

## ***Journal Watch***

### **Opioids and the immune system.**

Sacerdote, P. Palliat Med 2006; 20:S9-S15.

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Received during: Journal Rounds on the Tertiary Palliative Care Unit, July 26, 2006

### **Abstract**

Opioid compounds such as morphine produce powerful analgesia that is effective in treating various types of pain. In addition to their therapeutic efficacy, opioids can produce several well known adverse events, and, as has recently been recognized, can interfere with the immune response. The immunomodulatory activities of morphine have been characterized in animal and human studies. Morphine can decrease the effectiveness of several functions of both natural and adaptive immunity, and significantly reduces cellular immunity. Indeed, in animal studies morphine is consistently associated with increased morbidity and mortality due to infection and worsening of cancer. However, from several animal studies it emerges that not all opioids induce the same immunosuppressive effects, and evaluating each opioid's profile is important for appropriate analgesic selection. Buprenorphine is a potent opioid that is frequently prescribed for chronic pain. Acute intracerebroventricular administration of buprenorphine has been shown in rats not to affect cellular immune responses, while a statistically significant inhibition of the immune response was observed with morphine. In mouse studies, chronic administration of buprenorphine led to immune parameters important for antimicrobial responses or for anti-tumour surveillance (lymphoproliferation, natural killer (NK)-lymphocyte activity, cytokine production, lymphocyte number) being unaffected. In contrast, levels of these immune markers were significantly reduced when the potent  $\mu$ -agonist fentanyl was administered, but recovered after longer periods as tolerance developed. Because the intrinsic immunosuppressive activity varies between individual opioids, predicting the outcome on immunity can be difficult. To study this, the effects of morphine, fentanyl and buprenorphine on NK-lymphocyte activity depressed by experimental surgery were examined in rats. Treating animals immediately after surgery with equianalgesic doses of morphine and buprenorphine significantly reduced surgery-induced immunosuppression. However, buprenorphine reverted NK-lymphocyte activity was ameliorated, although not completely. In contrast, fentanyl did not prevent immunosuppression, induced by surgery. Overall, from several animal studies it emerges that buprenorphine has the more favourable profile, being a potent analgesic devoid of intrinsic immunosuppressive activity.

### **Comments**

Strengths/uniqueness:

Draws attention to an understudied aspect of pain control.

Weaknesses:

Article still mainly relies on animal studies.

It does not discuss the role of tolerance to immunosuppression. We know that many opioid users are chronic users and the role of tolerance must be considered more seriously.

Relevance to Palliative Care:

The significance of the immunosuppressive effect of opioids in palliative care medicine and the relevance to every day practice remain unclear. It is possible that future research may suggest advantages for some opioids over others due to different effects in the immune system.

This article should not prompt a change in opioid prescribing practices, as buprenorphine is not a recommended opioid for cancer pain.