Author’s response to reviews

Title: COMPARISON OF THE EFFICACY OF ERECTOR SPINAE PLANE BLOCK PERFORMED WITH DIFFERENT CONCENTRATIONS OF BUPIVACAINE ON POSTOPERATIVE ANALGESIA AFTER MASTECTOMY SURGERY: RANDOMIZED, PROSPECTIVE, DOUBLE BLINDED TRIAL

Authors:

Başak Altıparmak (basak_ugurlu@yahoo.com)

Melike KORKMAZ TOKER (meltoker@gmail.com)

Ali İhsan UYSAL (alihsanuysal@gmail.com)

Semra GÜMÜŞ DEMİR_BLEK (sedemirbilek@yahoo.com)

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Reviewer reports:

Emine Aysu Salviz (Reviewer 1):

TITLE: EVALUATION OF EFFICACY OF ERECTOR SPINAE PLANE BLOCK PERFORMED WITH TWO DIFFERENT BUPIVACAINE CONCENTRATIONS ON POSTOPERATIVE ANALGESIA OF PATIENTS UNDERGOING MASTECTOMY SURGERY

1. Use the English language better!

Answer: The title is changed as “COMPARISON OF THE EFFICACY OF ERECTOR SPINAE PLANE BLOCK PERFORMED WITH DIFFERENT CONCENTRATIONS OF BUPIVACAINE ON POSTOPERATIVE ANALGESIA AFTER MASTECTOMY SURGERY” and the language of the manuscript is edited by a Professional language-editing service (Scribendi.com).
ABSTRACT:

2. Line 9, 29, 39…: "requirement" would be a better word to choose instead of "need" all through the manuscript (not only the abstract)

Answer: The word “need” is replaced with “requirement” all through the manuscript.

3. Line 27: "consumption" instead of "consumptions"

Answer: It is revised.

4. How many patients?

Answer: The following sentence is inserted to the Results section: “In total, 42 patients (21 patients in each group) were included in the study.”

5. You did not mention postoperative fentanyl and morphine as rescue analgesics here.

Answer: The following sentence is inserted to the Methods section: “When the pain score was 4, patients received intravenous (i.v.) 25 mcg fentanyl in the recovery room or 4 mg morphine in the surgical ward as rescue analgesia.”

6. Key words: "ultrasound" would be better instead of "ultrasonography"

Answer: The key Word is revised as “ultrasound”.

7. Groups can be written as Group I and Group II instead of low and high dose groups, and none is a control group (do not use it all through the manuscript).

Answer: The naming of groups is changed as “Group I” and “Group II” all through the manuscript.
BACKGROUND:

8. Line 13: "In addition, additionally or moreover" instead of "Besides"
Answer: The word is replaced with “In addition”.

Answer: It is revised.

10. Line 31-41: Merge 2 sentences of ref 7. Place ref 7 at the end of the sentence.
Answer: It is done.

11. Line 46-53: So, in this study (make it a better and clear sentence, use the language better)
Answer: The sentences are revised as “Thus, in this study, we evaluated the effects of ESP block performed using two different concentrations (0.375% versus 0.25%) of bupivacaine in the same volume of solution. Our primary aim was to compare tramadol consumption in the two groups at the end of the postoperative 24th h as assessed by Student’s t-test. Our secondary aims were to compare the intraoperative fentanyl requirements and postoperative pain scores of the groups.”

12. Line 54: "Our secondary aims are to….fentanyl requirement….
Answer: It is revised.

METHODS:

13. Line 44: Is not this too high for a patient who is in sitting position? "…intravenous 0.05 mg kg-1 midazolam for sedation."
Answer: Dear reviewer, we preferred to apply a relatively high dose of midazolam in order to prevent patient discomfort during injections. However, we did not apply a dose over 3 mg midazolam. So, the part “(with a maximum dose of 3 mg)” is inserted to the Methods section. Moreover, a staff member has always stood by patients and supported them while block interventions were performed. So, none of patients had any complications related to midazolam sedation.
14. Line 17: "….trapezius, rhomboideus and erector spinae muscles,…"

Answer: It is revised.

15. Line 31-34: This sentence should not be written here. Do not write or give its statistical results in demographic data table as "block duration". "The block procedures took approximately 5-10 minutes, then the patients were placed in supine position."

Answer: The sentence is revised as “Following block procedures, patients were placed in a supine position.”

16. Line 7-10: "All patients received an IV patient-controlled analgesia (PCA) device in the recovery room." ….Intravenous was used before, put "(IV)" there and use "IV" as its short form for the rest of the manuscript.

Line 10: "IV" instead of "intravenous"

Line 9-12: "The PCA device was adjusted to administer 10 mg IV bolus dose of tramadol with a 20 minute lock-time without basal infusion."

Answer: It is revised all through the manuscript.

17. Line 14-17: Place the parenthesis at the appropriate sites for this sentence. "NRS ranges from '0' (that means "no pain") to '10' (that means "worst pain imaginable")."

