PEER REVIEW HISTORY

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ARTICLE DETAILS

| TITLE (PROVISIONAL)                          | Intrathecal Diamorphine For Perioperative Analgesia During Colorectal Surgery: A Cross-Sectional Survey of Current UK Practice |
|---------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| AUTHORS                                    | Alderman, Joseph; Sharma, Amit; Patel, Jaimin; Gao-Smith, Fang; Morgese, Ciro                                                      |

VERSION 1 – REVIEW

| REVIEWER                                  | Seki, Hiroyuki Kyorin University Faculty of Medicine Graduate School of Medicine, Anesthesiology                           |
|-------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| REVIEW RETURNED                           | 12-Jan-2022                                                                                                              |

GENERAL COMMENTS

Thank you for the opportunity to review this interesting article.

In this self-administered survey, the authors aimed to establish the dose of intrathecal diamorphine used for postoperative analgesia in laparoscopic colorectal surgery. Although the study has several limitations, the result is quite interesting, especially for readers outside the UK. I have some minor comments.

Minor comment
The authors should describe the selection criteria for the hospitals or procedure for selection.

The authors should clarify the number/rate of spinal anesthesia with or without local anesthetics.

| REVIEWER                                  | Reay, Michael Russells Hall Hospital, Anaesthesia and Critical Care                                                      |
|-------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| REVIEW RETURNED                           | 04-Feb-2022                                                                                                              |

GENERAL COMMENTS

Primary and secondary objectives clearly defined and achieved. Would have been interested to know rationale for dose selection and at what point of experience ( case /month dose) does the ITD dose increase above the median (500mcg).

| REVIEWER                                  | Kapila, Atul Royal Berkshire Hospital, Anaesthesia                                                                      |
|-------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|
| REVIEW RETURNED                           | 16-Feb-2022                                                                                                              |

GENERAL COMMENTS

To better understand the context of the responses to the survey - How were the 100 hospitals that the surveys were sent to chosen? Did that give rise to the opportunity to stratify responses by teaching hospital, large, medium or small DGH?
Or were there no identifiers in the survey monkey responses to help determine where the respondents were replying from? What proportion of all NHS hospitals is this? (assuming no private hospitals were included - the methods just states UK hospitals?) One of the survey questions is ‘specialty grade’ - but all the respondents are defined as consultant anaesthetists in the results. Did any other grade of anaesthetist respond? What is the response rate of 479 consultant anaesthetists as a proportion of all UK consultant anaesthetists?

It would be interesting to postulate why there were differences in opioid doses used for bowel resection surgery (hemicolecotomy, sigmoid and anterior resection) and pelvic surgery (AP resection, TATME) given that these often also have abdominal wounds?

Why do the authors think the reported correlation between activity and dosage of opioid administered exists?

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**VERSION 1 – AUTHOR RESPONSE**

Reviewer 1:
1. Selection criteria for hospitals approached:
Lists of UK NHS hospitals were obtained from the following websites:
https://www.nhs.uk/servicedirectories/pages/nhstrustlisting.aspx,
http://www.wales.nhs.uk/ourservices/directory/hospitals,
https://www.nimdta.gov.uk/international-graduates-page/trusts-hospitals/
and https://www.scot.nhs.uk/organisations/. From these lists, we excluded all the hospitals that do not provide surgical services (community and mental health hospitals, rehabilitation centres), maternity centres, single-specialty hospitals (e.g. eye hospitals, heart and lung centres, neuroscience hospitals) and those hospitals that did not have an anaesthetic department and those that were not contactable.
The anaesthetic departments of 138 acute NHS hospitals were eventually contacted, either by phone or email. Of these, 97 (70%) agreed to distribute an email invitation to their consultants to complete an electronic form of the survey.

Details herein are included in the Methods on page 6 of the submitted manuscript.

2. Reporting the rate of spinal anaesthesia with/without local anaesthetic:
Our questionnaire did not ask about differing combinations of opioids with local anaesthetic, though we did ask if anaesthetists use local anaesthetic only (with no opioid). We have added details of this latter point to page 9 (highlighted yellow in the version of the manuscript with tracked changes).

Reviewer 2:
1. Rationale for dose selection:
We agree that this is an important question. It would be best answered using a mixed-methods study, as questionnaires like ours lack the depth to truly understand clinicians’ reasoning.

2. Reporting the intersection between median ITD dose (500mcg) and activity of anaesthetists:
This is an interesting proposition which would require regression (using activity level as a proxy of anaesthetists’ experience as the independent variable) to investigate further. Given the high variability in the dose data, and that this analysis was not defined a priori as an objective of the investigation, the results of this regression would be vulnerable to overfitting. Descriptive analyses showed a significant difference between the median number of patients anaesthetised per month by consultants who use >500mcg and <=500mcg ITD (3 and 2, respectively; p=0.012). We were hesitant to include...
this analysis in the manuscript for the reasons highlighted above but will readily do so if the Editor
deems this of value.

Reviewer 3:
1. Understanding the context of the survey:
Details of how the hospitals were selected and what proportion of these are included in the survey
have been provided in our response to Reviewer 1 (point 1). No private hospitals were contacted.
Unfortunately, we did not ask respondents to report their Trust name, or the size of their hospital.
Therefore we cannot stratify the responses by type/size of hospital or identify the region in which the
respondents practice.

2. Respondents’ anaesthetic experience:
We only received responses from consultant anaesthetists. Other grades of anaesthetists were
welcome to submit responses but were not actively targeted to respond.

3. Response rate as a proportion of all UK anaesthetists:
According to the latest Royal College of Anaesthetists (RCoA) census there were 7959 anaesthetic
consultants in the UK in 2020 (https://www.rcoa.ac.uk/sites/default/files/documents/2020-11/Medical-
Workforce-Census-Report-2020.pdf). We received responses from 479 consultants. Although this
represents obviously a small proportion of all consultants (6%), it is still a large number across a large
geographic area. Our sampling strategy - contacting anaesthetic departments for response rather
than individual anaesthetists – optimised geographic spread of responses rather than absolute
number. It must be noted that of all the consultant anaesthetists in the UK, only a proportion of these
will be routinely involved in laparoscopic colorectal surgery, and so our sample represents a higher
(and, regrettfully, unquantifiable) proportion of experts in this type of anaesthesia.

4. Different opioid doses for bowel resection vs pelvic surgery:
We agree that this is an interesting question, but unfortunately beyond the scope of this survey.

5. Why is there a correlation between anaesthetists activity & ITD dose delivered:
Our team has several theories, but at present we have no evidence to support these. This may
indicate that more experienced anaesthetists believe the higher doses offer patients better quality and
longer duration of postoperative pain relief; or have a different opinion about risks of higher doses.
Ultimately, this should be the subject of future study, potentially as a study within a trial of optimal ITD
dosing for particular procedure subtypes.