Sedation from analgesics: patient preference survey

Joseph Burdon, Samuel Fingas, Rachel Parry, Constantina Pitsillides, Paul Taylor

ABSTRACT
Background The propensity for certain analgesics to cause sedation is well documented, yet physician–patient dialogue does not routinely include pre-emptive exploration of preferences regarding this side effect.
Objectives To investigate the extent to which palliative patients would accept sedation as a side effect of analgesia and to identify factors affecting decision-making.
Methods Patients (n=76) known to a specialist palliative care services were given hypothetical scenarios regarding pain and asked about the acceptability of varying levels of sedation occurring as an analgesic side effect. Demographic data, including diagnosis, performance status and experience of pain and sedation, were collated for evaluation of the influence of these factors on patient opinion.
Results Most patients (89.47%) would be quite or very likely to accept mild sedation. A significant minority (40.79%) would accept high levels of sedation. There is no significant association with the acceptability of sedation according to demographics. Almost half (40.79%) reported that their responses may change if the prognosis were extended, typically for less sedation with a longer prognosis.
Conclusions Increasing levels of sedation are less acceptable, although there is significant variation in views. Palliative care patients are likely to indicate preferences regarding their acceptability of sedation. Palliative physicians must explore preferences on an individualised basis.

BACKGROUND
Analgesia-induced sedation is a well-documented adverse effect in palliative care, arising from both opioids and co-analgesics. Fatigue is the most frequently reported symptom among patients with cancer and, as with pain, is associated with impaired quality of life. Over time, a person’s preferences regarding quality of life may change; for example, a preference to maintain alertness is balanced with symptom control, where higher drug doses are associated with sedating side effects.

WHAT THIS STUDY ADDS
The relatability of the study’s clinical context among physicians renders its conclusions accessible, understandable and transferable to clinical practice. The study draws patient views from across palliative care settings to enhance clinicians’ previously anecdotal perception of patient preference.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY
Conclusions drawn from this study support an individualised approach to analgesic prescribing at the end of life. Palliative care patients exhibit preferences regarding personal acceptability of sedation, and clinicians should be encouraged to explore this in clinical practice.

WHAT IS ALREADY KNOWN ON THIS TOPIC
- Sedation resulting from analgesic agents is well recognised, whereas exploration of patient acceptability of this side effect is limited.
- The need to balance analgesic benefits with the adverse effects of sedation is a commonly encountered clinical scenario in palliative care.

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drugs to ease distress may result in a significant reduction in awareness, with the potential to cause distress for patients, families and professionals alike. Similarly, prior experience of pain, either directly or through witnessing it in another, may impact an individual’s response to and perception of pain.1

There is significant research into the side effects of analgesics but limited information from patients themselves regarding their acceptability.9 Exploring preferences in palliative care is especially important given the potential for equipoise and the notion that some medical decisions demand the incorporation of personal preference.10 Patients deem decisions about treatment preferences of key importance to physician–patient dialogue in palliative care.11

We report a study exploring patient preferences regarding the extent to which they would accept sedation as a side effect of analgesic administration towards the end of life. The study does not explore patients’ views on continuous palliative sedation,12 which we regard as a distinct concept with additional legal and ethical considerations.

AIM
This study aims to explore patient perceptions regarding the acceptability of sedation as a side effect of analgesia in a palliative care context.

METHODS
Design
This was a survey study comprising structured patient interviews.

Settings
Participants (n=76) were recruited from a palliative care service in a city in the North of England, UK, between 2018 and 2021. Settings included specialist palliative care inpatient or hospice, hospital support team and hospice day therapy.

Participants
Participants were identified by their clinical team. Patients were excluded if they were considered to be in the dying phase of their illness (judged to be in the final days or short weeks of life) or unable to consent. Individuals were offered a participant information sheet and given at least 24 hours to decide whether to partake, with the opportunity to discuss further before agreeing. Participants were reassured that participation or non-participation would not impact the care received. A sample size of 76 was determined using the G*Power calculation.13 Statistical advice was sought to ensure the appropriateness and accuracy of subsequent analyses.

Data collection
Demographic information was collected from medical records. The current level of pain was ascertained with a five-point Likert-type scale. Participants’ personal experience of medication-induced drowsiness, experience of witnessing pain in others and experience of witnessing medication-induced drowsiness were recorded on similar five-point scales. Original data collection forms are included in online supplemental file 1. All data were pseudonymised using a unique participant code.

