Transport Accident Commission & WorkSafe Victoria

Evidence Service

Implantable pain therapies: Intrathecal (IT) infusions

Evidence summary

Report number: ***0611-002-R7.1***

Overview

This evidence review is an update of a previous review requested by the Transport Accident Commission (TAC) and WorkSafe Victoria (WSV) conducted in September 2008.[1] The current report has identified further evidence for the effectiveness of IT opioids and IT ketorolac, a non-steroidal anti-inflammatory drug (NSAID). No new evidence for the effectiveness of IT baclofen and IT ziconotide was identified since the previous report.

At present, the evidence available for the effectiveness of intrathecal (IT) infusions in patients with persistent, non-cancer pain is insufficient (IT opioids, baclofen, ziconotide, and ketorolac).

Definition

For a small proportion of patients with non-cancer pain who do not experience sufficient pain relief or have intolerable side effects with conventional treatments, intrathecal (IT) infusions may be an effective treatment. A pump is implanted under the skin usually in the abdominal region. Tubes from the implanted pump are programmed to trickle out the drug at a certain rate into the space around the spinal cord (intrathecal or IT) which may provide the patient with sufficient pain relief.

The following evidence review identified a total of fifteen studies (three evidence-based guidelines, three health technology assessments, eight systematic reviews and one randomised clinical trial) of IT infusions for persistent pain that met the selection criteria.

ANALGESICS (OPIOIDS):	The most recent high quality systematic review (SR)[2] was found to be well conducted. The included studies in the SR, which were case series (low level evidence), **provided limited evidence to determine whether IT opioids are effective for chronic, persistent non-cancer pain.**
ANTI-SPASMODICS (BACLOFEN):	Only low level evidence based on a single case series study[3, 4] exists for the effectiveness of IT baclofen in the treatment of persistent pain. Therefore, there is **insufficient evidence to determine whether IT baclofen is effective for chronic, persistent non-cancer pain.**
CALCIUM CHANNEL ANTAGONISTS (ZICONOTIDE):	The most comprehensive, up-to-date high quality SR[5] identified, found that "no studies for ziconotide met the inclusion criteria for either effectiveness or complications". No further primary studies were identified according to the inclusion criteria requested in this report. Hence, there is **insufficient evidence to determine the benefits of IT ziconotide treatment for chronic, persistent non-cancer pain.**

OTHER MEDICATIONS (KETOROLAC):	A small cross-over RCT[6] did not find a statistically significant difference in treatment effect following IT ketorolac or placebo with established, simultaneous IT morphine, although a trend for reduced pain intensity and unpleasantness was present following IT ketorolac. Overall, this led us to conclude that **there is insufficient evidence of effectiveness of IT ketorolac on persistent pain.**

In what clinical conditions is this intervention indicated for use?

Drug infusions through implantable pumps are indicated and approved for use by the TGA for baclofen only. Morphine (opioids), ziconotide and other medications (ketorolac) are not approved and are prescribed by some physicians in an "off label" capacity. For "off label" use appropriate patient consent is required.

Findings in the following report identify the target group for use of IT infusions (opioids and ketorolac) to be adults with chronic non-cancer pain that have not experienced pain relief with conventional treatments. Insufficient evidence is available to confirm which patients IT baclofen and IT ziconotide can be used for.

What is the efficacy and effectiveness of this intervention on persistent pain in these conditions?

ANALGESICS (OPIOIDS):	There is **insufficient evidence** to answer this question.
ANTI-SPASMODICS (BACLOFEN):	There is **insufficient evidence** to answer this question.
CALCIUM CHANNEL ANTAGONISTS (ZICONOTIDE):	There is **no evidence** to answer this question.
OTHER MEDICATIONS (KETOROLAC):	There is **insufficient evidence** to answer this question.

What is the effect of this intervention on function, quality of life, return to work, medication use and use of the healthcare system?

ANALGESICS (OPIOIDS):	There is **insufficient evidence** to answer this question.
ANTI-SPASMODICS (BACLOFEN):	There is **insufficient evidence** to answer this question.
CALCIUM CHANNEL ANTAGONISTS (ZICONOTIDE):	There is **no evidence** to answer this question.
OTHER MEDICATIONS (KETOROLAC):	There is **insufficient evidence** to answer this question.

In what patient groups/conditions is use of this intervention contraindicated?

Patient groups/conditions in which use of IT infusions are contraindicated are

- When infection is present[7]
- When the pump cannot be implanted 2.5 cm or less from the surface of the skin[7]

- When body size is not sufficient to accept pump bulk and weight[7]
- Allergy or hypersensitivity to the drug being used[7, 8]
- Blood thinning medications[9]
- In patients who have another implanted device, such as a pacemaker[8]
- Drugs with preservatives[7]
- Epilepsy refractory to therapy[8]
- Previous history of psychosis[9]

The Australian and New Zealand College of Anesthetists caution the use of IT therapy in patients where psychological factors are considered to be a major pain modifying factor. [10]

What are the risks associated with use of this intervention?

Device-related adverse events were only reported for IT opioids,[2] however the same device is utilised for all other IT drugs. Adverse events include pump and catheter malfunctions and malpositioning, surgical complications and postsurgical complications.

The following drug-related adverse events were reported with IT ketorolac[6] including mild sedation (n=2, lasting < 2 hours), mild dizziness (n=1, lasting < 30 minutes, and a hot sensation in the back, headache, urinary retention, and hives (n=1, lasting< 4 hours). Following saline infusion in the RCT, mild sedation (n=2, lasting < 1 hour, mild nausea (n=2, lasting < 1 hour), and mild headache (n=1, lasting < 2 hours) were reported.

The only serious adverse event reported following IT administration of opioids was hallucinations.[2]

As no evidence was available for IT baclofen or IT ziconotide, drug-related adverse events remain unknown.

Glossary of Findings	
Insufficient	Little or no evidence exists to answer this question
Limited evidence of effectiveness	There is some evidence of effectiveness but not enough to be sure. More high quality studies are needed before conclusions can be drawn.

Accompanying documents to this report	
Title	*Report number*
Implantable pain therapies: Intrathecal (IT) infusions – Full Report	Research Report No. *0611-002-R7*
Implantable pain therapies: Intrathecal (IT) infusions – Plain Language Summary	Research Report No. *0611-002-R7.2*
Implantable pain therapies: Intrathecal (IT) infusions – Technical Report	Research Report No. *0611-002-R7.3*