INTRATHECAL INFLAMMATORY MASSES: A LIGHT AT THE END OF THE CATHETER TIP

Rui Duarte[a], Jon Raphael[a], Jane Southall[b], Candice Baker[b], Dalvina Hanu-Cernat[c]
[a]Faculty of Health, Birmingham City University, Birmingham, UK
[b]Department of Pain Management, Russells Hall Hospital, Dudley, UK
[c]Pain Management Unit, University Hospital Birmingham, Birmingham, UK

BACKGROUND

The first reservoir for intrathecal analgesics delivery was implanted in 1981[1] and since then continuous intrathecal analgesia using opioids and other analgesics has become a recognized therapy for the management of severe and otherwise intractable chronic pain.

One of the possible long term side-effects of intrathecal drug delivery systems is the formation of an intrathecal inflammatory mass, also known as granuloma. Although rare, the magnitude of this complication can be serious, with potential for neurological morbidity[2].

The first granuloma report was published in 1991[3]. Early signs of granuloma can include increase in pain, the need for unusual or unanticipated dose escalation, appearance of new pain sensations near the level of the catheter tip, sensory loss and neurological changes[4-7].

The cause of granulomatous masses is uncertain but certain drugs, drug concentrations, duration of treatment, catheter tip location and cerebrospinal fluid (CSF) flow patterns are some of the current hypotheses as to the aetiology of intrathecal granulomas[5,7,8].

OBJECTIVES

To investigate the association between intrathecal drug, flow rate, drug concentration and drug dose with the formation of intrathecal inflammatory masses.

METHODS

A retrospective longitudinal study of 56 consecutive patients receiving long term intrathecal analgesic administration was undertaken through screening of medical records from date of implant until to June 2009. Data regarding drug flow rate, dose per day and concentration of drugs administered were recorded for morphine, diamorphine, bupivicaine, clonidine and baclofen and averages computed. For patients diagnosed with granuloma, only the data until date of diagnosis was considered for analysis. Dichotomous data were compared using Mann-Whitney. Inter-variable relationships were evaluated by Spearman's correlations. Statistical significance represented $p \leq .05$.

GRANULOMA DETECTION

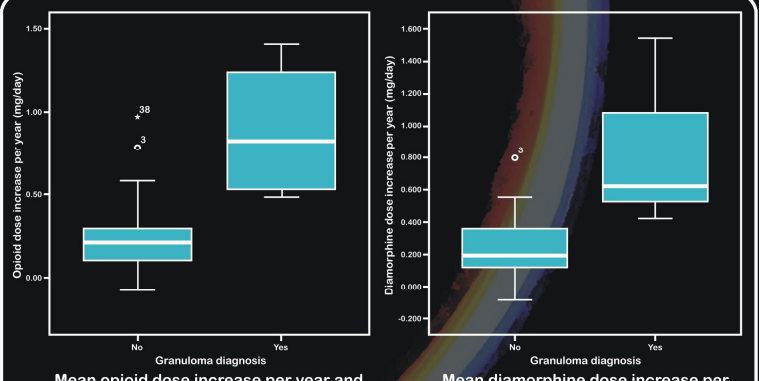
When attending for pump refill, all patients were asked if the pain was being controlled and if new symptoms had emerged, including new pain, altered sensation or weakness of limb. In case of an affirmative answer, a neurologic examination took place and if there was a clear change, a Magnetic Resonance Imaging (MRI) scan was performed. For this purpose, programmable pumps were turned off, non-programmable pumps were emptied and the imaging was carried out via a 1.5 Tesla MRI system through Short Tau Inversion Recovery (STIR) sequence. In the existence of doubts regarding the formation of intrathecal inflammatory masses, a second MRI would be completed with the contrast-enhancing agent Gadolinium.

RESULTS

The sample comprised 33 women (58.9%) and 23 men (41.1%) with an average age at time of implant of 50 ± 10 years (range: 30-72).

The average duration of chronic pain symptoms preceding date of implant was 14 ± 9 years (range: 2-36) and the average follow-up time post-implant was 91 ± 55 months (range: 9-209). Four of the 56 patients were diagnosed with intrathecal granuloma indicating a rate of 7%, the equivalent to 0.009 events per patient year. Twenty one of the patients had received morphine either alone or combined; 22 had received diamorphine either alone or mixed; and 13 crossed over from morphine to diamorphine or the inverse. None of the patients with granuloma crossed over before diagnosis. The mean time span until granuloma formation was 39.5 ± 13.5 months (range: 22-52). The mean time of treatment for the non-granuloma patients was 90 ± 57 months (range: 9-209).

A significant correlation was found between opioid dose ($r=.275$, $p<.05$), yearly increase of the opioid dose ($r=.433$, $p<.05$) and granuloma formation. Clonidine appeared to have a protective effect for the non-granuloma patients. No association was found with flow rate ($r=.056$) or opioid concentration ($r=.214$).



Mean opioid dose increase per year and granuloma formation

Mean diamorphine dose increase per year and granuloma formation

The mean opioid dose increase per year was significantly higher in patients diagnosed with granuloma (opioid median =.22, $U=6.00$, $p<.005$, $r=-.43$), as well as the mean diamorphine dose increase per year (diamorphine median =.207, $U=5.00$, $p<.05$, $r=-.44$).

CONCLUSION

This is the first detailed study showing an association of diamorphine with granulomas. This study supports the previous finding of intrathecal opioid dose being a risk factor for intrathecal granulomas and clonidine being protective. In addition we have found that the yearly increase in opioid dose is a risk factor for granulomas and could serve as an indicator for closer surveillance.

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ADDRESS CORRESPONDENCE: Rui Duarte, Centre for Health and Social Care Research, Birmingham City University, Room 311, Ravensbury House, Westbourne Road Campus, Birmingham B15 2TN, UK
E-MAIL: ruivduarte@gmail.com

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