

Opioid Adverse Effects

Health Professional Resources
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Adverse Effects

Whilst common adverse effects of chronic opioid therapy such as constipation and sedation have been recognised for many years, the full spectrum of potential problems remains incompletely defined¹. This article summarises current evidence.

Respiratory system effects

1. Respiratory depression and death can occur in overdose particularly when opioids are combined with benzodiazepines or other sedating medication^{2,3}.
2. Sleep apnoea can be worsened^{4,5} and an abnormal apnoea-hypopnoea index has been reported in 75% of a cohort of chronic opioid users⁶.

Gastrointestinal system effects

1. Opioid-induced bowel dysfunction (OBD) occurs in up to 80% of patients on chronic opioid therapy⁷. The cluster of OBD problems includes constipation, nausea and biliary dyskinesia.
2. Reduced production of saliva and poor nutrition contribute to the increased prevalence of dental caries⁸.

Nervous system effects

1. Although opioids can produce analgesia, they can also paradoxically amplify pain through sensitisation of the nervous system. This is known as opioid induced hyperalgesia⁹. The multiple mechanisms of hyperalgesia overlap with those of tolerance and contribute to declining opioid effectiveness over time.
2. Morphine is more likely to produce hyperalgesia than buprenorphine^{10,11}. It has been proposed that the κ antagonism of buprenorphine contributes to an anti-hyperalgesia effect¹¹.
3. Activation of the N-methyl-D-aspartate receptor in the dorsal horn of the spinal cord, contributes to both opioid tolerance and opioid induced hyperalgesia^{12,13,14}.
4. Glial cells in the central nervous system have previously been thought to play only a passive role in maintaining neuronal homeostasis. However, recent studies show that opioids activate glial cells and that these activated glia contribute to neuronal sensitisation and hyperalgesia¹⁵.
5. In addition to sensitisation of the nervous system there is evidence that opioids produce dose dependent changes in both the structure and function of reward and affect processing areas of the brain¹⁶. The clinical significance of these changes is as yet unclear.
6. Neurophysiological effects include the potential for driving impairment¹⁷⁻²⁰ and interference with sleep architecture.
7. There is an increased risk of falls and consequent fracture particularly in the elderly^{21,22}.
8. Neuropsychological problems include a potential contribution to mood disorders and opioid use to manage psychological distress (the "chemical coper")²³. The problems of opioid abuse and addiction have been under recognised in the pain management context²⁴.

Endocrine system effects

1. Opioid therapy can suppress the hypothalamic pituitary axis and cause hypopituitarism. This in turn can cause hypogonadism, impotence, infertility and osteoporosis^{25,26}.
2. Studies of intrathecal opioid administration^{27,28} have shown that hypogonadotropic hypogonadism is common in men (85% prevalence). Secondary amenorrhoea is similarly common in pre-menopausal women. Hypoadrenalism (ACTH deficiency) and growth hormone deficiency are less common (15% prevalence of both). TSH deficiency and increased prolactin levels are rare.
3. Prevalence of endocrine abnormalities with oral opioid use is not known although cases have been reported^{29,30}.

Immune system effects

1. The interaction between opioids and the immune system is complex. Trauma and pain in themselves cause immunosuppression. Pain relief in part alleviates this. Opioids however have additional direct effects on many aspects of immune function. These effects depend on multiple factors including structure of the individual opioid agent and dose range used³¹.
2. Opioid use (acute and chronic) can inhibit humoral and cellular immune response including antibody production, lymphocyte activity, and cytokine expression^{32,33}. Potential mechanisms include:
 - i. Modulation of the hypothalamic pituitary axis
 - ii. Stimulation of the sympathetic nervous system
 - iii. Direct action via μ receptors on immune cells

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