Title

More time in a community setting: a service evaluation of the impact of intrathecal drug delivery systems on place of care of patients with cancer pain.

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Title

More time in a community setting: a service evaluation of the impact of intrathecal drug delivery systems on place of care of patients with cancer pain.

Abstract

Background

Intrathecal Drug Delivery Systems are underutilised in the management of refractory cancer pain despite evidence of their efficacy. Not all patients who are offered this treatment modality accept it. There is no current evidence that indicates if the use of intrathecal drug delivery systems impacts on place of care for patients with cancer related pain.

Aims

This service evaluation compared place of care, place of death and morphine equivalent daily dose at end of life for patients in whom Intrathecal Drug Delivery was successfully established vs those who chose comprehensive medical management.

Setting/participants

A retrospective longitudinal cohort study of 45 patients with cancer pain comparing those who had ongoing analgesia successfully delivered via an implanted Intrathecal Drug Delivery System (n=28) with those who continued to receive comprehensive medical management (n=17).

Results

There was a markedly greater time spent in the community in the intrathecal group than the medical management group (median 126.5 days vs 25.5 days; *P* =0.002) and a lower morphine equivalent daily dose at end of life (median 127.5 vs 440.0 p=0.022).

Conclusion

In patients with advanced cancer, the successful establishment of intrathecal analgesia is associated with more time in the community and a lower morphine equivalent daily dose at end of life. The study has low numbers, and the sample was retrospectively selected. Nevertheless, these findings suggest the initial investment of time in an inpatient setting may be beneficial. Further research is required, using larger, prospective studies of patient outcomes in this setting.

Key Statements

What is already known about this topic?

- Intrathecal drug delivery systems can be used to manage cancer pain effectively and are under-utilised.
- Uncontrolled pain is a predictor of institutionalised care in patients with advanced cancer.

What this study adds?

- Patients with intrathecal drug delivery systems in situ live longer in the community than those who opted not to accept intrathecal drug delivery as a treatment modality

Implications for practice, policy or theory

- Time spent establishing Intrathecal drug delivery in an inpatient setting can be viewed positively in the light of time subsequently spent in the community
- Policymakers should aim for equity of access to services which can offer assessment for and delivery of Intrathecal drug delivery systems where appropriate

Introduction

Background

Palliative care services support patients with advanced cancer to achieve their preferred places of care and death. 58% of patients with advanced cancer expressed a preference for end of life care at home [1]. However patients with higher pain intensity scores are more likely to be cared for in an institution [2]. It is known that intrathecal drug delivery systems can offer both survival benefit and pain improvement in patients with advanced cancer, and that this modality is underutilised [3, 4,5]. Although some evidence exists for the efficacy of intrathecal drug delivery systems on pain control, drug toxicity, and survival, there is no evidence of the impact of intrathecal drug delivery systems on the location of care of patients receiving this treatment modality [6].

We run an established interventional cancer pain management service in Scotland following national guidelines [7]. We offer assessment and where appropriate intrathecal drug delivery for patients with refractory cancer pain.

Aim

This service evaluation compared place of care, place of death and morphine equivalent daily dose at end of life for patients in whom Intrathecal Drug Delivery was successfully established vs those who chose comprehensive medical management.

Methods

Study design

A service evaluation was undertaken using a retrospective comparison of two cohorts of patients with cancer pain who had potential to benefit from intrathecal drug delivery. The first group accepted intrathecal drug delivery and received this treatment until death. The comparison group turned down intrathecal drug delivery and received comprehensive medical management until death.

Setting

The interventional cancer pain management service is a multidisciplinary service. Patients with complex cancer-related pain are referred to the service by Palliative Medicine physicians for assessment and consideration of an intervention including intrathecal drug delivery. If intrathecal drug delivery is considered beneficial, patients are offered a trial of this treatment. Not all patients who are offered intrathecal drug delivery accept the intervention. Goals are set for patients who agree to a trial. If these are not met they do not go onto implantation. If the trial is successful a permanent Medtronic intrathecal pump is implanted, and patients receive a mixture of morphine and local anaesthetic via the pump until death.

The service evaluation period was 1st April 2015 to 18th October 2021.

Participants

Patients eligible for inclusion in the service evaluation were referred to the interventional cancer pain service over the evaluation period and were assessed as having potential to benefit from intrathecal drug delivery. The intrathecal group consisted of patients who after a successful trial had

a permanent pump implanted. The comprehensive medical management group turned intrathecal drug delivery down. Patients who were alive at the end of the study period were excluded as place of death and morphine equivalent daily dose at end of life were primary endpoints. Patients in both cohorts had input from community palliative care teams.

