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OPEN PEER REVIEW

Management of Incidental Uncontrolled Elevation of Intraoperative Blood Pressure: A Comparative Study on Nitroglycerine Versus Dexmedetomidine Infusion

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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Contents

1 **Original submission** Referee 1, Saied Amniati, Referee 2, Associate Editor, Editor-in-Chief 2
2 **Revision 1** Referee 1, Associate Editor 4
Authors' reply to reviewers 5
Reviewer and editor comments 11

1 Original submission

5 comments · 23 Jan 2023 – 1 Feb 2023

Referee 1 Reviewer

MAJOR REVISION 23 Jan 2023

Dear Author
The article presents a good concept, but some points need explanation and correction as follows:
1-The title of the article is not aligned with what is inferred from the article. The aim is to compare intraoperative hypertension control between two drugs, while the existing tables show the comparison of blood pressure in the postoperative period, and the bias is toward dexmedetomidine.
2- ASA is not defined for patients.
3- How do you calculate sample size, study power, and p-value?
4- The methods are not very well explained, and the timing of blood pressure and heart rate measurements is not mentioned.
5- How and by what means do you determine the adequacy of analgesia or anesthesia? (line 76)
6-What were the induction and maintenance drugs?
7- Table 3 shows the PACU hemodynamic changes between the two groups, but there is no comparison of the main objective during the operation.
8- The CONSORT diagram was unclear.
Thank you

Saied Amniati Reviewer

REJECT 30 Jan 2023

The topic of your article is not a new topic and has been mentioned many times in various books and articles.

Referee 2 Reviewer

MAJOR REVISION 1 Feb 2023

Dear authors
Please use references from the last 5 years.
Considering that these two drugs differ in terms of pharmacology, please mention the inclusion and exclusion criteria for the study.
Please mention how the unwanted side effects of the drugs are dealt with.

Associate Editor

MAJOR REVISION 1 Feb 2023

Dear EIC,
This study compares Nitroglycerine Infusion with Dexmedetomidine Infusion in the Intraoperative Management of Uncontrolled Hypertension. It is a useful study, but some points need explanation and correction, as mentioned by the reviewers (especially the Title, Table, and method of calculating the sample size).

Editor-in-Chief MAJOR REVISION 1 Feb 2023

Dear Author,
Please revise the manuscript based on the comments. We can decide about your manuscript after revision.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Editor in chief and Editorial board members of Anesthesiology and Pain medicine

We are extremely pleased to know that our manuscript **" A Comparative Study Between Nitroglycerine Infusion and Dexmedetomidine Infusion in Intraoperative Management of Uncontrolled Hypertension"** has been assessed by your eminent reviewers.

- Editorial corrections, comments and reviewers' reports, together with any additional comments were meticulously addressed by our team.
- We did our best efforts to fully address these points. A point-by-point response was included.

Associate Editor's Comments:

Associate Editor 1:

This study compares Nitroglycerine Infusion with Dexmedetomidine Infusion in Intraoperative Management of Uncontrolled Hypertension. It is a useful study but some points need to explanation and correction as mentioned by reviewers (especially Title, Table and the way of calculation sample size).

- Thank you for your comments:
  - The title was changed to “Management of incidental uncontrolled elevation of intraoperative blood pressure: A Comparative study between nitroglycerine versus dexmedetomidine infusion.”

  - Postoperative data was illustrated in table 3 to avoid adding an additional 4 figures under titles of postoperative heart rate values, postoperative systolic blood pressure, postoperative mean blood pressure and postoperative diastolic blood pressure. On the other hand, preoperative and intraoperative data for hemodynamics “Heart rate, systolic, mean and

diastolic blood pressure were all expressed in 4 graphs under the figures 1,2,3and 4.

- For the sample size: Sampling technique was explained as being done by consecutive methodology for one year in both groups to include all eligible patients fulfilling the inclusion criteria.

Reviewers Comments:

Reviewer 1:

Dear Author

It was an article with good conception but some points need to explanation and correction as follows:

1-The title of the article is not aligned with what is inferred from the article. The aim is to compare the control of hypertension interoperative between two drugs, while the existing tables show the comparison of blood pressure in the postoperative period, and the bias is towards dexmedetomidine.

- Thank you for your comment:
  - The title was changed to “Management of incidental uncontrolled elevation of intraoperative blood pressure: A Comparative study between nitroglycerine versus dexmedetomidine infusion.”
  - Comparison between the two groups was done throughout the perioperative period, however preoperative and intraoperative data were expressed in the form of graphs in figures 2,3,4 and 5 but postoperative data in PACU was expressed in table 3
  - The analyzation of collected data showed more hemodynamic stability with the dexmedetomidine administration regarding both blood pressure values and heart rate

2- ASA is not defined for patients.

- Thank you for your comment:
  - ASA was added to the methodology section: “ASA II patients”

3- How do you calculate sample size, study power, and p-value?

- Thank you for your comment:
  - Sample size: Sampling technique was explained as being done by consecutive methodology for one year in both groups to include all eligible patients fulfilling the inclusion criteria. A p-value less than 0.05 were considered statistically significant.

