Clinician-reported changes in octreotide prescribing for malignant bowel obstruction as a result of an adequately powered phase III study: a trans-national, online survey

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Word count (excluding abstract, tables, figures and references 1826
Abstract word count 247
Tables and figures 4

References 15

Key words: practice change, implementation science, phase III clinical trial, randomised controlled trial, malignant bowel obstruction, octreotide, somatostatin analogues

Running heading: Changes in practice after publication of an RCT

What is known about this topic?

- Changing clinical practice for existing clinicians usually entails a long lag time.
- Evidence from adequately powered, well-designed, randomized controlled trials can inform practice in palliative care
- Octreotide is widely used in the management of inoperable malignant bowel obstruction around the world on the basis of a number of small studies, all but one of which were underpowered

What this paper adds:

- This paper demonstrates that high quality clinical evidence from effectiveness (real-world) studies is assimilated by many clinicians practicing in palliative medicine
- Uptake varies by clinician factors that can be identified in the population (age, previous use of octreotide)

Implications for practice, theory or policy:

- This paper demonstrates that it is important to examine the uptake of new knowledge into practice
- One way of tracking the influence of a paper is to ask clinicians if they changed practice as a result of a new study with findings directly applicable to their practice.
- Clinician surveys are important in order to understand changes in knowledge and attitudes, and barriers and enablers to changes in clinical practice.

Abstract

Background
Translating research evidence into clinical practice often has a long lag time.

Aim
To determine the impact of a phase III randomised controlled trial on palliative care clinicians' self-reported practice change.

Design
Online survey about use of octreotide in managing inoperable malignant bowel obstruction due to cancer or its treatments distributed in November, 2016, two years after the first publication of the study in a peer-reviewed journal. Demographic, self-reported practice and the reasons underpinning this were collected. Responses were aggregated to 'practice modified' or 'practice not modified'. A multinomial regression model explored predictors of practice change.

Setting
Members of the Australian New Zealand Society of Palliative Medicine.

Results
Response rate was 20.8% (106/509): 55.6% were aged >50; 56.5% female; 77% had previously prescribed octreotide for this clinical indication. 52/106 (49.1%) modified practice (60.9% of those who had previously prescribed octreotide in this setting). In those who reported practice change, most frequently octreotide was now used when other therapies failed; for not changing practice 'more confirmatory evidence was needed' was most often cited.

In the regression model, older age (clinician age 50-59 (RR 0.147 (95% CI 0.024, 0.918; p 0.04) and having practices with lower proportions of people treated with octreotide (0-20%; RR 0.039 (95%CI 0.002, 0.768; p 0.033) predicted greater self-reported practice change.

Conclusion
Clinician-reported change in practice in the survey is seen in the majority of respondents. This suggests there are a cohort of 'early adopters' within palliative care practice as new evidence becomes available.

Introduction

Incorporating clinical trial evidence into clinical practice is challenging. Many strategies have been trialled to change clinicians' knowledge, attitudes and practices. These include audit and feedback;[1] education workshops;[2] engaging local key opinion leaders[3] and educational material, each with varying success in changing practice. Even though each requires significant resources, these approaches only manage to shift routine practice minimally. [1-3]

The translation of research evidence into practice is lengthy, regardless of the field of clinical practice. Estimates suggest that, on average, 17 years will elapse before research is fully incorporated into routine clinical care.[4] This significant lag time is unacceptable to patients, funders and policy makers, and requires more effective ways of bringing new knowledge to the bedside. Early adopters of new evidence are part of the spectrum of uptake of new knowledge and this paper sought to identify those clinicians who reported that their practice had changed in response to the findings of an adequately powered phase III study.

Malignant bowel obstruction secondary to cancer or its treatment is a relatively common problem amongst patients with advanced cancer (3-15%).[5] The prognosis of inoperable bowel obstruction is poor and is often associated with difficult to control vomiting (often faeculent), abdominal pain and distension. When surgical intervention is deemed inappropriate, treatment seeks to minimise symptoms, including reducing the volume and frequency of vomiting.

