



Opioids for non-cancer pain—should we or shouldn't we prescribe?

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The topic of prescribing opioids for chronic non cancer pain is going through troubled times. A recent *JAMA* paper (1) by Ray and colleagues compared all-cause mortality for patients with chronic non cancer pain on either opioids or alternative medications. They described a significant increase in deaths from the opioid group.

There are other issues related to these concerns. In the USA politicians are attacking the use of opioids with statements such as '80% of opioid abusers started on prescription medicines'. President Obama has also got in on the act with tweeted statements such as '120 Americans die every day from drug overdoses—most involving legal prescriptions' and '4 in 5 heroin users started out misusing prescription opioids'. This is only a half-truth as heroin use has been a societal problem for decades and not related to prescription opioids.

To add to this, there is good evidence across Europe that many patients who have been prescribed opioids for chronic non cancer pain are reporting consistently high pain scores indicating that the drugs are not providing pain relief. Physicians therefore have the difficult task of stopping those medicines as patients fear that their pain may get even worse.

The issue is not straightforward as it has political, legal, social, psychological and clinical implications. The anti-opioid approach has the potential to restrict opioids to those most in need- patients with severe cancer related pain.

Is it the patients fault? Patients' pain has to be taken seriously and the general rule in pain clinics is to believe the patient and not make prejudiced judgements. Severe pain affects the whole of life and reduction of pain leads to many other parameters such as sleep and ability to work

to be improved. However this is a balance and we wait for better analgesics than are currently available. Opioids may have a place in therapy but need careful handling. What do we know?

In the *JAMA* paper (1) mentioned above, Ray and colleagues undertook a retrospective cohort study between 1999 and 2012 of Medicaid patients with chronic non cancer pain in the USA. They monitored almost twenty three thousand new episodes of pain therapy in a cohort of over 131,000. Qualifying patients had a diagnosis of chronic pain in the previous 90 days reporting low back, other musculoskeletal, abdominal, headache or other neurological pains. The number of patients being treated with opioids for either abdominal or headache pains seem quite high but most were in the back or musculoskeletal groups.

Study drugs were long acting morphine, controlled release oxycodone, transdermal fentanyl or methadone. Comparators were either anti-epileptics or low dose cyclic antidepressants. The reason for this choice of comparator is not explained, neither is there any comment about the lack of NSAIDs as a comparator—a significant omission. Median doses were 50 mg morphine equivalent for the opioid and 600 mg gabapentin equivalents or amitriptyline 25 mg equivalent for the control. The doses for morphine and amitriptyline seem lower than expected and gabapentin higher. Authors reported 167.1 deaths per 10,000 person years in the opioid group and 107.9 deaths per 10,000 person years in the control group. The increased risk was confined to the first 180 days but doesn't appear to be dose related. About half the deaths were due to cardiovascular causes. The authors concluded that the use of long acting opioids is associated with a significant increase in all-cause mortality.

A systematic review by Häuser and colleagues (2) included 11 open label studies with 2,445 participants reporting low back pain, osteoarthritis or neuropathic pains. The median study duration was 26 weeks. Only around a quarter of those who participated in a long term study completed the full term but those who did reported some benefit from opioids. The authors conclude that there may be some benefits of long term opioids in carefully selected patients after a short trial of opioid therapy.

A small study (3) based around Leeds and Bradford in the UK was based on interviews with 23 patients and 15 general practitioners. Generally patient expectations were relatively simple; they wanted their pain managed and wanted an explanation for their symptoms. This is a common problem as many have a mechanistic view of life. If I have a pain then there must be an (usually) on-going cause. This is not actually the situation in neuropathic pains as nerves that have been damaged can continue to fire even though healing may have taken place. On the other hand GPs found it very difficult to know what messages to convey. They are aware that opioids are difficult to manage and not always appropriate but often don't have the time to deal with issues appropriately. They are aware of the need to take analgesics regularly but equally aware of the possibilities of addiction. Some refer patients to specialists such as pain management teams as a way out. It is clear that some GP—patient relations break down due to a lack of trust and a lack of continuity.

Campbell and colleagues (4) undertook a 2-year prospective study of just over 1,500 patients taking opioids for chronic non cancer pain in Australia. The results give an interesting profile of this group of patients. Around 60% of those of working age or nearing retirement were unemployed, and 40% of these said that their work status had changed due to pain. Many reported childhood abuse or neglect. The median duration of pain was 10 years and for the majority this was due to back or neck problems. Nearly half the sample reported moderate to severe depression. The most commonly prescribed strong opioids were oxycodone and buprenorphine. Many also self-medicated with 'Over the counter' pain remedies. The median length of strong opioid use was 48 months and nearly 10% reported a dose of greater than 200 mg of morphine equivalent per day. Virtually everyone reported adverse effects; the most common were constipation, drowsiness and fatigue. There was fear of becoming addicted or dependent by around a third of the sample.

The participants in this study demonstrate a complex

social and clinical profile but there are hints here of what issues can lead to problems when prescribing strong opioids

In an opinion piece Scholten and Henningfield (5) outline some of the challenges in what they describe as an unbalanced policy in the USA. It is clear that a number of problems have arisen from the non-medical use of prescription opioids opining that there is little distinction made between harms involving opioids and harms caused by opioids. Attempts to restrict diversion are leading to increasing difficulties for deserving patients to access opioids. Scholten *et al.* (5) make the following recommendations for responsible prescribing of opioids:

- Follow the dosage guidelines as recommended in guidelines;
- Assess the patients pain and functioning regularly and adjust dosage accordingly for optimal pain relief;
- Avoid prescription of more than is necessary to treat pain in order to avoid diversion or accumulation of stock;
- Avoid under treatment of pain in order to prevent 'doctor shopping';
- Instruct the patient and any caregivers to store opioid medicines safely and out of reach of others;
- Instruct the patient and any caregivers how to safely dispose of unused medicines so as to prevent medicines being diverted to illicit markets;
- Be aware that caregivers may potentially divert and/or misuse prescribed opioids;
- Consider prescribing naloxone kits along with education of the patients care givers and family members.

This seems a sensible approach and I would add two other recommendations made by Dr. C Stannard, a pain clinician based in Bristol UK:

- Before the first prescription, discuss with patients how opioids will be stopped if they prove to be ineffective;
- Supporting patients in reducing medicine that are not effective is a healthcare intervention in its own right even if there is nothing else to offer.

In summary the prescribing of opioids is under attack and we need to ensure that these medicines although imperfect continue to be available for patients who need them. For those with severe chronic non cancer pain these agents must be used with care.

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