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OPEN PEER REVIEW

Comparison of Intraperitoneal Bupivacaine and Intravenous Ketorolac for Postoperative Pain Management Following Laparoscopic Cholecystectomy

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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.

More about open peer review: brieflands.com/knowledgebase/opr

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1 Original submission

5 comments · 6 May 2021 – 18 May 2021

Referee 1 Reviewer

MAJOR REVISION 6 May 2021

Line 67:
Although {Many studies have shown that the preventive use of NSAIDs reduces the need for opioids after surgery}, reference No. 15 refers to intraperitoneal ketorolac, not to intravenous ketorolac! So this reference should be replaced by a relevant reference.

Referee 2 Reviewer

MAJOR REVISION 10 May 2021

Review of manuscript 114623;
1-In the introduction, the importance of this study and its novelty were not explicitly mentioned.
2-Any history of hypersensitivity or reaction to the drugs, as well as heart diseases and dysrhythmias, should be considered exclusion criteria.
3-No description has been given of the method of blinding in the study, apart from randomization.
4-The country and the manufacturer of the drugs utilized in the study must be indicated.
5-Further explanation of the methods used to conduct the study is needed, such as airway management, drugs used for induction, maintenance and emergence from anesthesia, and intravenous fluids.
6-The analgesic plan for the beginning and continuation of anesthesia is not clear.
7-What was the difference between the bupivacaine doses in this study and those in previous studies?
8-What were the method of administration and dose of fentanyl used to relieve pain that had not been relieved by bupivacaine and ketorolac?
9-How would the study investigators manage nausea and vomiting in patients if they occurred?
10-Table-2 should include the P-value.

Associate Editor

MAJOR REVISION 10 May 2021

Dear Author:
Thank you for this research. Could you please provide further explanations about some points?
Abstract:
1-Shoulder pain was not included in the aims that you mentioned in the abstract.
Randomization:
1-Did you use fentanyl as a drug for primary sedation? You also repeated this term (fentanyl sedation) in line 189 in the results section.
2- How much fentanyl did you use during surgery, with the exception of the induction dose?
3-Did the patients have a history of surgery and/or nausea and vomiting or problems in the GI system, given the effect of these problems on the incidence of nausea and vomiting?

Patients follow-up
1- In line 128, you mentioned that for cases with VAS>4, the drug dose was increased by 20%. Which drug did you mean? You also mentioned 25 mg meperidine. Both drugs were used in patients in all groups.

Results
- The amount of opioid consumption after surgery was not different between the three groups.

Based on this, group C, without any intervention, is the same as the other two groups with intervention. Is that correct?

Tables
- Table 2 did not have a P-value.

With Regards

Associate Editor

MAJOR REVISION 18 May 2021

Dear Editor in Chief
Thank you for inviting me. I read this article with interest, and my comments are as follows:
In the abstract, under methods, remove the hospital name, city, and date.
Study design: It is not necessary to describe ASA I and II.
The results section is too long!
Reduce the number of decimal places; that is, for 2.57±1.45, write only 2.5 ±1.4.
P value for Table 2?
Ref 24 is too old.
Please consider and add the following nine references:
Imani F, Zaman B, De Negri P. Postoperative Pain Management: Role of Dexmedetomidine as Adjuvant. Anesth Pain Med. 2020;10(6):e112176.
Imani F, Varrassi G. Ketamine as Adjuvant for Acute Pain Management, Anesth Pain Med. 2019;9(6):e100178.
Malik K M, Imani F, Beckerly R , Chovatiya R. Risk of Opioid Use Disorder from Exposure to Opioids in the Perioperative Period: A Systematic Review, Anesth Pain Med. 2020;10(1):e101339.
Tully J, Jung JW, Patel A, Tukan A, Kandula S, Doan A, et al. Utilization of Intravenous Lidocaine Infusion for the Treatment of Refractory Chronic Pain. Anesth Pain Med. 2020;10(6):e112290.
Murthy TKK, Kumar PVV. Effect of Perioperative Intravenous Lignocaine Infusion on Haemodynamic Responses and postoperative Analgesia in Laparoscopic Cholecystectomy Surgeries, Anesth Pain Med. 2018;8(2):e63490.
Urits I, Jung JW, Amgalan A, Fortier L, Anya A, Wesp B, et al. Utilization of Magnesium for the treatment of Chronic Pain. Anesth Pain Med. 2021;11(1):e112348.
Rahimzadeh P, Faiz SHR, Hoseini M, Mousavie SH, Imani F, Negah AR. Comparison of intraperitoneal bupivacaine, acetazolamide, and placebo on pain relief after laparoscopic cholecystectomy surgery: A clinical trial. Med J Islam Repub Iran. 2018 Nov 13;32:112.
Imani F, Faiz HR, M Sedaghat, Hajiashrafi M. Effects of Adding Ketamine to Fentanyl Plus Acetaminophen on Postoperative Pain by Patient Controlled Analgesia in Abdominal Surgery. Anesth Pain Med. 2014;4(1):e12162.
Albooghobeish M, Ghomeishi A, Adarvishi S, Neisi A, Mahmoodi K, et al. The Effect of Preoperative Zintoma Capsule on Postoperative Nausea and Vomiting After Laparoscopic Cholecystectomy, Anesth Pain Med. 2018;8(5):e67132.
Regards

Editor-in-Chief

MAJOR REVISION 18 May 2021

Major 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.

