JOURNAL OF CASE REPORTS 2012;2(2):86-88

Letter to Editor

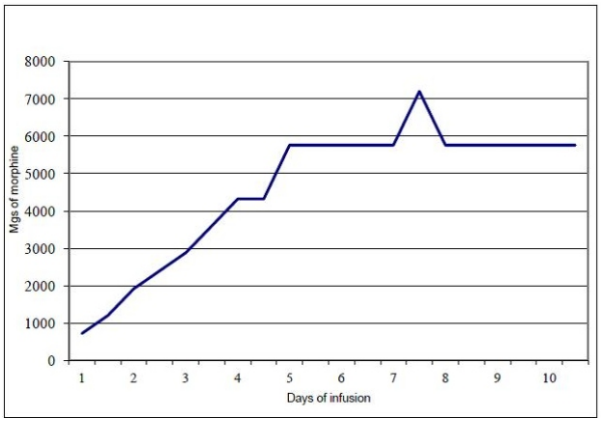
Hydromorphone and Verapamil Infusion in Severe Cancer Pain

Jairo Moyano, Maria Teresa Garcia
From the Department of Anaesthesia and Pain Clinic
University Hospital Fundación Santafé de Bogotá, Colombia.

This report is on synergy based approach to manage a clinical challenging situation in increased opiate use due to both progression of tumour growth and pharmacological tolerance in a patient suffering very severe cancer pain. CM was a 52 year-old man who 12 months before was diagnosed with rectal cancer and metastatic disease to the liver and L3 to S1 vertebrae. Antineoplastic treatments included an abdominal-perineal resection, multiple chemotherapy protocols and radiotherapy cycles on lumbar spine disease. CM was well informed on the diagnosis and he partially coped with his prognosis. He had been undergoing palliative care for 6 months due to severe, incidental lumbar pain and left radiculopathy interpreted as somatic-neuropathic pain, secondary to bony metastasis and lumbar plexus involvement. Initial treatment with hydromorphone 7.5 mg/PO/day and carbamazepine 300 mg/PO/day, achieved satisfactory pain relief with no relevant side effects during 10 days; but because of uncontrollable pain in the left dorso-lumbar region (intensity 10/10) in spite of repeated dose adjustments, he was admitted into hospital. At that moment the degree of sedation was a major limiting factor (Ramsay scale 3-4). Examination findings on admission revealed a normal mini mental state examination, hypoesthesia in left lower limb from L1-4, muscular atrophy, 3/5 proximal muscle strength. Magnetic resonance imaging confirmed infiltration of left psoas and lumbosacral plexus, increase in L1-L5 bony lesions. Electrolytes, kidney function tests, glycaemia and A.M/P.M serum cortisol levels were within normal limits.

Hydromorphone was progressively increased to 270 mg/PO/day. At this point, an infusion of hydromorphone was started at 6 mg/IV/hour, progressively readjusting it according to CM pain reports, until 600 mg/IV/hour were reached on the 5th day [Fig. 1]. In the meantime, multiple non-opioid analgesics were evaluated without clinical advantage (non-steroidal, ketamine, α-2-agonists, baclofen, and dexamethasone). Also, on the 3rd day, verapamil 2.5 mg/IV/bolus twice a day was added until a 5 mg/IV/bolus four times a day was reached on the 5th day. In parallel, carbamazepine was increased up to 800 mg/PO/day. A switch to morphine was planned. On the 5th day, an infusion with morphine was started at equianalgesic doses [Fig. 2]; after the 5th day of infusion, the average pain intensity was 3/10, there was an improvement in the patient's state of mind, and more hours of night sleep.

Corresponding Author: Dr. Jairo Moyano
Email: jairo_moyano@hotmail.com



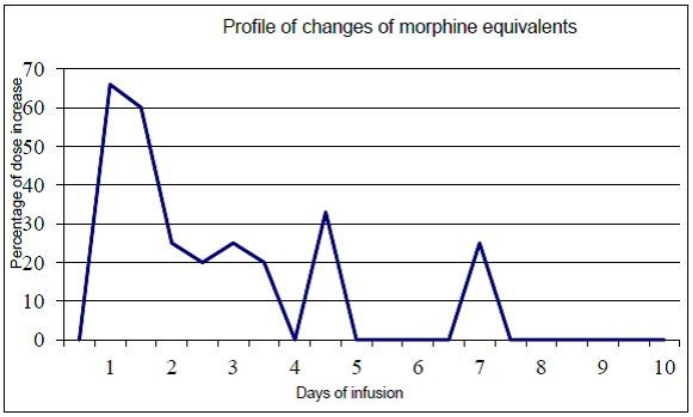


Fig. 1: Consumption of equianalgesic doses of IV morphine.
Fig. 2: Profile of changes of morphine equivalents

Most cancer pain patients can be treated effectively with a combination of opioid and non-opioid analgesics. However, increased analgesic requirements may result from worsening disease, tolerance and cognitive dysfunction. The voltage-gated calcium channels are a large group of ion channels found throughout the central and peripheral nervous system. The rationale for the use of calcium channels blockers in pain management can be summarized by their neuronal functions that include the control of neurotransmitters release in lamina I and II of spinal cord. L-type calcium channel blockers administered systemically produces blockade of Ca^{2+} entry via ion channels, and so plasma membrane Na/Ca^{2+} exchange [1,2]. Previous research showed that L-type Ca^{2+} channel blockers act as anti-inflammatory agents; the mechanism by which the L-type calcium channels blockers decrease inflammation is suppression of macrophage activation-induced up regulation of plasminogen (Plg) binding and Plg receptor (Plg-Rs) expression [3]. In addition, it has been reported that L-type Ca^{2+} channel blockers, have an analgesic effect at the central level mediated by an increase in the β-endorphins [4], and also at peripheral level, softening the activity of the C fibers while increasing the serum concentrations of the opioid, all of which leads to a reduction in opioid requirements and contributes to reduce its adverse effects.

In conclusion, we cannot recommend a dose of verapamil, however, we suggest that combining a low-dose of calcium channel blocker with morphine may be a useful method of minimizing the dose of opioids, starting at lower doses and monitoring hemodynamic changes to adjust doses. In difficult pain conditions, clinicians should not forget their knowledge of basic pharmacology to design strategies to alleviate the suffering of their patients by improving analgesic efficacy.

References

1. Hao S, Mamiya K, Takahata O, Iwasaki H, Mata M, Fink DJ. Nifedipine potentiates the antinociceptive effect of endomorphin-1 microinjected into the periaqueductal gray in rats. Anesth Analg. 2003;96:1065-1071.
2. Tadaoki Fukuizumi. Spinally Delivery N-, P/Q- and L-type Ca^{2+}-channel Blockers Potentiate Morphine Analgesia in Mice. Life Sciences 2003;73: 2873-2881.
3. Bkaily G, Jacques D. L-type calcium channel antagonists and suppression of expression of plasminogen receptors: is the missing link the L-type calcium channel? Circ Res. 2009;105:112-113.
4. Fukuizumi T, Ohkubo T, Kitamura K. Spinally delivered N-, P/Q- and L-type Ca2+-channel blockers potentiate morphine analgesia in mice. Life Sci. 2003;73:2873-2881.