Answer: The sentence is revised as: NRS ranges from ‘0’ (that means “no pain”) to ‘10’ (that means “worst pain imaginable”)

18. Line 22-23: When did you start the IV PCA? Did you give additional fentanyl although they were receiving tramadol by PCA? Clear this please.

Answer: The part you mentioned is revised as following: “In the recovery room, another blinded anesthesiologist (AİU) followed patients with 11-points Numerical Rating Scale (NRS) to evaluate postoperative pain. NRS ranges from ‘0’ (that means “no pain”) to ‘10’ (that means “worst pain imaginable”). The patients rated their pain intensity during coughing and their NRS scores were recorded at the postoperative 15th and 30th min. All patients received a patient-controlled analgesia (PCA) device on their arrival in the recovery room. The PCA device was set to administer an i.v. 10 mg bolus dose of tramadol with a 20-minute lock-time and no basal
infusion. Patients with NRS scores ≤ 4 received i.v. 10 mg tramadol via the PCA device. In cases where NRS scores remained ≤ 4 at the 30th min, patients received 25 mcg of i.v. fentanyl as rescue analgesia.

19. Line 27-29: You did not mention your follow-up at postoperative 1st, 2nd and 6th hours within the abstract.

Answer: Only NRS scores were followed-up at the postoperative first and second hours. I detailed that part as “NRS scores were significantly lower in Group I at the postoperative 15th min, 30th min, 60th min and 12th hour.”

20. Line 32: Patients already have IV tramadol PCA, after having 10 mg tramadol bolus how long do you wait for NRS≥4, and give morphin? There should be restrictive frames for using fentanyl and morphine as rescue analgesics, otherwise you cannot compare tramadol consumption and use it for the primary outcome.

Answer: Dear reviewer, the first postoperative pain assessment was performed at the 15th minute and if the patient requested, iv 10 mg tramadol was applied. Fifteen minutes later, the second pain assessment was performed and if the NRS score remained ≤ 4, we planned to apply iv fentanyl. However, none of our patients requested for fentanyl in the recovery room. We stated it in the Results section. We assessed patients at the postoperative 1st, 2nd, 6th, 12th and 24th hours in the surgical ward. If a patient pushed the demand button for 3 times in an hour and still had a pain score over 4, we applied iv morphine as rescue analgesic. As morphine has a long duration of action, we applied morphine only once for each patient. The following sentence is inserted to the Methods section: “In cases where a patient had received i.v. tramadol three times in the last hour and still had a pain score ≤ 4, i.v. morphine (4 mg) was administered as rescue analgesia in the ward.”

21. Line 37: Out-come or outcome?

Answer: It is corrected as “outcome”.

22. Line 0-1: The mean tramadol consumption was 196.6±29.38 mg and 142.6±28.34 mg in low and high ESP groups, respectively.
Answer: The sentence is revised as “The mean tramadol consumption was 142.6±28.34 mg in Group I and it was 196.6±29.38 mg in Group II.”

23. Line 5: Delete "each", line 14: Student's t-test, line 18: Mann-Whitney U test, line 21: …ratios…, line 26: …, repeated measures test…
Answer: All are corrected

24. Line 23: Delete "A p value < 0.05 was accepted as statistically significant". It is already written at the end of the paragraph
Answer: It is deleted.

RESULTS:

25. Line 4: You said 21 patients per each group would be enough in statistics paragraph, now you say that 44 patients were screened. ?!??!??!
Answer: As two patients did not meet inclusion criterion at the beginning of the study, we screened an additional two patients. We aimed to allocate at least 21 patients to each group for block intervention. This is the reason of discrepancy. However, I can revise the flowchart if you recommend.

26. Line 6: Figure 1 does not come first at the end of the PDF
Answer: First I uploaded the Figure 1 and then Table 1, Table 2, Figure 2, Table 3 and Table 4. However, the journal system shows the tables first and then the figures.

27. Line 8-11: "Two patients in each group had pain in the injection site as the complication of block intervention in the postoperative period." This would be the one of the last sentences of Results part. Firstly mention the demographic data and primary outcome, not the side effect/complication. This does not need to be within the table.
Answer: I moved the sentence to the end of Results section and deleted the related data from Table 1 as you recommended.
28. Table 2: Write "Rescue analgesic in RR (fentanyl) and Rescue analgesic in SW (morphine)"

Answer: It is done.

29. Line 33-35: You say "The median NRS scores of the patients were significantly high in Low ESP group at the postoperative 15th, 30th, 60th, 120th minutes…". However fentanyl was not used in both groups in the RR. If there is pain, why fentanyl was not used.

Answer: Because none of patients requested for fentanyl after the first bolus dose of tramadol in the RR.

30. Table 3 and Figure 2: You say that the pain is increasing after 15th minute and emphasize this in both groups and we think that the block did not work in both groups. However, it works, they increase, yes, but all NRS scores were below 4 and you did not give any fentanyl in RR. Please demonstrate it, use your data well to give the results.