Data collection

The records of patients referred to the interventional service during this period were examined. All patients had identical information collected at assessment including age, gender, Scottish Index of Multiple Deprivation score, cancer type, Karnofsky score, morphine equivalent daily dose, adjuvant analgesic medication, and pain scores using the short form of the Brief Pain Inventory.

Follow up data included date of death, place of death, number of acute or hospice admissions from assessment to death, time spent in the community, morphine equivalent daily dose and adjuvant analgesic medications at end of life. Data were collected using paper and electronic records across services.

Variables

Confounders/effect modifiers

The evaluation size was small. The data was gathered over several years as intrathecal drug delivery is a relatively uncommon procedure.

Data were not collected for patients who underwent a trial of intrathecal drug delivery but did not proceed to an implanted pump.

Consent

Patients receiving intrathecal drug delivery gave written consent for data analysis. The Caldicott Guardian approved data analysis for the comprehensive medical management group. The service evaluation was approved by the local Quality Improvement committee.

Statistical Methods

Continuous data are summarised using mean and standard deviation, or median and quartiles; categorical data are summarised as counts and percentages.

Mann-Whitney U tests and Fisher's exact tests were used to assess the statistical significance of differences in post-assessment survival, admission and time spent in place of care, place of death, and morphine equivalent daily dose at end of life between the two groups.

All statistical analyses were conducted using R version 4.2.1. A 2-sided significance level of $P < 0.05$ was used throughout.

Results

Participants

There were 28 patients in the intrathecal cohort and 17 patients in the comprehensive medical management cohort. Demographic and clinical characteristics of patients were similar between the

two study groups (Table 1). There was no significant difference in the total pain scores for each group at assessment (mean 14.5 vs 13.3, *P* =0.2).

Table 1

	N	IDDS, N = 28	CMM, N = 17	*P* value[1]
Age, mean (SD)	**45**	**59.8 (9.4)**	**58.8 (12.7)**	**0.8**
Gender, *n (%)*	**45**			**>0.9**
Female		**14 (50%)**	**9 (53%)**	
Male		**14 (50%)**	**8 (47%)**	
SIMD, *n (%)*	**45**			**0.2**
1 – Most deprived		**12 (43%)**	**4 (24%)**	
2		**3 (11%)**	**7 (41%)**	
3		**4 (14%)**	**1 (5.9%)**	
4		**3 (11%)**	**2 (12%)**	
5 – Least deprived		**6 (21%)**	**3 (18%)**	
Cancer group, *n (%)*	**45**			**0.6**
Gastrointestinal		**9 (32%)**	**6 (35%)**	
Gynaecological/urology		**13 (46%)**	**8 (47%)**	
Other		**3 (11%)**	**0 (0%)**	
Respiratory		**3 (11%)**	**3 (18%)**	
Karnofsky, *n (%)*	**45**			**0.15**
50		**7 (25%)**	**3 (18%)**	
60		**7 (25%)**	**6 (35%)**	
70		**8 (29%)**	**8 (47%)**	
80		**6 (21%)**	**0 (0%)**	
MEDD, median (IQR)	**45**	**295.0 (142.5, 498.8)**	**420.0 (170.0, 690.0)**	**0.3**
Adjuvant count, mean (SD)	**45**	**3.5 (1.5)**	**3.1 (1.1)**	**0.4**
Worst pain, mean (SD)	**45**	**9.0 (1.1)**	**8.2 (1.8)**	**0.11**
Least pain, mean (SD)	**45**	**4.9 (2.5)**	**4.4 (2.4)**	**0.4**
Average pain, mean (SD)	**45**	**6.6 (1.9)**	**6.4 (1.1)**	**>0.9**
Pain now, mean (SD)	**45**	**6.2 (2.5)**	**5.5 (2.6)**	**0.3**

	N	IDDS, N = 28	CMM, N = 17	*P* value[1]
Pain intensity, mean (SD)	**45**	**6.7 (1.5)**	**6.1 (1.5)**	**0.2**
Pain interference, mean (SD)	**45**	**7.8 (1.6)**	**7.3 (1.5)**	**0.2**
Total pain score, mean (SD)	**45**	**14.5 (2.8)**	**13.3 (2.4)**	**0.2**

IDDS: intrathecal drug delivery system; CMM: comprehensive medical management; N: number; SD: standard deviation; IQR: inter-quartile range; SIMD: Scottish index of multiple deprivation; MEDD: morphine equivalent daily dose

