What are the essential medications in palliative care?
A survey of Australian palliative care doctors

**BACKGROUND**

There is a disparity of availability and cost of drugs in the community for palliative care patients through the Pharmaceutical Benefits Scheme (PBS) compared to those available to inpatients in public hospitals.

**METHODS**

The Joint Therapeutics Committee of the Australian and New Zealand Society of Palliative Medicine, Palliative Care Australia and the Clinical Oncological Society of Australia surveyed palliative care practitioners in Australia to compile a list of drugs they considered essential.

**RESULTS**

Drugs nominated generally had good levels of evidence for use in palliative care, although many practitioners still used some without evidence of benefit.

**DISCUSSION**

We are now working with the Commonwealth Department of Health and Ageing to agree on a list of drugs for specific palliative care indications. As a result, the first ever section in the PBS for a specific patient population has been created. There is a need for high quality studies in palliative care to determine the best drugs to add to the list.

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Many palliative care doctors feel that patients receiving palliative care in the community are disadvantaged in accessing drugs because the Pharmaceutical Benefits Scheme (PBS) constrains them. Members of the Australian and New Zealand Society for Palliative Medicine (ANZSPM) started to advocate to redress this. Barriers to changing the PBS regulations were: some drugs on the list require Therapeutics Goods Administration approval for palliative care indications; others needed evidence of effectiveness, cost effectiveness and clinical place in therapy for PBS listing; and these drugs would require an industry sponsor to fund and take on responsibility for the application and subsequent use, as required by Australian law – a problem as many drugs were out of patent.

As a way forward, a Joint Therapeutics Committee of Palliative Care Australia, ANZSPM, and the Clinical Oncological Society of Australia formed to generate a list of essential drugs for palliative care. One had previously been generated from a world survey sent to 50 palliative care doctors in 25 different countries (including Australia), and a list of what was thought the ‘20 essential drugs in palliative care’ published.¹

We decided to survey palliative care doctors in Australia to compile a similar list of essential drugs, and also to assess the level of evidence for them, setting out which were available through the PBS.

**Method**

We surveyed members of ANZSPM, asking them what they thought were essential drugs for palliative care. The questionnaire used a list of the 22 most frequently encountered symptoms derived from the literature, ‘pain’ occupying three of these. Respondents could list up to five individual drugs for each symptom, together with their estimated level of evidence for the drug for that indication, using a ranking of the evidence (Table 1). This differs from

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**Table 1. Levels of evidence used in the questionnaire**

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>Evidence from systematic review of all relevant randomised controlled trials</td>
</tr>
<tr>
<td>Level 2</td>
<td>Evidence from at least one properly designed randomised controlled trial</td>
</tr>
<tr>
<td>Level 3</td>
<td>Evidence from nonrandomised controlled trials, cohort studies, case control studies</td>
</tr>
<tr>
<td>Level 4</td>
<td>Evidence from case reports/expert opinion</td>
</tr>
<tr>
<td>Level 5</td>
<td>Unknown to respondent what level of evidence exists</td>
</tr>
</tbody>
</table>

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The current National Health and Medical Research Council (NHMRC) guidelines\(^2\) in retaining the expert opinion no longer included in NHMRC guidelines. While these levels have been used throughout the article for consistency, where the only evidence available is expert opinion, that is denoted ‘4E’.

The questionnaire was hand delivered to registrants at a biennial scientific committee of ANZSPM held in Geelong (Victoria) in September 2000 and in addition, mailed to all other members not present.

The Hunter Area Research Ethics Committee gave ethics approval for this study.

**Results**

Out of 350 questionnaires, 102 were returned. Two were excluded because the address was unknown, giving a response rate of 100/350 (29%). Median age was 46 years (range 28–70), and median time since graduation was 21 years (range 5–49). Most respondents’ (58%) main area of practice was palliative medicine, while the rest were mostly general practitioners with experience in palliative care.

