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Duarte, Rui; Raphael, Jon; Eldabe, Sam

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**Intrathecal drug delivery for the management of pain and spasticity in adults: an executive summary of the British Pain Society's recommendations for best clinical practice**

Rui Duarte<sup>1</sup>, Jon Raphael<sup>2</sup>, Sam Eldabe<sup>3</sup>

<sup>1</sup> School of Health and Population Sciences, University of Birmingham, Birmingham, UK

<sup>2</sup> Department of Pain Medicine, Dudley Group of Hospitals, Dudley, UK

<sup>3</sup> Department of Pain and Anaesthesia, The James Cook University Hospital, Middlesbrough, UK

Corresponding author:

Sam Eldabe, Department of Pain and Anaesthesia, The James Cook University Hospital, Middlesbrough TS4 3BW, UK.

Email: seldabe@mac.com

**Abstract**

This article provides a summary of the updated British Pain Society Guidance on Intrathecal Drug Delivery for the management of pain and spasticity in adults.

We aim to highlight the areas of the guidance that have been updated and to provide a concise summary.

**Keywords**

Chronic pain, pain, intrathecal, analgesia, nociceptors

Accepted manuscript

## **Background**

The technique of intrathecal drug delivery (ITDD) is based on the principle that effective analgesia can be achieved by the action of some drugs at the dorsal horn and adequate concentrations cannot be achieved by systemic administration, or only by high systemic doses. Delivery of the drug by the intrathecal route is a means of achieving these enhanced therapeutic effects. The smaller doses needed for intrathecal administration also allow a reduction in side effects compared to systemic administration. There is evidence to support the use of this technique.

The document describes the clinical use of ITDD systems in the management of pain and spasticity, reviews the available drugs and ITDD technologies and provides recommendations for the context in which this therapy should be delivered. It covers the situations in which pain relief is the major indication for the technique.

The recommendations are primarily evidence based but where necessary comprise the opinion of the working group members. The recommendations are accompanied by information for patients and their carers, intended to inform and support patients in their decisions.

The current executive summary highlights the main updates in the British Pain Society's ITDD recommendations for best clinical practice.

## **Objectives**

This document is intended to define and support best practice and provide guidance for:

- practitioners and institutions delivering or planning to deliver the treatment;
- referrers, as to which patients might benefit;
- primary carers regarding the management of patients with implanted ITDD systems;
- purchasers of health care as to the nature of the technique and when it might be used.

## **Indications**

ITDD is a recognised intervention for the management of chronic non-malignant pain (CNMP), pain in patients with cancer and spasticity. ITDD can be used adjunctively and concurrently with other modes of pain management. Key indications for ITDD in CNMP are nociceptive pain, mixed aetiology cases of nociceptive and neuropathic pain, and neuropathic pain that has failed to respond to other management techniques including an adequate trial of spinal cord stimulation (SCS). A robust randomised controlled trial (RCT) of ITDD in CNMP is currently lacking from the available literature. A recently published RCT in CNMP observed that ITDD reduces pain in those patients who responded to the test dose.<sup>1</sup> The evidence for use of ITDD in CNMP is mostly limited to supportive prospective open studies. Because of the complexity of pain in these patients, selection remains challenging and experienced teams should make the decisions. The principal indication for using ITDD for pain in patients with cancer is failure of conventional routes of administration of analgesics to achieve satisfactory analgesia despite escalating doses of strong opioids, and/or dose limiting side effects. The use of ITDD for pain in patients with cancer is supported by RCT evidence.<sup>2</sup> There are on-going RCT's evaluating the

effectiveness of ITDD in spasticity. At the moment the evidence for effectiveness of ITDD in spasticity is limited to well-designed open studies.

### **Complications**

Prospective patients should be adequately informed of potential complications and these should be addressed in the informed consent. There must be clear pathways for dealing with complications, both in and out of hospital. It is recognised that it is not possible for one implanting doctor to be permanently on call; other non-implanting doctors with appropriate training in resuscitation, dealing with consequences of sudden drug withdrawal or overdose, and proficient in the use of implanted pumps can be responsible. The patient's primary care team should be aware of potential complications and have management plans.

*Drug related complications* - Sudden drug withdrawal or overdose are rarely observed in patients treated with ITDD. Recently reported mortality rates associated with the use of ITDD should be interpreted with caution. Mortality rates of patients treated with ITDD were higher when compared with patients treated with spinal cord stimulation (SCS) after 1-month (0.39% vs 0.09% respectively) and after 1-year (3.89% vs. 1.36% respectively).<sup>3</sup> The main cause of mortality for ITDD patients was respiratory depression due to opioid or central nervous system depressant drugs as a primary or contributing factor. It should be noted that from the 9 index cases reported, 7 patients received an initial intrathecal opioid dose that exceeded the 0.2 to 1mg/day dose recommended on the drug manufacturer's label; 2 patients had a history of prescription drug abuse or overuse, and the 2 patients with an initial intrathecal opioid dose within the suggested range were obese, which may contribute to decreased respiratory reserve.