[1]Wilcoxon rank sum test; Fisher's exact test

Admissions and time spent in place of care

Survival time from assessment to death was significantly lower in the medical management group (median, 181.0 days vs 61.0 days; *P* <0.001). There were significant differences in total number of admissions (median, 5.0 vs 1.0; *P* <0.001) and inpatient days (median, 58.0 days vs 15.0 days; *P* <0.001) between the intrathecal group and the comprehensive medical management group. The intrathecal group spent more time in acute hospital with planned admissions (median, 25.5 days vs 0 days; *P* <0.001). They also spent more time in the community (median, 126.5 days vs 25.5 days; *P* =0.002). However, there was no significant difference in proportion of time spent in the community (median, 61.0% vs 79.8%, *P* =0.6) between the two study groups. The intrathecal group spent more time in planned hospitalisations both in establishing the intrathecal system and its ongoing manipulation. This was not relevant to the patients receiving comprehensive medical management (median, 15.3% vs 0.0%; *P* <0.001). There were no significant differences in time spent in unplanned acute hospital admissions (median, 2.0 days vs 1.0 days; *P* >0.9) or hospice admissions (median, 19.0 days vs 10.5 days; *P* =0.2) between the two groups (Table 2).

End of life

The morphine equivalent daily dose at end of life was significantly lower in the intrathecal group than the comprehensive medical management group (median, 127.5 vs 440.0; *P* =0.022) at end of life (Table 2). No difference between the groups was found in place of death (*P* = 0.6).

Table 2

	N	IDDS, N = 28	CMM, N = 17	*P* value[1]
Admission and time spent in place of care				
Days from assessment to death, Median (IQR)	45	181.0 (110.5, 385.5)	61.0 (28.0, 74.0)	<0.001
Total number of admissions, Median (IQR)	44	5.0 (3.0, 7.2)	1.0 (1.0, 2.0)	<0.001
Unknown, *n*		0	1	
Total number of in-patient days, Median (IQR)	44	58.0 (39.2, 96.8)	15.0 (6.0, 25.2)	<0.001
Unknown, *n*		0	1	
Number of admissions to acute hospital – planned, Median (IQR)	45	3.0 (2.0, 4.0)	0.0 (0.0, 0.0)	<0.001
Days spent in acute setting – planned, Median (IQR)	45	25.5 (19.5, 37.0)	0.0 (0.0, 0.0)	<0.001
Percentage of days spent in acute setting – planned, Median (IQR)	45	15.3 (6.7, 30.5)	0.0 (0.0, 0.0)	<0.001
Number of admissions to acute hospital – unplanned, Median (IQR)	45	1.0 (0.0, 2.0)	1.0 (0.0, 1.0)	0.3
Days spent in acute setting – unplanned, Median (IQR)	45	2.0 (0.0, 7.2)	1.0 (0.0, 10.0)	>0.9
Percentage of days spent in acute setting – unplanned, Median (IQR)	45	0.3 (0.0, 3.4)	3.7 (0.0, 14.0)	0.3
Number of admissions to hospice, Median (IQR)	44	1.0 (0.8, 1.3)	1.0 (0.0, 1.0)	0.3
Unknown, *n*		0	1	
Days spent in hospice, Median (IQR)	44	19.0 (1.5, 41.0)	10.5 (0.0, 15.2)	0.2
Unknown, *n*		0	1	
Percentage of days spent in hospice, Median (IQR)	44	10.9 (0.7, 31.4)	9.6 (0.0, 71.3)	0.7

Table 2

	N	IDDS, N = 28	CMM, N = 17	*P* value[1]
Unknown, *n*		0	1	
Days spent in community, Median (IQR)	44	126.5 (54.8, 251.8)	25.5 (12.5, 57.0)	0.002
Unknown, *n*		0	1	
Percentage of days spent in community, Median (IQR)	44	61.0 (47.6, 81.2)	79.8 (19.2, 88.8)	0.6
Unknown, *n*		0	1	
End of life				
Days of EOL medication, Median (IQR)	41	10.0 (4.0, 14.0)	10.0 (10.0, 11.0)	0.5
Unknown, *n*		0	4	
MEDD, Median (IQR)	41	127.5 (40.0, 347.5)	440.0 (120.0, 1,056.0)	0.022
Unknown, *n*		0	4	
Adjuvant count, Median (IQR)	41	2.5 (1.0, 3.0)	4.0 (3.0, 4.0)	0.050
Unknown, *n*		0	4	
Place of death, *n (%)*	45			0.6
Acute		3 (11%)	3 (18%)	
Cancer Centre		2 (7.1%)	0 (0%)	
Home		5 (18%)	5 (29%)	
Hospice		18 (64%)	9 (53%)	

IDDS: intrathecal drug delivery system; CMM: comprehensive medical management; N: number; IQR: inter-quartile range; EOL: end of life; MEDD: morphine equivalent daily dose

[1]Wilcoxon rank sum test; Fisher's exact test

Discussion

Main findings.