Reviewers' Comments:

Authors are very grateful to the reviewer for careful review and helpful comments on this manuscript.

Reviewer 1:
Line 67:
Although {Many studies have shown that the preventive use of NSAIDs reduces the need for opioids after surgery} but the reference No. 15 refer to intraperitoneal ketorolac, not to intravenous ketorolac! So this reference should be replaced by a relevant reference.

Answer: **The relevant reference was replaced.**

Reviewer 2:
Review of manuscript 114623;
1-In introduction part, the importance of this study and its novelty was not explicitly mentioned.

*Answer:***The importance of the study in the use of intraperitoneal bupivacaine and its comparison with NSAIDs. Bupivacaine replaces NSAIDs if it achieves adequate efficacy to reduce the side effects of using NSAIDs in postoperative recovery. The use of intraperitoneal bupivacaine will also reduce shoulder pain.**

The novelty of this study is to achieve a more effective and useful dose of intraperitoneal bupivacaine than the dose of ketorolac.

2-Any history of hypersensitivity or reaction to the drugs besides heart diseases and dysrhythmias should be considered as excluding criteria.

*Answer:***These items have been excluded in our study, which was mentioned in the study design section.**

3-No description has been given for the method of blinding of the study apart from randomization.

Answer : ***Method of blinding*** **was added in the method section.**

4-The country and the manufacturer of the drugs utilized in the study must be indicated.

Answer: **The specifications of the drug manufacturer were added in the method section.**

5-Further explanation in relation with methods of implementation of study is needed, such as airway management, drugs used for induction, maintenance and emergence of anesthesia and intravenous fluids.

Answer: **The section was edited and suggested items were added to methods of implementation.**

6-It is not clear the analgesic plan for the beginning and continuation of anesthesia.

Answer: **The section was edited and suggested items were added to methods of implementation.**

7-What was the different between bupivacaine doses in this study with previous ones?

Answer: **The aim of this study was to compare the dose of *bupivacaine* used with ketorolac and opioids. Therefore, its purpose is not to compare with other doses of bupivacaine in other studies.**

8-What was the method and dose of fentanyl used to relieve the pain not had been achieved by bupivacaine and ketorolac?

Answer: **If analgesics were insufficient, the patient used bolus injection of fentanyl, and if insufficient, Meperidine was injected slowly at a dose of 0.5 mg/kg intravenously.**

9-How would the conductors of study manage nausea and vomiting in patients if it happened?

Answer: **If the patient had nausea and vomiting, *Metoclopramide* Injection were used intravenously and slowly.**

10-Table-2 should include P-value.

Answer: **P-value was included in Table-2.**

Associate Editor's Comments:

Associate Editor 1:
Dear Author:
Thank you for this research. Could you please give further explanation about some points :
Abstract:
1-Shoulder pain was not included in aims that you mentioned in the abstract.

Answer: **Abstract was revised and shoulder pain included.**

Randomization:
1-Did you use fentanyl as a drug for primary sedation? And you repeated this term(fentanyl sedation) in line 189 in section of results.

Answer: **Fentanyl was used as a drug for "primary analgesia" and corrected in line 189.**

2- How much of fentanyl did you use during surgery with the expiation of induction dose?

Answer: **Fentanyl is one of the inductive anesthetics that was used at a dose of 3µg/kg at the beginning of the surgery and then was injected with a dose of 1µg/kg along with intravenous atrocurium (0.2mg/kg) every half an hour during surgery.**

3-Did the patients have history of surgery and or nausea and vomiting or problems in GI system because of effect of these problem on incidence of nausea and vomiting.

Answer: **Patients with a history of PONV and GI disorder were excluded from the study. (These are listed in the exclusion criteria).**

Patients follow-up
1- In line 128: you mentioned for cases with VAS>4 , drug dose increased by 20%. Which drug did you mean? And 25 mg meperidine. Both of the drugs used on patients in all groups.

Answer: ***This section was corrected in manuscript.*** **If analgesics were insufficient, the patient used bolus injection of fentanyl, and if insufficient, Meperidine was injected slowly at a dose of 0.5 mg/kg intravenously.**

Results
- Amount of opioid consumption after surgery was not different between the three groups. With this concept, group C , without any intervention is same as other two groups with intervention. Is it right?