The first ranked drug for selected symptoms, PBS availability, and level of evidence at the

<table>
<thead>
<tr>
<th>Palliative symptom</th>
<th>Drug</th>
<th>% of respondents nominating this drug as first rank</th>
<th>PBS subsidy at time of survey (September 2000)</th>
<th>Level of evidence nominated by respondents</th>
<th>% responding</th>
<th>Level of evidence</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain using opioid analgesics</td>
<td>Morphine</td>
<td>98</td>
<td>Yes</td>
<td>43</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Pain using nonopioid analgesics</td>
<td>Paracetamol</td>
<td>88</td>
<td>Yes</td>
<td>43</td>
<td>1</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Pain using adjuvant analgesics</td>
<td>Valproate</td>
<td>61</td>
<td>Yes</td>
<td>8</td>
<td>1</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>Morphine</td>
<td>94</td>
<td>No</td>
<td>9</td>
<td>2</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>End stage respiratory reflexes (grunting, secretions)</td>
<td>Hyoscine, Hydrobromide</td>
<td>86</td>
<td>No</td>
<td>4</td>
<td>4</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Terminal restlessness</td>
<td>Midazolam</td>
<td>81</td>
<td>No</td>
<td>5</td>
<td>4</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Anorexia</td>
<td>Dexamethasone</td>
<td>69</td>
<td>Yes</td>
<td>6</td>
<td>2</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>Metoclopramide</td>
<td>86</td>
<td>Yes</td>
<td>19</td>
<td>3</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>
time of the survey are listed in Table 2. Table 2 shows a 60% agreement between respondents in regards to the number one medication used in each category, apart from anxiety, depression, dry mouth, and constipation.

The 20 most frequently nominated drugs and level of evidence are shown in Table 3.1

**Discussion**

The response rate of the survey was low, therefore we cannot be sure this represents Australian palliative care doctors. Nevertheless, a broad spectrum of palliative care doctors responded and our findings were similar to the international survey.1 There were differences among the 20 essential drugs with only 10 common to both lists (the top eight, followed by diazepam and fentanyl). There are many possible explanations, including different availability and formulations, costs and different preferences (perhaps based on clinical experience rather than evidence). Laxatives such as lactulose are commonly prescribed worldwide, while in Australia, docusate and senna is most commonly prescribed. There is no evidence that adding docusate to senna provides benefit. Any difference between lactulose and senna appears to be minimal in the small amount of data available.3

There seems to be a relatively low level of evidence for some important medications in palliative care (eg. midazolam) although the majority of first ranked drugs have at least level 2 evidence. Apart from the most frequently used medications, there was a large discrepancy between the respondents’ belief about the available evidence and what is actually available. For example paracetamol for pain, where level 1 evidence is available, but the majority of respondents rated evidence as levels 3-6, while more than one in 3 respondents thought morphine only had level 4 or 5 evidence for anaegia, whereas the evidence is level 2. About a third thought there was level 1-3 evidence for hyoscine hydrobromide (level 4) and midazolam (level 4).

We have used these lists to facilitate a process to increase their PBS listing with a group made up of the medical profession and the Rural Health and Palliative Care Branch of the Department of Health and Ageing in association with the Australian government. This has lead to a section in the PBS specifically for palliative care with an initial list of approved drugs.

For many widely used drugs the best level of evidence is not sufficient to justify further subsidy. Reasons may be that studies have not yet been undertaken – we should address this.

**Implications for general practice**

- Access to drugs for palliative care is harder in the community (through the PBS) than in hospital.
- A survey of palliative care doctors produced a list of drugs they thought essential.
- Their perception of the evidence for their use was variable.
- Collaborative work has led to the creation of the first ever section in the PBS for a specific patient population.
- There is a need for high quality studies to justify PBS listing of palliative care drugs.

<table>
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<tr>
<th>Palliative symptom</th>
<th>Drug</th>
<th>% of respondents nominating this drug as first rank</th>
<th>PBS subsidy at time of survey (September 2000)</th>
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<th>Level of evidence</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>Docusate and senna</td>
<td>58</td>
<td>No</td>
<td></td>
<td>1</td>
<td>9</td>
<td>4E</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>Artificial saliva</td>
<td>39</td>
<td>No</td>
<td></td>
<td>1</td>
<td>–</td>
<td>2</td>
</tr>
<tr>
<td>Delirium</td>
<td>Haloperidol</td>
<td>84</td>
<td>Yes</td>
<td></td>
<td>1</td>
<td>21</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>Sertraline</td>
<td>40</td>
<td>Yes</td>
<td></td>
<td>1</td>
<td>25</td>
<td>2</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Diazepam</td>
<td>52</td>
<td>Yes</td>
<td></td>
<td>1</td>
<td>23</td>
<td>2</td>
</tr>
</tbody>
</table>
Conflict of interest: David Woods – speaker fees and travel assistance to attend meetings has been paid for by Mundipharma and Janssen-Cilag.

Acknowledgments

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References