To date, there has been no standardized clinical approach to managing vomiting in inoperable bowel obstruction due to cancer or its treatments. One systematic review suggested that there was potential benefit from the use of dexamethasone[6] to aid resolution of bowel obstruction, and theoretical benefit from the use of ranitidine to reduce the volume of upper gastro-intestinal secretions.[7] Octreotide has previously been prescribed widely for symptomatic treatment in inoperable bowel obstruction due to cancer or its treatments without empiric evidence. This incomplete evidence base led the Australian national Palliative Care Clinical Studies Collaborative (PaCCSC)[8] to investigate the net effects of octreotide or placebo on inoperable bowel obstruction due to cancer or its treatments in an adequately powered multi-site phase III study.

This RCT was conducted across 12 Australian specialist palliative care services with a primary end point of days free of vomiting at 72 hours. The study's results did not demonstrate any statistically or clinically significant difference between groups, confirmed by other studies of somatostatin analogues conducted simultaneously.[9] Further, the participants receiving octreotide had a statistically significant increase in the use of hyoscine butylbromide, the protocol-defined treatment for people with colicky abdominal pain. The survey was to quantify clinicians' response to these new findings in the short term (two years after the publication of the results) with expectation that there would be a range from no response from changes in practice through to maintaining the *status quo*.

Few studies to date have demonstrated the short term changes in self-reported clinical practice as a result of such a study. In addition to publication in a peer-reviewed journal and presentation of findings at international conferences, an article was prepared for the Australian and New Zealand Society of Palliative Medicine's newsletter. The aim of this current survey was to determine whether this phase III study had influenced clinicians' self-reported knowledge and attitudes or behaviours. Participants were palliative care specialists or trainees in Australasia surveyed two years after publication. The null hypothesis was that there has been no change in clinical practice.

Methods

The results from the octreotide RCT were first presented at an international conference in June 2012. This paper was published online as a peer-reviewed publication in November 2014 and, subsequently, in the printed edition in May 2015.

Survey

Australasian palliative care clinicians' utilisation of octreotide in the management of inoperable bowel obstruction due to cancer or its treatments was explored in an online survey in Australasia in November, 2016. This was the only issues explored in this survey. One email reminder was sent out two weeks after the initial email invitation. The survey was sent by the Society to all Australian New Zealand Society of Palliative Medicine (ANZSPM) members working in palliative medicine or with a special interest in this field. The email linked to an online survey through a secured portal on CareSearch (www.caresearch.com.au). No pilot nor clinometric testing was done.

The survey sought to assess any self-reported changes in clinicians' pharmacological management of inoperable bowel obstruction due to cancer or its treatments in response to this phase III RCT. Of note, no details about the trial nor its results were given in the survey. Basic demographic information about the clinician and information about his/her previous and current prescribing practices of octreotide were gathered. Options for response about any change to practice (positive or negative) were aggregated to 'practice modified' or 'practice not modified' and could include no change or increased use of octreotide.

Analysis

Data were summarised descriptively. A sub-group of particular interest was consultant physicians who had previously prescribed octreotide for the symptomatic treatment of inoperable bowel obstruction due to cancer or its treatments and provided responses. A multinomial regression model was used to explore the relationship between respondent characteristics and practice change and to identify any factors to identify factors increasing the likelihood of practice modification.

No data were imputed. Data were collated in Excel spreadsheets (Excel 2010, Microsoft, Seattle, Washington, USA. 2010) and analysed in SPSS (Version 23.0, IBM Corp, Armonk, New York, USA. 2014)

Ethics approval and reporting

Ethics approval was granted by the Social Behavioural Research Ethics Committee, Flinders University, Adelaide, South Australia. Given that the audience for the survey was established medical practitioners, an information sheet was sent with the web link, and participation taken as informed consent. The results are presented using the studies Strengthening the Reporting of Observational studies in Epidemiology (STROBE) framework for reporting observational data and the Checklist for Reporting Results of Internet E-Surveys (CHERRIES).[10,11]

Results

In total, 20.8% (106/509) of members of ANZSPM in November, 2016 responded. Of note given their roles as local key opinion leaders, 88 respondents were consultants in palliative medicine, representing 41.3% of the estimated consultant workforce nationally in palliative care.[12] Over half of respondents were aged over 50 years (55.6%) and were female (56.6%). The respondents covered medical practitioners with a range of clinical seniority and time commitment to clinical care (Table 1). The majority of respondents worked more than 0.81 of a full time equivalent (FTE) role (72/106 (68%)). Seventy seven percent of respondents had previously used octreotide for the treatment of inoperable bowel obstruction due to cancer or its treatments.

