sodium channels to prevent membrane depolarization and action potential propagation. As afferent noxious stimuli transmission depends on this process, if the sodium channels are blocked, then noxious stimuli cannot be transmitted to the central nervous system. Lidocaine binds to the intracellular portion of voltage-gated sodium channels to prevent ion movement through the channel. In addition to this classic mechanism of action, lidocaine augments the inhibitory, cholinergic, descending pain pathway; releases endogenous opioids; and reduces post-synaptic NMDA depolarization in the spinal cord [7]. A recent meta-analysis examined the effects of a peri-operative lidocaine infusion and concluded that lidocaine decreased post-operative pain and opioid requirements. Additional benefits included decreased ileus, decreased postoperative nausea and vomiting (PONV), and decreased hospital length of stay [8].

Repeated, ongoing injury and exposure to inflammatory mediators sensitizes functional peripheral nociceptors and activates dormant ones. Through neural plasticity, inflammatory nociceptor sensitization decreases threshold and increases responsiveness so that subsequent afferent, nociceptive inputs are amplified [9]. Ketorolac is used to decrease inflammation and potentially prevent peripheral sensitization. A recent meta-analysis demonstrated that a single systemic ketorolac dose reduced postoperative pain, opioid consumption, and PONV [10].

This case series demonstrated that MLK can safely and efficaciously manage opioid resistant post-operative pain. While opioids were often initially effective in the patients presented, peripheral and central sensitization most likely lead to opioid resistance. The MLK bolus was effective in patients with PMH of anxiety, depression, and chronic pain. While one patient experienced only transient benefits from the one-time MLK bolus, continuous magnesium or lidocaine infusion possibly could have produced longer-lasting analgesia. Additionally, the PACU physician administered the boluses over 4.5 minutes. This extra time at the bedside allowed for discussion of the MLK bolus and provision of emotional comfort.

Perhaps this additional physician-patient interaction accounts for some of the benefits observed in this case series.

Appropriate pain management is critical; it maintains patient functional status, improves emotional well being, enhances quality of life, decreases hospital stay, and prevents readmission (ASA). Additionally, the preponderance of evidence demonstrates that acute post-surgical pain predicts chronic pain. More efficacious acute pain treatment is humane, prevents chronic pain, decreases complications, and facilitates recovery. The department's anecdotal results with the magnesium, lidocaine, and ketorolac combination have proven so compelling that a randomized, prospective, placebo-controlled trial is being prepared to test this novel, non-opioid combination on uncontrolled post-operative pain.

IRB

This case series (HS-11-00707) was approved by the USC IRB on 23 December 2011. The IRB Administrator was Marie Reyes. She may be reached via email at marierey@usc.edu.

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