Answer: Amount of opioid consumption was different between the three groups and is listed in Table 3.

Tables
- Table 2 did not have P-value

Answer: **P-value was included in Table-2.**

With Regards

Associate Editor 2:
Dear Editor in Chief
Thank you for inviting me. I read with interest this article and my comments are as below:

In abstract, at methods, remove the name of hospital, city and date.

Answer: The abstract was edited and changes were made.

Study design: It is not need to describe the ASA I and II
Result section is too long!

Answer: The study design and result section were edited.

Delete decimal numbers, it means for 2.57±1.45, write only 2.5 ±1.4
P value for Table 2???!!
Ref 24 is too old

Answer: Decimal numbers were deleted and new reference was replaced.

Please consider and add below nine references:
Imani F, Zaman B, De Negri P. Postoperative Pain Management: Role of Dexmedetomidine as Adjuvant. Anesth Pain Med. 2020;10(6):e112176.
Imani F, Varrassi G. Ketamine as Adjuvant for Acute Pain Management, Anesth Pain Med. 2019;9(6):e100178.
Malik K M, Imani F, Beckerly R , Chovatiya R. Risk of Opioid Use Disorder from Exposure to Opioids in the Perioperative Period: A Systematic Review, Anesth Pain Med. 2020;10(1):e101339.
Tully J, Jung JW, Patel A, Tukan A, Kandula S, Doan A, et al. Utilization of Intravenous Lidocaine Infusion for the Treatment of Refractory Chronic Pain. Anesth Pain Med. 2020;10(6):e112290.
Murthy TKK, Kumar PVV. Effect of Perioperative Intravenous Lignocaine Infusion on Haemodynamic Responses and postoperative Analgesia in Laparoscopic Cholecystectomy Surgeries, Anesth Pain Med. 2018;8(2):e63490.

Urits I, Jung JW, Amgalan A, Fortier L, Anya A, Wesp B, et al. Utilization of Magnesium for the treatment of Chronic Pain. Anesth Pain Med. 2021;11(1):e112348.
Rahimzadeh P, Faiz SHR, Hoseini M, Mousavie SH, Imani F, Negah AR. Comparison of intraperitoneal bupivacaine, acetazolamide, and placebo on pain relief after laparoscopic cholecystectomy surgery: A clinical trial. Med J Islam Repub Iran. 2018 Nov 13;32:112.
Imani F, Faiz HR, M Sedaghat, Hajiashrafi M. Effects of Adding Ketamine to Fentanyl Plus Acetaminophen on Postoperative Pain by Patient Controlled Analgesia in Abdominal Surgery. Anesth Pain Med. 2014;4(1):e12162.
Albooghobeish M, Ghomeishi A, Adarvishi S, Neisi A, Mahmoodi K, et al. The Effect of Preoperative Zintoma Capsule on Postoperative Nausea and Vomiting After Laparoscopic Cholecystectomy, Anesth Pain Med. 2018;8(5):e67132.

Answer: All references included in the manuscript.

2 Revision 1

3 comments · 11 Nov 2021 – 11 Nov 2021

Referee 3 Reviewer

REJECT 11 Nov 2021

Dear Editor in Chief
I read with interest this revised manuscript, but unfortunately there are a lot of problems. In its current form, this article needs fundamental and structural corrections. Therefore, I strongly suggest that the authors consult an expert writer.
In my opinion, it should be rejected for publication.
Sincerely

Associate Editor

MAJOR REVISION 11 Nov 2021

Dear Editorials
Based on reviewers' comments, this article needs some revision.
Final decision: Major revision.
Regards
AE

Editor-in-Chief

MAJOR REVISION 11 Nov 2021

Major Revision

3

Revision 2

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.

Reply to reviewers

Authors are very grateful to the reviewer for careful review and helpful comments on this manuscript.

Reviewers' Comments

Reviewer 1:

Dear Editor in Chief

I read with interest this revised manuscript, but unfortunately there are a lot of problems. At this format, this article need fundamental and structural corrections. Therefor strongly suggest to authors to consult by an expert writter.

In my opinn it is rejeced for publishing.

Sincerely

Answer: The manuscript was revised by expert writter and all possible problems were solved. Also all corrections were highlited.

Associate Editor's Comments:

AE:

Dear Editorials

Based on reviewers comments this article (ID #114623) need some revision.

Final decisin: Major revision.

Regards

AE

Answer: First of all we have to thanks for your attention and careful reviewing. Following reviewers' comments, at this revision, we tried to correct all objections, and redisned the majority of our manuscript. Also, corrections were highlighted.

3 Revision 2

1 comment · 9 Dec 2021

Editor-in-Chief

ACCEPT 9 Dec 2021

Dear Editorials
Fortunately, the author was able to respond to all requested items, and this revised version can be acceptable.