Review Article

Medication and Monitoring in Palliative Sedation Therapy: A Systematic Review and Quality Assessment of Published Guidelines

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Abstract

Context. Palliative sedation therapy (PST) is increasingly used in patients at the end of life. However, consensus about medications and monitoring is lacking.

Objectives. To assess published PST guidelines with regard to quality and recommendations on drugs and monitoring.

Methods. We searched CINAHL, the Cochrane Library, Embase, PsycINFO, PubMed, and references of included articles until July 2014. Search terms included "palliative sedation" or "sedation" and "guideline" or "policy" or "framework." Guideline selection was based on English or German publications that included a PST guideline. Two investigators independently assessed the quality of the guidelines according to the Appraisal of Guidelines for Research and Evaluation II instrument (AGREE II) and extracted information on drug selection and monitoring.

Results. Nine guidelines were eligible. Eight guidelines received high quality scores for the domain "scope and purpose" (median 69%, range 28–83%), whereas in the other domains the guidelines' quality differed considerably. The majority of guidelines suggest midazolam as drug of first choice. Recommendations on dosage and alternatives vary. The guidelines' recommendations regarding monitoring of PST show wide variation in the number and details of outcome parameters and methods of assessment.

Conclusion. The published guidelines on PST vary considerably regarding their quality and content on drugs and monitoring. Given the need for clear guidance regarding PST in patients at the end of life, this comparative analysis may serve as a starting point for further improvement. J Pain Symptom Manage 2015;49:734–746.

Key Words
Palliative sedation, practice guidelines, drug monitoring, quality assurance

Introduction

Some patients in their last weeks of life experience intolerable suffering from one or more severe symptoms that cannot be controlled by standard palliative care treatment. As a treatment of last resort for "refractory symptoms," palliative sedation therapy (PST) may be considered.[1] A "refractory symptom" has been defined as a "symptom that cannot be adequately controlled despite aggressive efforts to identify a tolerable therapy that does not compromise consciousness. (…) the clinician must perceive that further invasive or non-invasive interventions are either 1) incapable of providing adequate relief, 2) associated with excessive and intolerable acute or chronic morbidity, or 3) unlikely to provide relief within a tolerable time frame."[2] Terminology and definitions for PST, which is, for example, also called palliative sedation or terminal sedation, vary in the literature.[1] Herein, we define PST as the "monitored use of medications intended to induce a state of decreased or absent awareness (unconsciousness) to relieve the burden of otherwise intractable suffering […]."[3]

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In recent years, international medical associations, national bodies, and local institutions have taken up the task of developing guidelines and policies with the aim of informing practitioners about the appropriate practice of PST in oncology as well as other fields of medicine.[3–5] As reported elsewhere, current guidance on PST varies considerably with regard to definitions of and indications for PST.[6]

In this article, we present the findings of a systematic review of published PST guidelines on recommended drug selection, dosage, and monitoring. The objectives are to inform palliative care professionals about the similarities and differences of these recommendations, and to assess the quality of the available guidelines against established criteria for guideline development. The findings shall inform the debate on good clinical practice of PST in patients at the end of life and may contribute to the improvement of future PST guidelines.

Methods

Data Sources and Searches

As described in the first publication of the results of this systematic review, which focused on recommendations on ethical and communication aspects of indication and decision making,[6] we conducted a systematic literature search in CINAHL, the Cochrane Library, Embase, PsycINFO, and PubMed to identify and collect published guidelines in English and German. The database search covered the period from January 1, 1980 to July 31, 2014. Search terms were "palliative sedation" or "sedation" and "guideline" or "policy" or "framework." Additionally, the reference lists of eligible articles were screened for further published guidelines. For this article, the guideline definition for the Medical Subject Heading "Practice Guideline" in MEDLINE was used.

Study Selection, Data Extraction, and Synthesis

As a first step, the first and second authors independently reviewed all resulting citations according to title and abstract. Disagreements regarding the eligibility of articles were resolved by consensus after reading the full text. Each guideline received a label according to the developers (e.g., "European Association for Palliative Care [EAPC] framework," "Japanese guideline;" Table 1) to facilitate reference to the specific guideline. Data extraction of the guidelines' contents on medication and monitoring relevant to this article was performed independently by the first and the last author. Disagreements were resolved by discussion amog all three authors. For reporting, we followed the criteria as described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.[7]

Quality Assessment

The quality of published guidelines was assessed independently by the first and the last author using the Appraisal of Guidelines for Research and Evaluation II instrument (AGREE II).[8] Each item was assessed on a seven-point scale from 1 = strongly disagree to 7 = strongly agree. It was decided in advance that if an AGREE II item was not applicable to the particular guideline, it would be rated as 1, as suggested in the AGREE II instructions.[8] Domain scores for each of the six AGREE II domains were calculated using the scores from both assessors as recommended by AGREE II.

Results

Literature Search and Quality of Guidelines

Nine publications on PST guidelines were included in the review.[1,3–5,9–13] Figure 1 provides an overview of the study selection process. The most frequent reason for exclusion of publications after reading the full text was lack of compliance with the definition of "Practice Guideline" as defined in MEDLINE. The quality assessment according to the AGREE II instrument shows that most guidelines received high scores for the domain "Scope and Purpose" (median 69%, range 28–83%), whereas the domain "Applicability" received the lowest scores (median 15%, range 0–25%). The median values for the other four domains were 28% (Stakeholder Involvement), 23% (Rigor of Development), 42% (Clarity of Presentation), and 25% (Editorial Independence). Five guidelines obtained scores higher than 60% in two domains;[1,3,4,10,13] one of these received a score higher than 60% in a third domain.[10] Four guidelines received scores between 40% and 60% for the domain "Rigor of Development."[1,3,4,10] Table 1 summarizes the overall and guideline-specific results of the quality assessment.

Drug Selection, Dosage, and Titration

Seven of the nine guidelines provide recommendations on specific drugs and also, partly, their respective indications in the context of PST.[1,3–5,9–11] One of the two guidelines that do not present any such recommendations states the lack of evidence as a reason.[12] Five of the seven guidelines that provide drug-specific recommendations name midazolam as the primary agent, either generally or in specific situations[1,5,9–11] (Table 2). The other two of the seven guidelines with drug-specific recommendations state that midazolam is the most frequently used drug.[3,4]