This service evaluation is the first evidence we have of any association between intrathecal drug delivery and place of care for patients with difficult to control cancer pain. The intrathecal group demonstrated a significant difference in survival which translated to a significant increase in the median number of days spent in the community.

The morphine equivalent daily dose at end of life was statistically different between the two groups. Sedation is a well-recognised side effect of opioid medication and can occur in up to 60% of patients [8]. It may be that the higher end of life opioid doses in the comprehensive medical management group are linked to an increase in sedation which in turn is linked to a reduction in performance status, impacting on survival.

What this study adds

Uncontrolled pain is a predictor of institutionalisation in patients with advanced cancer. Intrathecal drug delivery is an effective method of pain control for these patients. Repeated studies demonstrate a patient preference for home as a preferred place of care[9, 10]. Our results show that time invested in establishing an intrathecal drug delivery system translates to significant additional time spent in the community.

One of the documented reasons for turning down an intrathecal drug delivery system was a reluctance to spend time in the acute hospital setting. Our results inform discussions with patients that the in-patient stay associated with establishing intrathecal drug delivery can be viewed positively.

Randomised trials of intrathecal drug delivery are challenging. Investment is required to establish large-scale, national or international registries of cancer patients undergoing pain interventions, which could be used to assess patient outcomes in relation to treatment decisions. Future studies should include health economic analyses, and follow-up of patients with cancer pain who do not receive intrathecal drug delivery.

Strengths/weaknesses/limitations

This is a small non-randomised service evaluation and the comprehensive medical management group is self-selected.

There is a lack of data for preferred place of care and death and the reasons for turning down intrathecal drug delivery.

A reduction in analgesic side effects is a well-documented benefit of intrathecal drug delivery. A specific tool to measure these side effects would be advantageous.

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Declarations

Authorship and roles

Dr Alison Mitchell
(i) Made a substantial contribution to the concept or design of the work, acquisition, analysis, and interpretation of data,
(ii) Drafted the article or revised it critically for important intellectual content,
(iii) Approved the version to be published,
(iv) Has participated sufficiently in the work to take public responsibility for appropriate portions of the content.

Ms Lesley Somerville
(i) Made a substantial contribution to the concept and design of the work, and acquisition, of data,
(ii) Revised the article critically for important intellectual content,
(iii) Approved the version to be published,
(iv) Has participated sufficiently in the work to take public responsibility for appropriate portions of the content.

Dr Nicola Williams
(i) Made a substantial contribution to the acquisition of data.
(ii) Revised the article critically for important intellectual content,
(iii) Approved the version to be published,
(iv) Has participated sufficiently in the work to take public responsibility for appropriate portions of the content.

Dr Jonathan McGhie
(i) Made a substantial contribution to the concept and design of the work,
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(iii) Approved the version to be published,
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Professor Alex McConnachie
(i) Made a substantial contribution to the analysis and interpretation of data,
(ii) Revised the article critically for important intellectual content,
(iii) Approved the version to be published,
(iv) Has participated sufficiently in the work to take public responsibility for appropriate portions of the content**.**

Dr Gordon McGinn
(i) Made a substantial contribution to the concept and design of the work,

(ii) Revised the article critically for important intellectual content,
(iii) Approved the version to be published,
(iv) Has participated sufficiently in the work to take public responsibility for appropriate portions of the content.
Ms Jiyoung Lee
(i) Made a substantial contribution to the analysis and interpretation of data,
(ii) Revised the article critically for important intellectual content,
(iii) Approved the version to be published,
(iv) Has participated sufficiently in the work to take public responsibility for appropriate portions of the content**.**

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Conflicts of Interest
The Authors declare that there are no conflicts of interest

Ethics and consent
Patients receiving IDDS gave written consent for data to be analysed. The Caldicott Guardian approved data collection and analysis for the CMM group. The service evaluation project was approved by NHSGGC Regional Services Quality Improvement Committee.

Data sharing
Anonymised statistical data files are available within the Health Board website

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