Prescribing...

Opioids for Long Term Pain February 2016

- The Faculty of Pain Medicine, funded by Public Health England, has recently released an Opioids Awareness resource.
- This document, from a globally respected source, should be considered essential reading to support a safe and effective prescribing decision.
- This bulletin summarises the key points and specifically looks at effectiveness of opioids for long term pain.

The resource advises that

1. Opioids are very good analgesics for acute pain and for pain at the end of life but there is very little evidence that they are helpful for long term pain.
2. A small proportion of poeple may obtain good pain relief with opioids in the long-term if the dose can be kept low and especially if their use is intermittent. However it is difficult to identify these people people at the point of opioid initiation.
3. The risk of harm increases substantially at doses above an oral morphine equivalent of 120mg / day , but there is no increased benefit.
4. If a patient is using opioids but is still in pain , the opioids are not effective and should be discontinued, even if no other treatment is available.
5. Chroinic pain is very complex and if patients have refractory and disabling symptoms, particularly if they are on a high opioid doses , a very detailed assessment of the many emotional influence on their pain is essential.

It also reviews the **effectiveness of Opioids for Long Term Pain**, as follows.

There are now a large number of randomised control trials and systematic reviews that conclude that opioids may reduce pain for some patients in the short and medium term (usually less than 12 weeks) for a number of chronic painful conditions. The trials included in these syntheses are sometimes large and without conventional sources of bias but the results need more detailed analysis to understand the role of opioids in routine clinical practice. This is important because in trials of opioids in chronic pain withdrawal rates due to adverse events are high. For example, with oxycodone in musculoskeletal conditions about 45% withdraw in the first 3 weeks, and about 65% overall.

Understanding how the data from treatment withdrawals are handled is critical for interpreting trial data for use in real life. Conventionally, these withdrawals from clinical trials are dealt with using the "last-observation-carried-forward" (LOCF) method. Very often, patients have pain relief early on, but then cannot take the drug because of adverse effects. So a patient who has pain relief at (say) 3 weeks, but who withdraws from the trial because of adverse effects is recorded as a treatment success as the pain relief at 3 weeks is assumed to have continued had they not withdrawn from the trial. The result is significantly better pain relief at 12 weeks than placebo, but based in part on inferred data from those withdrawing from the trial.

This is critically important for clinical practice as if a drug is stopped because of adverse effects this represents a treatment failure. If trial data are interpreted such that treatment success should include BOTH pain relief at 12 weeks AND ability to keep taking the tablets, then opioids are no better than placebo. EVERY single RCT in chronic pain using this interpretation comes to this same result.

A further limitation of the data from RCTs is that in general, patients in these trials have discrete pain diagnoses and lack many of the physical and emotional co-morbidities of patients seen in clinical practice. Furthermore, progress of therapy in clinical trials is monitored more closely than is usual in clinical practice and dose titration is closely supervised. Data in relation to improved functional outcomes and quality of life as a result of opioid therapy in these trials are sparse.

Given the limited duration of clinical trials, data on efficacy of long term opioid use are available only from case series and open-label extensions of controlled trials. These latter have been systematically reviewed. Open-label extension data suggest that a small proportion of patients may derive continuing benefit from opioids in the long term but the relevance to clinical practice is uncertain as patients with co-morbidities that may predispose to problematic opioid use are generally excluded from clinical trials and evaluation of long term use does not, in these studies, identify potential benefits from placebo effect, benefits of additional therapies or spontaneous resolution of symptoms.

Analysis of open label data does not enable firm conclusions regarding improvement in function or quality of life with long term opioid treatment. Data from prospective cohort studies suggest that opioids retard return to work after injury and may prolong functional recovery or worsen physical functioning. A Danish cross-sectional study has suggested that when comparing opioid users with non-opioid users, opioid use appears to be associated with poorer self-related quality of life and employment status, increased healthcare use, and worse pain. These studies do not demonstrate causality in relation to opioids and poor function in a number of domains but indicate that the hoped for end points of pain reduction and improvement in function are not being met with long term opioid treatment.

There are always challenges when using what we know from clinical trials in routine practice. Clinical trials always have a limited sensitivity, and there are likely to be patients for whom drugs that cannot be shown to be efficacious in RCTs 'work' for them. This means that opioids may reasonably be included in the repertoire of cautious attempts to find some therapy that works when all the obvious ones have been tried. Given the harms of prolonged opioid treatment and the probability of therapeutic disappointment in the long term, exploration of opioid therapy for a patient with refractory pain should be planned carefully and closely monitored. With the evidence we have there should be no trial of traditional opioids in chronic pain beyond modest doses over about 2-4 weeks and the therapeutic trial should be informed by important practice points:

- Patients who do not achieve useful pain relief from opioids within 2-4 weeks are unlikely to gain benefit in the long term.
- Patients who may benefit from opioids in the long term will demonstrate a favourable response within 2-4 weeks.
- Short-term efficacy does not guarantee long-term efficacy.
- Data regarding improvement in quality of life with long-term opioid use are inconclusive.
- There is no good evidence of dose-response with opioids, beyond doses used in clinical trials, usually up to 120mg/day morphine equivalent. There is no evidence for efficacy of high dose opioids in long-term pain.

Reference : Opioids Aware : http://www.fpm.ac.uk/faculty-of-pain-medicine/opioids-aware

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