Participants were given a questionnaire for self-completion, supported by a member of the research team if needed. The questionnaire included a hypothetical scenario of illness provoking severe pain in the last few days to short weeks of life, defined as preventing the patient from completing daily tasks such as eating, maintaining personal care and mobilising. Participants were asked questions regarding their acceptance of varying levels of sedation occurring as a side effect of the offered analgesia in this hypothetical scenario. The extent of sedation was conveyed via four descriptions of progressive levels of analgesia-induced drowsiness, from dozing and difficulty concentrating to sleeping all of the time.

Descriptions were illustrated with examples of the impact of such drowsiness on activities of daily living. For each scenario of medication-induced drowsiness, participants rated their likelihood of acceptance of sedation on a five-point Likert-type scale from very likely to very unlikely. Following completion, participants were asked if, overall, their answers would differ if the prognosis changed from days to short weeks to weeks to months.

RESULTS
The study recruited 76 participants across four settings. Of the participants, 43 (56.58%) were male and 33 (43.42%) were female. Ages ranged from 32 to 86 (mean 64.4). The majority of participants (70, 92.11%) had malignant disease. The majority (53, 69.74%) had an Australia-modified Karnofsky Performance Status (AKPS) score between 40% and 60%. The majority of participants (43, 56.58%) were in an unstable phase of illness. Demographic details, prior experiences of pain or drowsiness and levels of pain or drowsiness observed in others are provided in online supplement 1.

For the primary outcome, results showed a clear association between increased levels of sedation and reduced acceptability (figure 1). The majority (68, 89.47%) reported that they would be quite or very likely to accept mild sedation to control pain. A significant majority (45, 59.21%) would not accept the highest level of sedation. A Kruskal-Wallis test confirms this pattern is significant at the p<0.0001 level. Interestingly, the numbers reporting being neither likely nor unlikely to accept a given level of sedation were consistently small (3.29% of all responses). Individuals were much more likely to express a preference either way than to be ambivalent.
Additional pre-hoc analyses involved testing for an association between the acceptability of sedation and participant characteristics. Details are provided in online supplement 1. Analyses showed no significant association with the acceptability of sedation in each scenario according to age (≥65 vs <65) and gender (male vs female) by the Mann-Whitney U test (p>0.05). No association was found with a cancer diagnosis either, although the small number of patients without cancer limits the validity of this finding.

There was no association between the acceptability of sedation in each scenario and current pain level, previous experiences of drug-induced drowsiness, phase of illness or AKPS by Kruskal-Wallis test (p>0.05).

Further analyses explored the link between the acceptability of sedation and previously witnessed pain and sedation. Where participants had observed overwhelming pain in another, they were more likely to find higher sedation acceptable (p=0.025). Other analyses in this group, however, did not show significance. Given the number of subgroup analyses undertaken, this finding should be interpreted with caution but may represent an area for further exploration.

Overall, 31 respondents (40.79%) reported that their responses may change if their prognosis were measured in weeks to months rather than days to short weeks. Where a preference was expressed, this was typically for less sedation when the prognosis was longer.

**DISCUSSION**

Palliative care patients express preferences regarding the common clinical dilemma of the acceptability of sedation as a side effect of analgesia. The majority are willing to accept mild sedation as a side effect of analgesia for severe pain, while greater degrees of sedation are less acceptable. Critically, few people expressed ambivalence towards sedation as a side effect. Preferences evolve over time and should be explored early and revisited as clinical conditions progress.

The study builds upon literature that has sought to offer explanations for patient attitudes towards opioid analgesia in palliative care and previously reported negative perceptions of opioid analgesia in palliative care offer context for our findings. The study’s findings concur with the observations of Wegier et al regarding the cognitive side effects of analgesia, as well as the diverse nature of views among palliative care patients. Our study supplements this knowledge through confirmation that such views cannot be inferred without direct exploration with the patient, reiterating the need for an individualised, patient-centred approach.

The study encompasses views from a broad spectrum of palliative care patients in a variety of clinical contexts. The study addressed a common clinical encounter and, although small, was adequately powered. However, a focus on the experiences of palliative care patients means the findings should not be applied uncritically to other contexts. Furthermore, the survey required some simplification; describing
sédation arising only from pain medication is not truly reflective of clinical practice.

