

Systematic Reviews on Palliative Sedation: What do They Tell Us?

Sir,

I read with interest the recently published systematic review by Barathi and Chandra^[1] (called henceforth as second review) which was directed to address a commonly arising clinical query: “Does palliative sedation shorten the survival time?” and the paper provided a detailed search methodology and description of the data synthesis to arrive at authors’ conclusion that mean survival time (MST) was not statistically different between sedated and non-sedated groups which supposedly implied that palliative sedation was not associated with survival time (an odds ratio would have been ideal to identify the association between palliative sedation given versus not given and survival short versus long). Arriving at odds ratio was presumably limited due to lack of meta-analysis, but re-reporting the between-group comparisons (with *P* values) in a table does not adequately describe the situation.

However, the authors suggested the future prospective studies in the absence of randomized controlled trials in this area, but specifically longitudinal cohort studies with the survival analysis would aim to appropriately answer such a research question. Systematic reviews of such cohort

studies should use relative risk estimates while pooling the data for summative interpretation.

It is however surprising to note that another recently published systematic review by Maltoni *et al.*^[2] (called herein as first review) was neither referenced in introduction nor in discussion section of the paper (the paper was available on ePub online by March 2012 which was included in the search period). Their systematic review involved searching two databases for the period 1980-2010 involving search terms ‘cancer and neoplasm’ among many other terms, and found 11 articles describing 1,807 consecutive patients in 10 retrospective or prospective nonrandomized studies, of whom 621 (34.4%) patients were given sedation. The second systematic review searched six databases including the two used in second one, across the same search period extended until April 2012, and search terms included the exhaustive words related to cancer except the word ‘cancer’ *per se*. The second review also found 11 articles but did not report the overall number of patients sedated (since statistical pooling was not attempted). The number sedated overall is 907 (can be found from the table) in the second review.

The third point is the use of quality appraisal checklist which was non-specific (one of Hawker *et al.* used in the second review), rather than the globally recommended Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist,^[5] which was also validated for scoring purposes. Use of quality appraisal tool and mentioning that one study was excluded since it was of poor quality and insufficient. The authors should have instead put a table summarizing the study-wise findings for the checklist and categorized them into high, average or poor quality. The other alternative is levels of evidence and grades of recommendation. The authors should have discussed their limitations in not using PRISMA, or the levels of evidence for the included studies. This situation is warranted since only one study among the included list of papers had an opposite direction of the effect (by Kohara *et al.*, in the second review which reported longer survival times in non-sedated group).

The first review had reported common indication for sedation was delirium which was also found in the second review. The most common drug found in first review was Benzodiazepines but the second review drug found was Midazolam. Hence, controlled trials if needed must compare the two drugs in the future.

Reporting of results in the second review require scientific upliftment of statistical terminology. Example, means are to be reported with confidence intervals or standard error of mean, and not the range. Medians are to be reported with range and interquartiles.

Both reviews however found similar conclusions-The first review concluded, “comparing survival of sedated and non-sedated patients, the sedation approach was not shown to be associated with worse survival” whereas the second review concluded, “Mean survival time (MST) was not statistically different between sedated and non-sedated groups in any of the included studies in this review.” The study by Mercadante *et al.* (included in the second review) however found $P = 0.003$ in Table 5 (in contrast to all other included studies) which was neglected and reported as a unidirectional conclusion.

The second review also was prone to risk of selection bias for including studies since blinded or independent search methodology was not used or not reported. The search strategy was a non-validated one, and these should be discussed as limitations rather than mentioning use of multiple databases as a scientific merit of the article.

I wish to bring into attention, to the readers of Indian Journal of Palliative Care on many other systematic reviews

on palliative sedation,^[4-7] which would also aid clinical decision making on relatives' experiences,^[4] observational scales,^[5] home follow-up^[6] and Propofol drug use,^[7] in palliative and end-of-life care settings.

I request the authors of second review if they could provide explanations for the issues raised in this letter so that an effective evidence-informed palliative care be evaluated and implemented in the developing countries. I thank the Indian Journal of Palliative Care for establishing a powerful platform for dissemination of high level evidence and an ongoing interdisciplinary discussion on the issues related to palliative care.

**Senthil P Kumar, Krishna Prasad¹,
Kamalaksha Shenoy², Mariella D'Souza³,
Vijaya K Kumar⁴**

Srinivas College of Physiotherapy and Research Centre, Departments of ¹Medicine, ²Radiation Oncology, ³Psychiatry and ⁴Physiotherapy, Srinivas College of Physiotherapy and Research Center, Pandeshwar, Kasturba Medical College (Manipal University), Mangalore, Karnataka, India

Address for correspondence:

Dr. Senthil P Kumar;

E-mail: senthilparamasivamkumar@gmail.com

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