4- The methods of work is not very well explained and the timing of blood pressure and heart rate measurements is not mentioned.

- Thank you for your comment:
  Explanation was added to the methodology section
  - In the operating theatre all patients were monitored using electrocardiogram (ECG), non- invasive blood pressure monitoring, capnography and oxygen saturation using pulse oximeter.

  -Upon administration of drugs for hemodynamic control (either nitroglycerine or dexmedetomidine), invasive blood pressure monitoring using the Datex- Ohmeda 3030, Carestation 620 B40 monitor (General Electric: Madison, USA) was connected. Heart rate and blood pressure were continuously monitored and documented every 10 minutes.

5- How and by what means do you determine the adequacy of analgesia or anesthesia? (line 76)

- Thank you for your comment:

  - This paragraph was added for illustration “Intraoperative analgesia was attained using either intravenous morphine 0.1 mg/kg or through epidural analgesia and some cases received regional wall blocks. In case of an

increase in either blood pressure or heart rate above 20% from the baseline 50µ fentanyl was administered to exclude inadequate analgesia".

6-What were the induction and maintenance drugs?

- Thank you for your comment:

  - Induction of anesthesia was conducted according to our institutional protocol using intravenous anesthesia by propofol 2mg/kg, rocuronium 0.6 mg/kg while maintenance of anesthesia was achieved through controlled mechanical ventilation using inhalational anesthesia by either sevoflurane or isoflurane with 50% Fio2. Intraoperative analgesia was attained using either intravenous morphine 0.1 mg/kg, through epidural analgesia and some cases received regional wall blocks. In case of an increase in either blood pressure or heart rate above 20% from the baseline 50µ fentanyl was administered to exclude inadequate analgesia.

7- Table 3 shows the PACU haemodynamic changes between the two groups, but there is no comparison of the main objective during operation.

- Thank you for your comment:

  - Comparisons between the two groups were done throughout the perioperative period, however preoperative and intraoperative data were expressed in the form of graphs in figures 2,3,4 and 5 but postoperative data in PACU was expressed in table 3

8- The consort diagram was unclear.

- Thank you for your comment:
  - Changes were made for more clarification.

Reviewer 2:
Dear authors

Please use references from the last 5 years

- Thank you for your comment:
  - References were revised, old references were found to be related either to the history of drug usage or related to drug pharmacology thus more recent literature were found to be citing same old ones.

Considering that these two drugs are different in terms of pharmacology, please mention the criteria for entering and exiting the study

- Thank you for your comment:
  - Study population included patients above 18 years old who underwent cancer resection surgical procedures under general anesthesia and developed accidental uncontrolled elevation in their blood pressure. Exclusion criteria were patients on beta blockers with heart rate below 55 beats per minute, patients with kidney or liver function impairment, bradycardia, any degree of heart block and severe cardiorespiratory disease. Additionally, patients diagnosed with pheochromocytoma, patients who suffered major blood loss and patients with major fluid shift were excluded from the study.

Please mention how the unwanted side effects of the drugs are dealt with

- Thank you for your comment:
  - Initially, dexmedetomidine infusion was started after elevation of blood pressure 20% above the baseline and titrated according to blood pressure values. The infusion was deescalated when blood pressure values reached the baseline and/ or heart rate values lowered below 50 bpm. The infusion was stopped in cases where the blood pressure values decreased

20% below the baseline or reported persistent bradycardia with heart rate less than 45 bpm. In case of persistent bradycardia after cessation of infusion, a bolus of intravenous atropine 0.5 mg was administered and repeated as needed. For the nitroglycerine group, data retrieved included patients who received nitroglycerine infusion due to uncontrolled intraoperative elevation of blood pressure. Patients received nitroglycerin infusion (0.3-1 µg/kg/min) titrated according to each patient's hemodynamic response. Initially, nitroglycerine infusion was started according to our institutional protocol after reported elevation of blood pressure 20% above the baseline and titrated according to blood pressure values, the infusion was deescalated when blood pressure values reached the baseline and stopped in cases where the blood pressure values decreased 20% below the baseline values. In both groups the protocol of management of lowered mean arterial blood pressure (MAP) values not responding to cessation of infusion or in cases of MAP less than 60 mmHg a bolus dose of ephedrine 10 mg repeated as needed was used and documented.

Reviewer 3:
The topic of your article is not a new topic and has been mentioned many times in various books and articles

- Thanks for your comment,
  - The topic could be not new for comparison in research work concerning techniques for hypotensive anesthesia, but for our knowledge this topic was not much investigated regarding the management of accidental increase of intraoperative blood pressure in previously controlled hypertensive patients.

2 Revision 1

2 comments · 8 Feb 2023 – 12 Feb 2023

Referee 1 Reviewer

REJECT 8 Feb 2023

Dear Author

Unfortunately, I have to say that this article does not meet the criteria for an article and an academic work, and it needs major changes, which makes it unacceptable from my point of view.

Thank you

Associate Editor

ACCEPT 12 Feb 2023

Dear EIC,
The manuscript is acceptable now.