Introduction

Methadone is a strong synthetic opioid used for treatment of cancer pain that has responded poorly to morphine or other strong opioids despite dose escalation and use of appropriate adjuvant analgesics. In many ways it is an ideal drug for opioid rotation because of its efficacy, rapid onset of action, good oral bioavailability, lack of known active metabolites, lack of accumulation in those with renal impairment and low cost. However, methadone is generally not used as a first-line analgesic due to its highly variable pharmacokinetics, drug interactions and its long half-life with risk of accumulation. Indications for methadone use in palliative care include neuropathic pain, cough and renal impairment. Methadone may also be used in patients who develop unacceptable side effects with other opioids. Given that methadone can be beneficial for many patients, but is also a complex drug, it is important to look into how it can be used to its maximal benefit, whilst it is prescribed in the most appropriate manner.

Aims

1. To evaluate the clinical benefits when converting to methadone from another opioid, in terms of improvement of analgesia and tolerability.
2. To establish current methadone use in Scotland’s palliative care services.

Methods

An audit pro-forma was completed for all patients started on methadone for pain in St Columba’s Hospice from January 2006–January 2010 (96 patients in total). Pain intensity was measured daily for 14 days after methadone initiation using the patient’s self-reported visual-analogue scale, and the clinical benefit of methadone was assessed by the clinician and patient. Statistical analysis for pain scores on Day 1 versus Day 7 and Day 14 was performed using the Wilcoxon signed rank test on SPSS. Reasons for initiation and discontinuation of methadone were noted. A questionnaire was sent to all Scottish hospices asking clinicians about methadone use in their service.

Results

Pain-scores

Figure 1 compares the pain-scores of Days 7, 10, 12 and 14 with those of Day 1, showing whether the scores were better, worse or the same. By Day 7, 59% of patients on methadone had statistically significant improved pain-scores when compared to Day 1 (p<0.003). The mean pain-score at Day 7 was 5.63 as opposed to 8.03 at Day 1. By Day 14, 47% of patients had statistically significant improved pain-scores when compared to Day 1 (p<0.031) and the mean pain-score at Day 14 was 5.88 as opposed to 8.03 at Day 1.

Figure 1

Analgesic response to methadone

The clinician tended to give a more positive assessment of benefit from methadone, judging 76% of patients to have responded to methadone, whereas only 61% of patients felt that methadone improved their pain.

Figure 2

Reasons for discontinuation of methadone

Figure 2 illustrates the change in pain severity (as assessed by the clinician) from Day 1 to Day 14. There was a decrease in the number of patients with severe pain-scores after 14 days, and an increase in the mild and pain-free categories when compared to Day 1.

Figure 2

Discussion

The effectiveness of methadone was demonstrated by both a reduction in mean pain score and pain severity level over the 14 days. Clinicians felt the overall benefit derived from methadone was greater than that which was reported by the patients. This is reflected in the literature, as health professionals have been shown to underestimate the level of cancer pain experienced by patients. In this study 33% of pain-scores did not correspond to the overall clinical picture. For patients such as those it may be helpful not only to use a visual-analogue scale to record pain, but also to record functional capacity via an Activities of Daily Living (ADL) scale such as the ECOG performance status, or a pain-score with a functional element, e.g. the Brief Pain Inventory. This would give a clearer picture of the effect of methadone both on pain and on functional capacity.

The main reasons for starting methadone at St Columba’s Hospice were opioid toxicity and neuropathic pain, both of which are well-known indications for methadone use in cancer pain. Uncontrolled pain was the most common reason for methadone discontinuation. These findings were consistent with the Scottish hospice survey.

Methadone does not work for everyone, and it is important to identify those patients who are not responding, re-evaluate their pain, convert them to alternative analgesic regimes. 78% of patients had tried two or more opioids before commencing methadone and 25% had tried three or four. The effectiveness of methadone was inversely proportional to the number of opioids previously tried, suggesting that patients trying a greater number of opioids have pain that is more difficult to manage. There is wide variation in methadone use throughout Scotland. It would be interesting to explore reasons for this, e.g. availability of guidelines or accessible training.

Conclusion

Methadone can be a successful analgesic, especially for patients with neuropathic pain and those who are opioid toxic. The results suggest, however, that the response to methadone may depend on the number of opioids that have previously been tried. This study has shown that methadone use varies significantly throughout Scotland, with no one protocol or guideline being followed nationally.

Reasons for discontinuation of methadone

Figure 3

Reasons for conversion to methadone

The main reasons for starting methadone in St Columba’s Hospice were opioid toxicity and neuropathic pain (Figure 3). Most patients (92%) had more than one reason for converting to methadone.

Figure 3

Reasons for conversion to methadone

Figure 4

Methadone Use in Scottish Hospices

The response rate from the questionnaire survey was 76%. The mean number of patients started on methadone in Scottish hospices was 9 per year, (range 0 to 40 patients per year). 71% of hospices started 30-40 patients a year. The main reason for initiating methadone was neuropathic pain and the main reason for discontinuation was uncontrolled pain. Methadone use varied considerably throughout Scotland, and was dependent on the individual clinician. The Morley-Makin method was the most frequently used approach for methadone titration (94%). There are no universal methadone guidelines used in palliative care throughout Scotland, but the main reported sources of information about methadone were www.palliativedrugs.com and local guidelines.

Figure 4

References