Long-term opioids: friend or foe?

Over the previous decades, prescribed opioid use for non-cancer pain has risen astronomically in the developed world. However, there has also been increasing realization of a rise in opioid-induced morbidity and mortality with chronic usage. Deaths from prescription opioids in the USA rose from 4041 in 1999 to 14 459 in 2007 (Manchikanti et al, 2012). In the USA, prescription opioids are said to contribute directly to more deaths than illegal recreational drugs, alcoholic liver disease or human immunodeficiency virus (HIV) infection (Dhalla et al, 2011). So is this escalation in opioid use justified?

Yes, the increased use is justified

Opioids are strong and undoubtedly very effective analgesic drugs with well-established use in acute and cancer pain. However, non-cancer chronic pain is often hard to manage prompting some physicians to initiate opioid analgesics. Patients often respond favourably initially but perhaps the longer term sequelae need to be considered.

No, the increased use is not justified

There is little evidence to support the long-term efficacy of opioids for chronic pain as most studies are in the acute or cancer pain setting. Eighty per cent of people taking opioids will experience at least one side effect. Common and well-known side effects include nausea, constipation, somnolence, dizziness, pruritus and urinary retention. In excess they can cause respiratory depression and hypotension.

More worrying are the long-term side effects of opioid use which are not commonly discussed. Chronic use leads to the predictable tolerance and dependence contributing to dose escalation (British Pain Society, 2010). Often co-existing is opioid-induced hyperalgesia; a poorly recognized condition where the chronic use of opioids induces a generalized whole body pain state as well as a worsening of the original pain (Lee et al, 2011). It is often mistaken for drug tolerance and the dose is increased, exacerbating the problem. The only treatment is to reduce the opioid dose (Lee et al, 2011).

'Opioids are very useful analgesics which will benefit some patients tremendously but they are often prescribed long term without much thought, resulting in side effects and even premature death.'

Less widely discussed are the immunosuppressive effects. Endogenous opioids activate the immune system but exogenous opioids have an immunosuppressive effect. Mechanisms include reduced antibody production, natural killer cell activity and cell-mediated immunity (Brack et al, 2011). The negative effects of opioids on immunity have been delineated more in in vitro and animal models but there is little research on the immune consequences of chronic opioid usage in humans. There is obvious concern over the risk of infections and tumour recurrence in cancer patients. Opioids are also thought to contribute to recurrent infections seen in heroin addicts and the exacerbation of immunosuppression in HIV-infected patients.

The endocrine system is also significantly affected. Opioids suppress the pulsatile secretion of gonadotrophin-releasing hormone which leads to a drop in the secretion of luteinizing hormone and thus falls in oestrogen, progesterone and testosterone (Seyfried and Hester, 2012). This can cause fatigue, night sweats and hot flushes, loss of libido, impotence, reduced muscle bulk, oligomenorrhoea and infertility. As sex hormones are required for maintenance of bone density, suppression can also lead to osteopenia and osteoporosis.

Effects on other hormones are more complex but cortisol and growth hormone secretion can be reduced. Prolactin levels can rise, leading to galactorrhoea. There is also a strong association between opioid use and weight gain, insulin resistance, hyperglycaemia and worsening of diabetes.

Conclusions

Opioids are very useful analgesics which will benefit some patients tremendously but they are often prescribed long term without much thought, resulting in side effects and even premature death. The recommendations by the British Pain Society (2010) for the prescription of opioids for chronic pain seek to ameliorate this, and recommend:

- Use of opioids with caution after exhausting all alternatives and at the minimum dose, carefully considering long-term consequences
- Consideration of a contract between doctors and patient before starting opioids
- A trial with an opioid to assess efficacy and side effects before starting it long term
- Monitoring all patients for adverse effects including regular endocrine blood tests and consideration of bone densitometry measurement. BJHM

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