What are the equivalent doses of oral morphine to other oral opioids when used as analgesics in adult palliative care?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals

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Background

Morphine is generally the strong opioid of choice and a common question is how to convert a dose of another opioid to morphine or vice versa. Other opioids may be preferred, for example, if a patient obtains insufficient pain relief with morphine and/or is suffering severe adverse effects. However, switching to an alternative opioid is only one approach to managing opioid adverse effects (1,2). Other strategies include:

- Reducing the dose of opioid (and possibly adding non-opioid or adjuvant analgesics).
- Symptomatic management of the adverse effect(s).
- Switching the route of administration.

If the strategies above have not worked, or are impractical, then a decision to convert to an alternative opioid may be taken, preferably with advice from a palliative care or pain team.

Answer

Advice on opioid conversion

NB: Before using Table 1, read the notes below and the Limitations statement at the end of this document.

- Equivalent doses of opioids are given in Table 1. These are an approximate guide only because comprehensive data are lacking and there is inter-individual variation. There is no widely accepted algorithm or guideline for equianalgesic conversions (3), borne out by the fact that sources differ in the equivalent doses they quote.

- When converting from one opioid to oral morphine, or vice versa, the initial dose depends on the relative potency of the two drugs (4) and route of administration (see Table 1). This Q&A deals only with oral administration.

- Some authors have suggested that, in most cases, the calculated dose-equivalent of a new drug derived from e.g. Table 1 must be reduced to ensure safety. A dose reduction of at least 50% is recommended when switching at high doses (e.g. morphine or equivalent doses of 1g/24 hours or more), in elderly or frail patients, or because of intolerable undesirable effects (4). A similar dose reduction is recommended when there has been a recent rapid escalation of the first opioid. As requiredï¼šdoses should be used to make up any deficit while re-titrating to a satisfactory dose of the new opioid (4).

- Based on clinical experience, the starting point for dose reduction from the calculated equianalgesic dose is 25-50% (3,5). This dose reduction is particularly important when high doses are used.
However, the reduction may not be appropriate if the original opioid failed to control pain (see below). Reasons for this suggested dose reduction include:

- Incomplete cross-tolerance between opioid drugs, which would lead to effects (including adverse effects) that would be greater than expected when a switch to a new drug is made (2,3,5).
- There appears to be a large inter-individual variability in the relative potencies among opioids (2,5).
- There is a need to adjust for conditions that increase opioid risk (e.g. elderly patients, co-existing medical conditions) (5).
- Most data are derived from single-dose studies and these values can only approximate to the clinical situation (5).

- When considering opioid conversions, the degree of unrelieved pain should also be taken into account (5). For example, if pain is not controlled by the current opioid then it may be appropriate to administer the calculated equianalgesic dose of the new opioid or even increase the calculated dose by 25-50% (3).
- The half-life of the two drugs needs to be considered when converting so that the patient does not experience breakthrough pain or receive too much opioid during the conversion period.
- The time to onset of action needs to be considered, for example, if moving from a non-modified release to a modified release preparation. The timing of doses will therefore need to be carefully considered.
- The total daily dose of the current opioid(s), including all long-acting and breakthrough doses, must be determined prior to conversion. If the patient is on multiple opioids, convert all to morphine equivalents (see Table 1) (3).
- Ensure that ‘as required’ doses of an opioid are prescribed for breakthrough pain. These should not be modified release preparations or transdermal patches.
- Once the conversion has occurred, the dose of new opioid should be titrated carefully according to individual response and the patient monitored closely for the first 7-14 days for side effects and efficacy especially when switching at high doses (6). Careful monitoring is also particularly necessary when there has been a recent rapid escalation of the first opioid (4). It is common for upwards or downwards dosage adjustment of a new long-acting opioid to be necessary during the initial 24-48 hours after conversion (3).
- Ensure naloxone is available.
Table 1. Approximate equivalent potencies of oral opioids to oral morphine (see advice above).

