Meeting date: 30 Nov 2010

Intervention: Lignocaine infusion for neuropathic pain

Background:
Lignocaine is a local anaesthetic drug which is quite rapidly cleared from the body/bloodstream. Infusions allow administration over an extended time via either an intravenous drip or pump under safe monitoring conditions. This procedure is used for both diagnostic and treatment purposes.

IPM 2010 update – summary of findings:
The 2010 update has found that overall there is conflicting evidence on the short term effectiveness of lignocaine infusion for neuropathic pain. The four new studies identified provide no additional evidence and, like the evidence examined in 2005, report on short term intervention and relief. The conclusion is therefore that the 2005 clinical recommendation, not recommended for the general treatment of neuropathic pain, should remain in place:

<table>
<thead>
<tr>
<th>Volume of evidence</th>
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<tr>
<td>Comment here on any issues concerning the quantity of evidence available on this topic.</td>
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</table>

Four eligible studies of efficacy/effectiveness, one systematic review (Attal, Mazaltarine et al. 2009) and three randomised controlled trials (Gottrup, Bach et al. 2006; Tremont-Lukats, Hutson et al. 2006; Attal, Mazaltarine et al. 2009; Gormsen, Finnerup et al. 2009) were identified by the updated search.

The three randomised trials were all placebo controlled double blind studies, i.e. NHMRC evidence level II. These studies examined the effectiveness of lignocaine infusions in patients with neuropathic pain arising from peripheral (three studies) or central (one study) injury.

A further six studies, small case series or case reports not eligible for inclusion for effectiveness, were identified as potentially relevant to issues relating to the safety of lignocaine (Cahana, Carota et al. 2004; Kiefer, Rohr et al. 2008; Shirani, Salamone et al. 2008; Gil-Gouveia and Goadsby 2009; Schafranski, Malucelli et al. 2009; Schwartzman, Patel et al. 2009).

The systematic review, while published in 2009 (Attal, Mazaltarine et al. 2009), did not contribute any studies that were (a) not previously reported in the IPM Guidance of 2005 or (b) eligible for this update.
**Consistency of evidence**

Comment here on the degree of consistency demonstrated by the availability of evidence. Where there are conflicting results, indicate how the group formed a judgement as to the overall direction of the evidence.

<table>
<thead>
<tr>
<th>These studies reported on two different patient populations i.e. those with neuropathic pain arising from damage to the peripheral nervous system and those with neuropathic pain arising from SCI. The studies were heterogeneous in a number of other respects including lignocaine dose and etiology. All of these trials were of very short durations. Two of the three trials were carried out in Aarhus University Hospital Denmark these were both crossover trials.</th>
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<tr>
<td>These studies presented conflicting evidence on the effectiveness of lignocaine.</td>
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**Applicability of evidence**

Comment here on the extent to which the evidence is directly applicable in the New Zealand setting. Comment here on how reasonable it is to generalise from the results of the studies used as evidence to the target population for this guideline.

| These studies were carried out in University hospitals in a largely research setting and examined the short-term effect of lignocaine infusions; the clinical significance of such short term studies in the context of ACC’s target populations is questionable. |

**Cost**

Comment on any economic costs associated with this service, product or procedure

<table>
<thead>
<tr>
<th>The unit cost of this procedure is $300.</th>
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<tr>
<td>Anticipated volume for the year 2011-2012 is 26 procedures with a total cost of $7,800.</td>
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</table>

**Clinical Impact**

Comment here on the potential clinical impact that the intervention in question might have – e.g. size of patient population; magnitude of effect; relative benefit over other management options; resource implications; balance of risk and benefit.

**Peripheral neuropathic pain:** of the three eligible studies (Gottrup, Bach et al. 2006; Tremont-Lukats, Hutson et al. 2006; Gormsen, Finnerup et al. 2009), only one reported positive results for Lignocaine (Tremont-Lukats, Hutson et al. 2006). This was a short duration dose-finding study.

**Summary**

The systematic review concluded that, similar to ketamine, Lignocaine infusions for neuropathic SCI pain should only be used in specialized centres. However, this review does not add any additional evidence to that used to inform the original 2005 IPM Guidance.

The included RCTs examined the effect of Lignocaine on neuropathic pain of peripheral origin. In one study the effect of Lignocaine at different infusion rates was compared to a placebo (Tremont-Lukats, Hutson et al. 2006), in two studies Lignocaine was compared in crossover trials with the active comparators AMP receptor antagonist (NS1209) (Gormsen, Finnerup et al. 2009) and ketamine (Gottrup, Bach et al. 2006).

The evidence provided by two of the reviewed RCTs (Gottrup, Bach et al. 2006; Gormsen, Finnerup et al. 2009) was largely negative with respect to Lignocaine and these studies if included would not change the current IPM Guideline recommendations for Lignocaine.

The evidence provided in the remaining study (Tremont-Lukats, Hutson et al. 2006) was positive in relation to the effects of Lignocaine on neuropathic pain. However this study was a short term (10 hours) dose finding study with only the highest dose group of 7 patients showing improved results over placebo . The evidence reported in this study is considered to be unlikely to change the current recommendations for Lignocaine.

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4 Thus the clinical significance is questionable.
**Serious Adverse events and complications not previously reported**

The six studies identified as potentially of interest for the safety review either (a) did not report serious adverse events or any new adverse events, or (b) were not, upon review, eligible.

**Other Factors**

*Indicate here any other factors that you took into account when assessing the evidence base.*

<table>
<thead>
<tr>
<th>Evidence statement</th>
<th>Weight &amp; consistency of evidence</th>
<th>Evidence Level</th>
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<tbody>
<tr>
<td>Four studies identified for the 2010 IPM Guidance update do not provide any additional evidence for this intervention in this population. Similar to the evidence provided in the 2005 guidance, these studies reported on short-term intervention and relief. Overall, there is conflicting evidence of short term effectiveness of lignocaine infusion for neuropathic pain.</td>
<td>-</td>
<td>NHMRC evidence level II</td>
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**Practice recommendation (for IPM website)**

*What clinical practice recommendation(s) can be drawn from this evidence? Please indicate the grade of recommendation(s).*

- The 2005 recommendation remains unchanged:
  - The general use of intravenous infusion of lignocaine is not recommended for the treatment of neuropathic pain

**Purchasing recommendation**

*What recommendation(s) does the Purchasing Guidance Advisory Group (PGAG) draw from this evidence?*

- Do not purchase intravenous infusion of lignocaine for the general treatment of adults with persistent neuropathic pain.
References