One half of all the respondents (52/106; 49.1%) indicated practice change (Table 2) as a result of incorporating the results of the study into their clinical work. When the analysis was limited to

palliative care consultants who had prescribed octreotide previously, this proportion increased to 60.9% (42/69) of respondents. In those who indicated practice modification, the most frequent response was that 'octreotide was now only used when other therapies had failed' (35/106; 33.0%). The most frequently cited reason for not modifying practice was that 'more confirmatory evidence was needed' (21/106; 19.8%), followed by practitioners being convinced of the benefit from their own observations (15/106; 14.2%).

Indication of practice modification by age of prescriber who had previously prescribed octreotide for inoperable bowel obstruction due to cancer or its treatments differed (Table 3; p=0.027) but not in those who previously prescribed octreotide less frequently for this indication (Table 4; p=0.165). In the regression model with practice change as the dependent variable, adjusting for sex and full time equivalent roles, older age (relative risk clinician age 50-59 (RR 0.147 (95% CI 0.024, 0.918; p 0.04) and having a practice where a lower proportion of people were already treated with octreotide (0-20% of patients with inoperable bowel obstruction due to cancer or its treatments; RR 0.039 (95%CI 0.002, 0.768; p 0.033) predicted greater likelihood of indicating practice change. The model was statistically significantly better than an intercept only model and explained 33.4% of the variance. (p=0.023; McFadden R-square 0.334).

Discussion

Given the relatively small number of people who present with inoperable bowel obstruction due to cancer or its treatments and the subjective nature of the responses, above all, this survey provides important insights into the self-reported practice of palliative practitioners who treat people with malignant bowel obstruction. The level of reported practice modification within a two year timeframe from the publication of an adequately powered, multi-site, placebo controlled study of octreotide for inoperable bowel obstruction due to cancer or its treatments is clinically significant, given the overall change achieved with targeted interventions for existing practitioners.[1-3] Many clinicians reported modified practice within a relatively short period of time. With 77.4% of clinicians reporting having used octreotide for this indication previously, changing knowledge and attitudes in 60.9% of previous prescribers suggests the likelihood of real changes to clinical practice. A sizable proportion of clinicians who self-reported prescribing octreotide in this clinical setting indicated that their practices would not change.

A large number of practitioners did not respond, and it cannot be estimated what their knowledge, attitudes or current practice is. Even if the 52 people who indicated practice change were the *only* people to change within the potential respondent group of 509, this would still mean that at least 10.2% (52/509) of clinicians had modified their practice in response to new data from the cited phase III study, demonstrating a greater level of change than seen in implementation science interventions.[1-3]

Given that the natural history of untreated inoperable bowel obstruction due to cancer or its treatments is poorly described in the clinical literature and an objective outcome measure was used in the phase III RCT, the placebo arm describes the natural history of bowel obstruction in this clinical setting, and provides evidence of the additional effects (benefits and harms) that can be directly attributed to octreotide. The response rate in both arms was equal, so it is interesting to see that practitioners who did not change practice did so because they themselves had attributed benefit to octreotide when they had prescribed it.

The results should be interpreted in the light of one other key publication in the palliative care literature.[9] The paper by Obita *et al* systematically reviewed the clinical trial evidence for the net effects of somatostatin analogues in the symptomatic treatment of inoperable bowel obstruction due to cancer or its treatments and may also have had an impact on clinicians' responses to the survey given that the Obita paper was published electronically in September 2016, two months before the survey.

There are barriers to the uptake of results from adequately powered RCT into day-to-day clinical practices. The response from some clinicians seeking further research before implementing changes in prescribing practices is interesting given the paucity of evidence in favour of octreotide in this clinical setting to date. Individual personal beliefs in the value of certain therapies may be more difficult to challenge, with confirmation bias one factor that needs to be taken into account.[13,14]

Limitations

Due to a number of factors, engaging clinicians in research surveys is difficult. Demographic information about the total ANZSPM membership such as sex and age distribution was unavailable to make comparisons between those who did and did not respond to the survey. The results only reflect the self-reported practice (itself a limitation without objective corroboration) and does not reflect the self-reported practice of nurse practitioners (who have pharmaceutical prescribing rights), pharmacists, nor ward or community nurses as they dispense and administer these medications respectively.