<table>
<thead>
<tr>
<th>Oral Drug (refs)</th>
<th>Duration of action (hours) (standard release preparations)</th>
<th>Potency equivalence to morphine (oral to oral)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine (4)</td>
<td>6 - 8</td>
<td>80 (sublingual)</td>
<td>Only one literature source suggests a conversion (4) but this potency equivalence has been cited for a number of years. No published dose equivalence studies in analgesia have been undertaken, but one study in opioid dependence suggests a potency equivalence of 30 (10). The relevance of this to analgesic equivalents is uncertain.</td>
</tr>
<tr>
<td>Codeine (4,7,8,9,19)</td>
<td>3 ÷ 6</td>
<td>0.08 - 0.15</td>
<td>Codeine is partly metabolised to morphine (4).</td>
</tr>
<tr>
<td>Dihydrocodeine (4,9)</td>
<td>3 - 6</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>Hydromorphone (2,4,6,7,8,9,11,12,16,18,19,23)</td>
<td>4 - 5</td>
<td>3.5 - 10</td>
<td>Some sources suggest a potency equivalence of 5 when converting from morphine to hydromorphone, but only 3.5-4 if switching from hydromorphone to morphine (4,16,18). The manufacturer states an approximate potency equivalence of 5-10 (11).</td>
</tr>
<tr>
<td>Morphine (4)</td>
<td>3 - 6</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Oxycodone (2,4,6,7,8,9,12,13,19,23)</td>
<td>3 - 6</td>
<td>1.3 - 2</td>
<td>Note high oral bioavailability compared to morphine (13). Manufacturer advises a potency equivalence of 2 (13).</td>
</tr>
<tr>
<td>Tapentadol (4,20)</td>
<td>Not available</td>
<td>0.3 - 0.4</td>
<td>Manufacturer states that direct opioid conversion has not been studied so potency equivalence has been calculated indirectly (20). Switching from another µ agonist (e.g., morphine) may cause low-grade opioid withdrawal. Role of tapentadol in palliative care is unclear (4).</td>
</tr>
<tr>
<td>Tramadol (4,7,8,9,19,21)</td>
<td>4 - 9</td>
<td>0.1 - 0.25</td>
<td>Manufacturer advises a potency equivalence of 0.1 - 0.17 (21).</td>
</tr>
</tbody>
</table>

Equivalent potencies are only approximate and can be unpredictable. When converting from one opioid to another, it is often appropriate to use a lower dose than the suggested equivalence above. Close monitoring for side effects and efficacy is mandatory, especially at higher doses.
Example conversion:

Converting from morphine m/r 15mg bd to oral oxycodone:

- Total daily dose of morphine is 30mg.
- From Table 1, oxycodone potency equivalence = 1.3 ÷ 2.
- Divide 30mg/1.3 = 23mg and 30mg/2 = 15mg.
- Therefore the approximate equivalent total daily dose of oral oxycodone is 15 - 23mg in divided doses. See notes above on how this should be used in practice.

Limitations

- Evidence for the effectiveness of switching opioids when managing cancer pain or chronic non-cancer pain is limited (14,15,22). There are currently no evidence-based guidelines for opioid choices when considering opioid conversion (22).
- Much of the dose equivalence information was derived from single dose studies and therefore may have limitations in applicability to repetitive administration (16). Also, some studies were not designed for the detection of relative opioid potencies and in some cases opioid equianalgesic conversion dosing recommendations may have emerged as secondary observations (3).
- The studies that are available have differing patient populations, study methods and small sample sizes. The duration of opioid exposure and the issue of tolerance are also factors in the interpretation of data (17).
- It has been suggested that the directional quality of cross tolerance may not be equal and has not been fully explored. Ratios may change according to the direction of an opioid switch; however the clinical relevance of this is not clear (17,18). Although it is unlikely to have a major impact when switching at lower doses, it is possible that failure to recognise the directional difference may result in negative consequences when switching at higher doses (18).
- Dose conversion tables are not meant to provide recommended initiation doses for a given opioid or patient (16).
- Randomised trials are needed to standardise conversion ratios when switching from one opioid to another (15,22).
- The data presented are derived from adults and so may not be applicable to children.

References

10. Personal communication, Reckitt Benckiser Medical Information department. 28th September 2011.
20. Personal communication, Grünenthal Ltd Medical Information department. 23rd September 2011.

Quality Assurance

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Search strategy

- Embase - search strategy: opioid.af AND equivalence.af
  - (exp opiate agonist/ OR exp narcotic analgesic agent/ OR exp narcotic agent/) AND equivalence.af (limited to H=Y and LG=EN)
  - (exp opiate agonist/ OR exp narcotic analgesic agent/ OR exp narcotic agent/) AND exp bioequivalence/ (limited to H=Y and LG=EN)

- Medline - search strategy: opioid.af AND equivalence.af
  - (exp analgesics, opioid/ OR exp narcotics/) AND exp therapeutic-equivalency/ (limited to H=Y and LG=EN)

- Specialist textbooks