*Procedure and device related complications* - Serious procedure and device related complications are rare. Minor complications are common. Device-related complications include catheter kinking, disconnection, dislodgement or pump failure, programme error and overflow or incorrect refill. In a multicentre study with cancer and non-cancer pain patients, procedure related complications occurred at a rate of 0.29 events per patient year and catheter related complications at a rate of 0.05 events per patient year.<sup>4</sup> The rate of complications / side effects in a non-cancer study with a 13-year follow-up was 0.111 events per patient year.<sup>5</sup>

*Infections* - Possible infections include meningitis epidural abscess pump pocket infection or pump reservoir infection. The rate of meningitis reported by studies ranged from 2.3% to 15.4% and for wound infections from 4.2% to 8.8%.<sup>6</sup> When considering only CNMP studies, the percentage of patients with meningitis ranged from 0% to 4% and for wound infections, from 0% to 22%. Infections may require explantation of the device.<sup>7</sup>

*Neurological damage* - Neurological deficits, although rare can occur from the procedure and from inflammatory mass development at catheter tip. Guidelines should be in place to permit rapid access to neuroradiological expertise and neurosurgical treatment if either is suspected. There are reports of neurotoxicity following intrathecal infusions of local anaesthetics. Several drugs have demonstrated neurotoxicity and except in special cases, are not recommended for intrathecal use. There are also reports of permanent

neurological damage following intrathecal local anaesthetic administration.

### **Drug pump compatibility**

Consideration must be given to stability, compatibility and sterility of intrathecal drugs. Morphine, hydromorphone, clonidine and baclofen are stable at room and body temperature for three months. Bupivacaine is stable for 60 days. Refill intervals should not exceed the period of stability. In recent years there have been a number of studies published designed to address stability of admixtures, although more work is needed in this area. Only Infumorph, baclofen and Ziconotide are approved for delivery with the Medtronic Synchronomed II device. A recent pump manufacturer urgent field safety notice warned of a higher rate of device failure resulting in therapy withdrawal when the particular device (Medtronic Synchronomed II) is used to deliver unapproved drugs and drug formulations including: compounded drugs, some formulations of baclofen and morphine; admixtures for severe spasticity therapy containing baclofen with clonidine, and baclofen mixed with other drugs; admixtures for chronic pain therapy containing fentanyl and/or sufentanil, bupivacaine, clonidine, hydromorphone, morphine, and baclofen. The risk of continuing to use this device to deliver unapproved drugs/mixtures should be carefully assessed on a case-by-case basis. Possible risk and the action needed in case of therapy withdrawal should be considered and discussed with patients on an individual basis.

### **Magnetic Resonance compatibility issues**

Some ITDD systems are at risk of significant damage and malfunction from Magnetic Resonance Imaging (MRI) scanners. Pump manufacturer guidance should be sought and will vary according to pump type and model, field strength of the magnet, sequences to be used and body part to be imaged, specifically whether near the implant and whether local coils will be used. Advice should be taken from local scanning departments; all should have access to manufacturer guidelines on this. Implanting teams should consider the type of pump and act accordingly. Patients with fixed rate delivery systems should have both the reservoir and catheter emptied prior to the scan and then refilled once completed. However if the catheter is emptied then issues relating to potential drug withdrawal and resulting increase in pain and spasms need to be addressed. Due to heating effect, patients with this type of pumps need to be monitored for 24 hours for potential respiratory effects. For patients with programmable devices, the pump specific manufacturer guidance should be followed in consultation with local radiology department. The device should be checked following imaging to confirm that it has not stalled.

### **Conclusions:**

Intrathecal drug delivery is an effective means of delivering analgesics in patients with severe pain either related to cancer or of non-malignant origin. The technique should only be carried out by experienced multidisciplinary teams, with appropriate expertise in patient selection, counselling, surgical techniques and long term follow up.

The implanting team must be aware of potential complications arising from surgery, hardware, drugs or drug hardware interactions. Teams should have access to neurosurgical and neuroradiology expertise where necessary. Although largely a safe technique, ITDD carries a higher risk than other interventional pain techniques such as spinal cord stimulation. Appropriate arrangements must be in place to deal with potential complications at all times.

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