November 2013

Development of dependence following treatment with opioid dependence following treatment with opioid analgesics for pain relief: a systematic review.

The Problem

As the debate in *JAMA* (below) shows there is no clinical or academic consensus as to what the key issues are with regards to risks of prescribing opioids for long term non cancer pain and what the solutions are – greater assessments of patients and their risk profile or restrictions on the use of drugs themselves.

Goal

To assess the incidence and prevalence of opioid dependence in adults with and without previous history of substance abuse following treatment with opioid analgesics for pain relief. This was done through a systematic review of 17 studies involving 88, 235 participants (a total of nearly 2,000 abstracts were initially looked at, 135 studies were scrutinised but 114 were excluded from the review, leaving only 17).

What they found

The results from the 17 studies were extremely varied. Data on dependence cited incidences ranging from zero to 24 per cent and prevalence of dependence varied from zero to 31 per cent. The data was inadequate to determine risk related to specific drugs or method of administration. Nor was it possible to retrieve information about the time following prescription of opioids after which dependence occurred. As well it was not possible to determine the specific risk among patients which a history of drug abuse as only one study reported data from this group separately.

The data on incidence and prevalence of dependence can be applied only to patients with chronic non cane pain who had used opioids for more than three months.

The authors conclude that the most solid finding is the absence of good quality studies. This stands in contrast to widespread concern of doctors relating to use of opioids for pain management. The authors argue the need for better designed prospective observational studies. In the meantime doctors should still consider using opioids to manage chronic pain because of their effectiveness and their potential to contribute to the quality of life of patients. Existing guidelines with regard to monitoring their use and dose and screening patients for potential comorbidities should be adhered to.

Development of dependence following treatment with opioid dependence following treatment with opioid analgesics for pain relief: a systematic review. Silvia Minozzi et al. *Addiction,108, 688-698*

Viewpoint. Curbing the opioid epidemic in the US. The risk evaluation and migration strategy

The problem

Even when used a prescribed, opioids are associated with significant morbidity and mortality

In the 1980s a combination of factors led to the beginning of what was by the late 1990s to become an explosion in the US of the use of prescription opioids for non-cancer pain, although there was limited evidence of the effectiveness of opioids for this indication. Sales of opioid analgesics including both regular and extended release formulations, increased fourfold between 1999 and 2010. In 2008 more than 14,000 deaths were related to the misuse of prescription medications, the vast majority prescription opioids

What they did

While the Food and Drug Administration (FDA) has responsibility for ensuring that medications are effective and safe, it is prevented from interfering with the practice of medicine. In 2007 an amendment to the Act governing the FDA gave it the authority to require post-marketing surveillance studies and to implement a risk evaluation and migration strategy (REMS) for drugs that are effective but have the potential for serious harm. Two opioid related REMS have been introduced – one for extended release formulation and the other for immediate release products such as fentanyl

Progress to date

Manufacturers have been given responsibility for educating prescribers in patient selection, counselling and risk assessment for dependency. Putting this in the hands of the pharmaceutical industry is considered controversial. As well participation in the REMS is voluntary for health care providers

What does it mean for health care professionals?

There is a possibility that a physician may be unwilling to prescribe a drug if they are unwilling to or unsure of how to meet the REMS requirements – e.g. onerous continuing education requirements. This could mean patients would miss out or be prescribed less effective medications. However if implemented appropriately the author believes that REMS may have an important contribution to make in curbing the opioid epidemic in the US.

Citation:

Curbing the opioid epidemic in the US. Lewis S Nelson (MD). *JAMA, August 1, 2012, VOL 308, no 5.*

Viewpoint: Opioid analgesics – risky drugs not risky patients

The problem

Opioid dependence and potential fatal respiratory depression are serious and well known risks of opioid analgesics, responsible for 16,000 deaths a year in the US. Screening tools have been developed in the US to help physicians distinguish between patients at low risk of developing problems with prescription opioids and those at high risk of developing problems such as patients with a history of addiction and substance abuse or a history of mental health problems. Yet opioid dependency is thought to affect more than one third of people with chronic pain and the author argues that no screening tool is sufficiently sensitive to rule out problems with opioids. Also screening a patient for risk of opioid abuse prior to prescribing pain treatment has the potential to stigmatise them.

Progress to date

The authors suggest that the issue is not necessarily with the patients who are high risk but with the drugs themselves and whether there is sufficient evidence to support their use in non-chronic cancer pain. For example one study shows that newly prescribed opioids after short stay surgery are associated with a 44 per cent increase in becoming long term opioid dependent within a year. She suggests that rather than assessing a patient's risk of dependence before prescribing the drugs it would be more useful to assess whether the benefits of prescribing opioids for pain outweigh the risks.

What does this mean for physicians?

The problems and the solution to prescribing opioids for chronic pain is still highly contentious in the absence of high quality long terms studies. The authors suggest that the problem stems from the drugs themselves not the patients. Low risk patients given large enough doses will have a high risk of overdose as will patients given moderate doses over a prolonged period. While a patient's risk should be considered physicians, should pay close attention to the drug dose and duration of treatment.

Opioid analgesics – risky drugs not risky patients. Deborah Dowell MD.
Hilary V Kunis MD; Thomas A Fairley MD. *JAMA 2013, 309 (21) 2219-2220*

Letters published in* JAMA *in response to Dr Dowell

Dr Russell Portenky of the Beth Israel Medical Centre in New York argues (*JAMA* 2013, 310, 16) that Dr Dowell did not clarify that the statistic of dependence affecting more than one third of people with chronic pain refers to life time prevalence not addiction during treatment. He also takes issue with the figure of a 44 per cent increase in the risk of long term opioid dependence after postoperative treatment with opioids because it only refers to 7.7 per cent of the study sample. He writes that there is considerable debate over the view that tolerance is a typical result of opioid therapy. He says the goal should be safe and effective opioid prescribing based on careful patient selection and continuing management based on an assessment of risks and benefits.

Dr Marcin Chwistek in a letter published in the same issue of *JAMA* also writes that shifting the focus from opioid related deaths to more limited prescribing will not protect patients or help physicians manage patients with long term chronic pain. He argues that a more systematic team based approach is needed that is also patient-centred and can be used in a community setting.