Journal of the Formosan Medical Association (2011) **110**, 666

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LETTER TO THE EDITOR

The mechanisms of ultra-low dose opioid agonist-antagonist

The major drawback of PCA for postoperative pain management is opioid related side effects, such as nausea, vomiting and pruritis etc, which discourage patients' use of PCA. Therefore, reduction of the opioid related side effect during PCA using is a major issue to improve the quality. Combination various adjuvant with morphine in PCA regimen to reduce the dose of morphine and thus decrease the incidence and severity of morphine related side effect is frequently used. Article published in JFMA (2009; 118) found that combination of low-dose nalbuphine and morphine in PCA decreases the incidence of opioid-related nausea without affecting the analgesia and PCA requirement and concluded this combination improving the quality of PCA with less incidence of nausea in postoperative pain control.[1] They suggested that the mechanism might be similar to the effect of ultra low dose naloxone, which improves the analgesic effect of morphine by inhibiting the excitatory action of morphine.[2] As known, combination of adjuvant with morphine administration in pain management reduces the morphine related side effects the main mechanism is the morphine spare effect. In this article, small dose nalbuphine, a mixed kappa opioid agonist and mu-opioid antagonist, inhibited the action of morphine on mu-opioid receptor induced side effects, which may also antagonize the analgesic effect of morphine, however, the partial kappa opioid receptor antagonist effect may restore the morphine analgesia. However, in this article, authors failed to observe the morphine sparing effect, lesser dose of morphine and better VAS pain score, by the small dose nalbuphin coadministration.

As discussed by author, the mechanism of ultra low dose naloxone in enhancing of morphine's analgesic effect is due to antagonize the excitatory effect of morphine, however, it was failed to demonstrate in clinical patient pain management. In our recent animal studies, we found that ultra low dose naloxone cotreatment with morphine can inhibit neuropathic thermal hyperalgesia[3] and morphine tolerance as well,[4] which might be through its antiinflammtory action in the spinal cord glia and moreover, ultra low dose naloxone can reinitiate the classical mu-opioid receptor and Gi-protein coupling in the pertussis toxin induced neuropathic pain animals.[5] Therefore, reduction of the incidence of nausea in this article may be just simply the nalbuphine binding to the mu-opioid receptors, and possibly less reduction of morphine's analgesic effect which however was restored by the partial agonist property of kappa opioid receptor of nalbuphine.

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12 May 2011

doi:10.1016/j.jfma.2011.08.013