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Oxycodone for cancer-related pain in adults

Background

Many people with cancer experience moderate to severe pain that requires treatment with strong painkillers that are classified as opioids.

Oxycodone and morphine are examples of these opioids that are used for the relief of cancer pain. However, strong painkillers are not effective for pain in all people neither are they well-tolerated by all people. The aim of this review was to assess whether oxycodone is associated with better pain relief and tolerability than other strong painkillers for adults with cancer pain.

Study characteristics

For this update, in November 2016, we found six more relevant studies. In total, we included 23 studies with 2648 participants. These studies compared the painkilling ability (benefit) and side effects (harms) of different types of oxycodone to each other or to other strong painkillers.

Key results

Generally, the studies showed that oxycodone is an equally effective strong painkiller whether taken every six or every 12 hours, and equally effective as other strong pain killers, such as morphine.

All the strong painkillers examined in the studies were also associated with a number of unwanted effects, such as vomiting, constipation, and drowsiness. Overall, these do not differ between oxycodone and the other strong painkillers. Hallucinations (where people experience imaginary things, e.g. hearing voices) are much less common as a side effect but we found that they were less likely with oxycodone than within morphine.

Overall, we found that the current evidence is comprised of studies that contained small numbers of participants of which many (19%) did not complete the studies. However, since there was very little difference between oxycodone and morphine, more research in this area is unlikely. Studies looking at oxycodone compared to other strong pain killers may be useful.

Quality of the evidence

We rated the quality of the evidence from studies using four levels: very low, low, moderate, or high. Very low quality evidence means that we are very uncertain about the results. High quality evidence means that we are very

confident in the results. Overall the quality of the evidence was low or very low, downgraded because of issues with study quality and size.

Authors' conclusions:

The conclusions have not changed since the previous version of this review. The data suggest that oxycodone offers similar levels of pain relief and overall adverse events to other strong opioids including morphine. Although we identified a clinically insignificant benefit on pain relief in favour of CR morphine over CR oxycodone, this did not persist following sensitivity analysis and so we do not consider this important. However, in this updated analysis, we found that hallucinations occurred less often with CR oxycodone than with CR morphine, but the quality of this evidence was very low so this finding should be treated with utmost caution. Our conclusions are consistent with other reviews and suggest that while the reliability of the evidence base is low, given the absence of important differences within this analysis it seems unlikely that larger head to head studies of oxycodone versus morphine are justified, although well-designed trials comparing oxycodone to other strong analgesics may well be useful. For clinical purposes, oxycodone or morphine can be used as first-line oral opioids for relief of cancer pain in adults.

Read the full abstract...

Background:

Many people with cancer experience moderate to severe pain that requires treatment with strong opioids, such as oxycodone and morphine. Strong opioids are, however, not effective for pain in all people, neither are they well-tolerated by all people. The aim of this review was to assess whether oxycodone is associated with better pain relief and tolerability than other analgesic options for adults with cancer pain. This is an updated version of the original Cochrane review published in 2015, Issue 2 on oxycodone for cancer-related pain.

Objectives:

To assess the effectiveness and tolerability of oxycodone by any route of administration for pain in adults with cancer.

Search strategy:

For this update, we searched the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE and MEDLINE In-Process (Ovid), Embase (Ovid), Science Citation Index, Conference Proceedings Citation Index - Science (ISI Web of Science), BIOSIS (ISI), and PsycINFO (Ovid) to November 2016. We also searched four trial registries, checked the bibliographic references of relevant studies, and contacted the authors of the included studies. We applied no language, date, or publication status restrictions.

Selection criteria:

We included randomised controlled trials (parallel group or cross-over) comparing oxycodone (any formulation or route of administration) with placebo or an active drug (including oxycodone) for cancer background pain in adults by examining pain intensity/relief, adverse events, quality of life, and participant preference.

Data collection and analysis:

Two review authors independently extracted data and assessed the included studies using standard Cochrane methodology. We meta-analysed pain intensity data using the generic inverse variance method, and adverse events using the Mantel-Haenszel method, or summarised these data narratively along with the quality of life and participant preference data. We assessed the overall quality of the evidence using GRADE.

Main results:

For this update, we identified six new studies (1258 participants) for inclusion. In total, we included 23 studies which enrolled/randomised 2648 participants, with 2144 of these analysed for efficacy and 2363 for safety. The studies examined a number of different drug comparisons.

Pooled analysis of three of the four studies comparing controlled-release (CR) oxycodone to immediate-release (IR) oxycodone showed that the ability of CR and IR oxycodone to provide pain relief were similar (standardised mean difference (SMD) 0.1, 95% confidence interval (CI) -0.06 to 0.26; low quality evidence). Pooled analyses of adverse events showed no significant differences between CR and IR oxycodone for asthenia (risk ratio (RR) 0.58, 95% CI 0.2 to 1.68), confusion (RR 0.78, 95% CI 0.2 to 3.02), constipation (RR 0.71, 95% CI 0.45 to 1.13), dizziness/lightheadedness (RR 0.74, 95% CI 0.4 to 1.37), drowsiness/somnolence (RR 1.03, 95% CI 0.69 to 1.54), dry mouth (RR 1.14, 95% CI 0.48 to 2.75), insomnia (RR 1.04, 95% CI 0.31 to 3.53), nausea (RR 0.85, 95% CI 0.56 to 1.28), nervousness (RR 0.57, 95% CI 0.2 to 1.64), pruritus (RR 1.46, 95% CI 0.65 to 3.25), vomiting (RR 0.66, 95% CI 0.38 to 1.15), and discontinuation due to adverse events (RR 0.6, 95% CI 0.29 to 1.22). The quality of the evidence was very low for all these adverse events. Three of the four studies found similar results for treatment acceptability.

Pooled analysis of seven of the nine studies comparing CR oxycodone to CR morphine indicated that pain relief was significantly better after treatment with CR morphine than CR oxycodone (SMD 0.14, 95% CI 0.01 to 0.27; low quality evidence). However, sensitivity analysis did not corroborate this result (SMD 0.12, 95% CI -0.02 to 0.26).

Pooled analyses of adverse events showed no significant differences between CR oxycodone and CR morphine for confusion (RR 1.01 95% CI 0.78 to 1.31), constipation (RR 0.98, 95% CI 0.82 to 1.16), dizziness/lightheadedness (RR 0.76, 95% CI 0.33 to 1.76), drowsiness/somnolence (RR 0.9, 95% CI 0.75 to 1.08),

dry mouth (RR 1.01, 95% CI 0.8 to 1.26), dysuria (RR 0.71, 95% CI 0.4 to 1.26), nausea (RR 1.02, 95% CI 0.82 to 1.26), pruritus (RR 0.81, 95% CI 0.51 to 1.29), vomiting (RR 0.94, 95% CI 0.68 to 1.29), and discontinuation due to adverse events (RR 1.06, 95% CI 0.43 to 2.6). However, the RR for hallucinations was significantly lower after treatment with CR oxycodone compared to CR morphine (RR 0.52, 95% CI 0.28 to 0.97). The quality of the evidence was very low for all these adverse events. There were no marked differences in treatment acceptability or quality of life ratings.

The remaining studies either compared oxycodone in various formulations or compared oxycodone to different alternative opioids. None found any clear superiority or inferiority of oxycodone for cancer pain, neither as an analgesic agent nor in terms of adverse event rates and treatment acceptability.

The quality of this evidence base was limited by the high or unclear risk of bias of the studies and by imprecision due to low or very low event rates or participant numbers for many outcomes.

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