Strengths

These results were gathered from a trans-national professional body of clinicians and the results provide responses from a diverse cross section of the medical practitioners most commonly prescribing octreotide in palliative care patients. The level of modification to clinical practice reported in this survey is greater than the effect of the practice change studies that are part of the Cochrane reviews of key opinion leaders, audit and feedback and academic detailing.

Implications for clinical practice

It is encouraging that many clinicians have assimilated this new knowledge into their clinical knowledge and attitudes. The self-reported changes in practice are not radical, but where new effectiveness data become available, many palliative care clinicians indicated that this impacts on their practice.

This survey assesses self-reports of clinicians' knowledge and attitudes to prescribing octreotide for inoperable bowel obstruction due to cancer or its treatments. Access to real-time prescribing data from clinical settings where octreotide is used for this clinical indication would help to corroborate these findings. Understanding the continued trends in practice change (and whether the changes described here are sustained) are important future questions.

Conclusion

The results of this survey reflect real change in knowledge and attitudes in practitioners as a result of an adequately powered phase III effectiveness RCT. Uptake of the results into practice varied between practitioners with age and previous prescribing habits predictors of change. The findings support the need for expanding good quality clinical research in palliative medicine, a specialty which is increasingly relying on high quality, high level evidence to improve care.[15]

Declarations

Authorship (ICJME)

Substantial contributions to the:	
	conception or design of the work; OR
	the acquisition, analysis, OR
	interpretation of data for the work; AND
Drafting the work or revising it critically for important intellectual content; AND	
Final approval of the version to be published; AND	
Agreement to be accountable for all aspects of the work in ensuring that questions re work are appropriately investigated and resolved.	

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Funding
The Palliative Care Clinical Studies Collaborative was funded under the national palliative care program of the Commonwealth Department of Health.

Declaration of conflicts of interest
The authors declare that there is no conflict of interest regarding the publication of this paper.

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Octreotide Online Survey questions

What age are you?	
What is your sex?	
What is your principle medical role?	
Are you a registrar?	
What Full Time equivalent (FTE) hours do you work?	
Have you ever prescribed octreotide?	
Are you aware of the randomised control trial assessing the use of octreotide in malignant bowel obstruction published in the Journal of Pain and Symptom Management in May 2015?	
Prior to becoming aware of this trial did you ever use octreotide in the management of malignant bowel obstruction?	
Malignant bowel obstruction. In what context do you prescribe octreotide?	
Other. In what context do you prescribe octreotide?	
What percentage of patients with malignant inoperable bowel obstruction and vomiting do you treat with octreotide?	
Have you prescribed octreotide in the last year?	
How many people do you estimate you prescribed octreotide for in an average year?	
What dose of octreotide, in a twenty four period, would you most commonly prescribe?	
Do you use an infusion or divided doses of octreotide?	
On average, how long would you administer octreotide for to determine whether it was beneficial for the patient?	
Has the trial changed your prescribing practices with regards to octreotide prescribing in the setting of malignant bowel obstruction?	
Please tick the statements which apply to you.	
Since becoming aware of the trial I prescribe octreotide less often	
Since becoming aware I never prescribe octreotide in the context of malignant bowel obstruction	
Since becoming aware of the trial I prescribe a lower dose of octreotide	
Since becoming aware of the trial I only prescribe octreotide when other treatments have failed	
Since becoming aware of the trial I am more selective in the patients in whom I prescribe octreotide	
Since becoming aware of the trial I prescribe a higher dose of octreotide	
Since becoming aware of the trial I prescribe octreotide more frequently	
Please tick the statements that apply to you	
I have not changed my practice because there is a lack of alternative therapeutic options	
I have not changed my practice because I believe the trial was not of sufficient quality	
I have not changed my practice because I believe more confirmatory evidence is required	

I have not changed my practice because the population I treat is different than that of the study	
I have not changed my practice because I am convinced of the benefit from my own observations	