When applying these findings clinically, patient preference should be explored on a case-by-case basis and allow for evolution over time. It should also be noted that, while pain management is pivotal in the provision of good palliative care, some individuals are not accepting of sedation as a side effect; this reinforces the need to consider alternative approaches to pain management.

In future research into symptom management, the impact of sedation is clearly important and should be considered as a study outcome; this should not be limited to pain control. Furthermore, there is a need to understand whether and how experiences of witnessed symptoms may influence personal preferences.

CONCLUSION

This study has explored the preferences of palliative care patients when weighing the sedating side effects of analgesia against pain control. Increasing levels of sedation are progressively less acceptable but, at all levels, individuals express strong preferences. Ensuring symptom management decisions are patient-centred and undergo regular review as the clinical context evolves is therefore essential to good palliative care.

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Contributors JB and SF designed the study. JB, SF, RP and CP recruited patients. PT analysed and reported the data. The authors have not declared a specific grant for this research from any funding agency in the public, commercial or profit sectors.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by HRA ethics approval obtained from the East of England, Cambridge Central Research Ethics Committee (REC Reference 18/EE/0006). This study was also approved by the research committees of the participating hospices and the NHS Trust. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; internally peer reviewed.

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11 Steinhauser KE. Factors considered important at the end of life by patients, family, physicians, and other care providers. JAMA 2000;284:2476.
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Table 1. Participant characteristics

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<td><strong>Total</strong></td>
<td><strong>76</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

1. Please rate your current level of pain by ticking the appropriate box.
   - No pain at all (0)
   - Slight (1)
   - Moderate (2)
   - Severe (3)
   - Overwhelming (4)

2. In your opinion, what is the greatest extent to which you have experienced drowsiness as a side effect of medication? Please tick the appropriate box.

3. What is the greatest level of pain a close friend or relative has experienced pain as witnessed by you? Please tick the appropriate box.

4. What is the greatest extent to which you have witnessed drowsiness as a side effect of medication in your friends or relatives? Please tick the appropriate box.

**Text box 2. Prior experiences of pain and sedation; all used same Likert scale.**

**Participant response form**

- You have severe pain as a result of your disease. You are in the last few days to short weeks of life. The pain is preventing you from completing normal daily tasks such as eating, toileting, and moving about. You are sleeping well at night.
- Your doctor has offered you some pain-relieving medication.
- "Sedation" is a potential side effect of this medication.
- How likely are you to accept the level of sedation described below- if it will provide you with symptom relief?
1. Dozing and difficulty concentrating whilst doing activities such as:
   - Sitting and reading or watching TV for 1 hour
   - Sitting quietly after lunch

   Very unlikely  Quite unlikely  Neither likely or unlikely  Quite likely  Very likely

2. Dozing and difficulty concentrating whilst doing activities such as:
   - Sitting and reading or watching TV for 15-30 minutes
   - Maintaining an interesting conversation for 15-30 minutes.

3. Asleep for most of the day. The sedation prevents you from undertaking activities such as:
   - Sitting and reading or watching TV
   - Holding a conversation for more than 1-2 minutes but can hear, understand and communicate your needs.

4. Asleep all of the time. The sedation prevents you from interacting with the world around you. Others are anticipating your care needs and maintaining your dignity.

If each scenario was the same but your life expectancy was extended from days to short weeks to weeks to months would your responses change?

Yes / No

Please explain your decision.

Text box 1. Pain scenarios for participant response form. Questions 1-4 used the same Likert scale.
Graph 2. Participant reported levels of experienced/observed pain and drowsiness.

<table>
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<tr>
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<th>Scenario 1</th>
<th>Scenario 2</th>
<th>Scenario 3</th>
<th>Scenario 4</th>
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<td>Age (MWU) (&gt;65/&lt;65)</td>
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<td>Current pain (KW)</td>
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<tr>
<td>Experienced drowsiness (KW)</td>
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<td>0.8174</td>
<td>0.5658</td>
<td>0.6252</td>
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<td>Observed pain (KW)</td>
<td>0.9069</td>
<td>0.5333</td>
<td>0.1351</td>
<td>0.0247*</td>
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<tr>
<td>Observed drowsiness (KW)</td>
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Table 2. Results of Mann-Whitney U and Kruskal-Wallis tests of significance comparing responses to each scenario with participant characteristics. MWU = Mann-Whitney U test. KW = Kruskal Wallis test.