Cost-effectiveness of subcutaneous ketamine in the management of chronic cancer pain

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Overview

• Context
• Study design
• Main results
• Cost-effectiveness
• Limitations
• Implications
Context

Palliative Care Clinical Studies Collaborative (PaCCSC)

– Pain
– Bowel obstruction
– Delirium
– Anorexia
Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Toxicity of Subcutaneous Ketamine in the Management of Cancer Pain

Hardy J, Quinn S, Fazekas B, Plummer J, Eckermann S, Agar M, Spruyt O, Rowett D, Currow D

Population

Exclusion criteria
- Ketamine \( \leq 6 \) months
- Radiotherapy for pain \( \leq 2 \) weeks
- Other procedure or therapy likely to affect pain
- Contraindicating comorbidities

Reproduced with acknowledgement of the Pain Research Group, The University of Texas MD Anderson Cancer Center, USA

Cleeland CS & Ryan KM 1994; Hardy et al 2012
## Cost-effectiveness analysis

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Costs (2014 AU$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health-related quality of life</td>
<td>Ketamine use</td>
</tr>
<tr>
<td>Responder rates*</td>
<td>Hospital admissions</td>
</tr>
<tr>
<td>Adverse events</td>
<td>Medication use</td>
</tr>
</tbody>
</table>

* ≥2 points from baseline in the absence of >4 breakthrough doses of analgesia over the previous 24 hours

Groenvold et al. 2006; Lyons et al. 2009; **McCaffrey** et al 2014
### Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Ketamine (n=93)</th>
<th>Placebo (n=92)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>63.1 (13.4)</td>
<td>64.4 (9.8)</td>
</tr>
<tr>
<td>Male, %</td>
<td>55.1</td>
<td>59.8</td>
</tr>
<tr>
<td>Lung, %</td>
<td>23.7</td>
<td>19.6</td>
</tr>
<tr>
<td>Prostate, %</td>
<td>14.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Colorectal, %</td>
<td>8.8</td>
<td>15.6</td>
</tr>
<tr>
<td>AKPS, median (IQR)</td>
<td>60 (50-60)</td>
<td>60 (50-60)</td>
</tr>
<tr>
<td>BPI average pain score (SD)</td>
<td>5.4 (1.3)</td>
<td>5.2 (1.4)</td>
</tr>
<tr>
<td>FACIT-Pal score#, mean (SD)</td>
<td>109.9 (18.3)</td>
<td>109.6 (18.9)</td>
</tr>
</tbody>
</table>

$0-100; \#0-184;$

AKPS = Australian-modified Karnofsky Performance Status; IQR = interquartile range; SD = standard deviation
## Maximum dose received

<table>
<thead>
<tr>
<th>Ketamine/ placebo dose (mg)*</th>
<th>Number received ketamine</th>
<th>Number received placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>6#</td>
<td>7$</td>
</tr>
<tr>
<td>100</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>300</td>
<td>35</td>
<td>19</td>
</tr>
<tr>
<td>500</td>
<td>36</td>
<td>54</td>
</tr>
</tbody>
</table>

* Participants were required to have received at least 80% of planned dose to complete the first dose level; # two patients withdrew before start of treatment and four withdrew during day 1 before 80% of dose step 1; $ two patients withdrew before start of treatment and five withdrew during day 1 before 80% of dose step 1
## Results: Outcomes and costs

<table>
<thead>
<tr>
<th>Treatment arm</th>
<th>Ketamine (n=93)</th>
<th>Placebo (n=92)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcomes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FACIT-Pal score (SD)</td>
<td>108.4 (17.7)</td>
<td>113.4 (18.3)</td>
</tr>
<tr>
<td>Responder rates*, %</td>
<td>31.2 (21.5, 39.8)</td>
<td>27.2 (19.6, 38.0)</td>
</tr>
<tr>
<td>Adverse events#, n</td>
<td>172</td>
<td>103</td>
</tr>
<tr>
<td><strong>Costs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>$476</td>
<td>$0</td>
</tr>
<tr>
<td>Hospital stays</td>
<td>$8,295</td>
<td>$8,196</td>
</tr>
<tr>
<td>Medication usage</td>
<td>$78</td>
<td>$118</td>
</tr>
<tr>
<td>Total</td>
<td><strong>$8,849</strong></td>
<td><strong>$8,314</strong></td>
</tr>
</tbody>
</table>

*ns, p=0.55; Day 1 incidence rate ratio 1.95 p<0.01 (95% CI 1.46, 2.61)  
McCaffrey et al 2014
## Results: Incremental analysis

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Increment* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>FACIT-Pal score#, mean change</td>
<td>-5.3 (-9.4, -0.8)</td>
</tr>
<tr>
<td>Responders, %</td>
<td>4 (-9, 17)</td>
</tr>
<tr>
<td><strong>Costs</strong></td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>$476</td>
</tr>
<tr>
<td>Hospital stays</td>
<td>$99 (-$166, $387)</td>
</tr>
<tr>
<td>Medication usage</td>
<td>-$40 (-$79, $12)</td>
</tr>
<tr>
<td>Total</td>
<td>$535 ($291, $821)</td>
</tr>
</tbody>
</table>

* difference between ketamine and placebo; $ 0-100; # 0-184; SD = standard deviation

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Cost-effectiveness acceptability plane

NW quadrant: intervention costs more and gains less

Incremental cost (AU$)

difference in FACIT-Pal QOL score after 5 days treatment

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Cost-effectiveness acceptability curve

probability ketamine is the preferred treatment

threshold value per additional unit gain in QOL after 5 days treatment
(thousands of AU$)

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A few caveats...

– Cost data
  – multiple imputation

– Generalisability

– Other treatment options
  – paucity of evidence

Kaambwa et al 2012; Burton et al 2007
Better informing decision making with multiple outcome cost-effectiveness analysis under uncertainty in cost-disutility space

McCaffrey N, Agar M, Harlum J, Karnon J, Currow D, Eckermann S

*PLoS ONE* 10(3):e0115544. doi:10.1371/journal.pone.0115544

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Study implications

– No statistically significant difference in responder rates but higher toxicity and worse QOL

– Higher ketamine costs despite lower costs for other medications

– When costs and QOL are jointly considered, ketamine is neither effective nor cost-effective
References


Dr Nikki McCaffrey May 2015
References


Dr Nikki McCaffrey May 2015


Kaambwa B, Bryan S,Billingham L. Do the methods used to analyse missing data really matter? An examination of data from an observational study of Intermediate Care patients. BMC research notes 2012;5:330.

References


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