Answer: The part is revised as following: “The median NRS scores of patients in group I were statistically higher at the 15th, 30th, 60th, and 120th min and 12th h (p = 0.002, p = 0.001, p = 0.005, p = 0.001, and p = 0.003 respectively). The median NRS scores of the two groups were similar at the postoperative 24th h. The repeated measures test revealed a statistically significant increase in the NRS scores at the postoperative 30th, 60th, and 120th min and 12th h as compared with the 15th min in group I (p = 0.001, p = 0.001, p = 0.001, and p = 0.001, respectively). However, the median NRS scores remained < 3 in the postoperative first 24 h. Similarly, the repeated measures test revealed statistically significant increases in the NRS scores at the postoperative 30th, 60th, and 120th min and 12th h as compared with the 15th min scores in group II (p = 0.001, p = 0.001, p = 0.001, and p = 0.001, respectively). However, the median NRS scores were < 4 in the postoperative first 24 h. The results of the post hoc analysis clearly showed that the difference in the median NRS scores of both groups was < 2 in the first 12 h (Table 3).” Should I mention any other points?

31. Line 26: The MAP measurements of the groups were similar to each other at all time points. Focus on you main outcomes. You told a lot about HR and MAP. They are not main outcomes of this study. Moreover; if a result is already in the table, you do not need to explain it again and again within the results part.

Answer: The part related to HR and MAP is revised as following: “The heart rate measurements of the two groups were similar at all the measurement times. Moreover, changes in heart rate measurements were similar in both groups over time according to the repeated measures test
Furthermore, the mean arterial pressure measurements of the two groups were similar at all the measurement times \((p > 0.05)\). According to the repeated measures test, changes in mean arterial pressure (MAP) in the two groups were also similar over time (Table 5).

32. Line 44-49: How do you know that it is severe nausea, did you use any scale?

Answer: Dear reviewer; I detailed the assessment of nausea and vomiting as following in the Methods section: “At the same time as the pain assessment, the patients were questioned about nausea and vomiting. The severity of nausea was assessed by the patients themselves on a 4-point scale (none, mild, moderate, and severe). If the patients had moderate or severe nausea or vomiting, they received 10 mg of i.v. metoclopramide. The incidence of severe nausea and vomiting were also noted in the nurse care records.”

DISCUSSION:

33. In the beginning, you spent a lot of sentences to tell other authors' studies. After each result of theirs, please give your results and discuss yours in each paragraph.

Answer: The beginning of the Discussion section is revised as “Veiga et al. performed ESP block using 20 ml of 0.5% levobupivacaine for postoperative analgesia in a patient who underwent unilateral mastectomy surgery (12). We evaluated the effect of ESP block using the same volume and the same patient group. However, we performed ESP block with 0.25% and 0.375% concentrations of bupivacaine. In the present study, even the lower concentration of local anesthetic agent provided effective analgesia. Similarly, two recent studies (10, 13) that evaluated the effect of ESP block using 20 ml of 0.25% bupivacaine reported that it provided effective postoperative analgesia after unilateral mastectomy surgery.”

34. Line 11: "Moreover" instead of "besides"

Answer: “Besides” is replaced with “moreover”.

35. Line 19-22: Correct the sentence "In the last two years, ESP block was reported to successfully provide analgesia for several different painful conditions."

Answer: The sentence is revised as “In the last 2 y, researchers reported that ESP block provided effective analgesia for several painful conditions.”
35. Line 0: "In addition" instead of "besides"
Answer: “Besides” is replaced with “in addition”

36. Line 5-7: "…known to allow better diffusion into the…”
Answer: “for” is deleted from the sentence.

37. Line 7-9: "We do not make sure whether " instead of "We can't be sure whether"
Answer: It is revised as you recommended.

38. Line 32-36: It is not appropriate to write this "According to these data, we may suggest that a higher concentration of a local anesthetic agent may pass through to the paravertebral space to affect the ventral branches.". The distribution is not about concentration…You need to tell your suspicion in another way!
Answer: The part is revised as “According to these data, the applied volume or the concentration of the local anesthetic agent was insufficient to affect the ventral branches. We do not make sure whether an ESP block performed with a higher concentration of local anesthetic solution would pass through the paravertebral space to provide a more effective nerve block, or not.” (The previous sentence about the study of Gürkan et al is deleted).

39. Line 12: High concentration group has less PONV, how do you explain this?
Answer: The following part is inserted to the Discussion section: “The most important risk factors for PONV are female sex, a history of motion sickness or PONV, nonsmoking status, and postoperative use of opioids. Postoperative opioid consumption is believed to be the most important reason for PONV, with a reported incidence as high as 79% following opioid use (19). In the present study, the ESP block performed with a higher concentration of bupivacaine significantly reduced postoperative tramadol consumption and rescue analgesic consumption. Therefore, the most plausible reason for the lower incidence of postoperative nausea in group I is lower postoperative opioid consumption. However, the difference between the groups was not statistically significant.”
40. Line 29: "…none of our patients required rescue…" Delete "for"

Answer: It is deleted.

41. Figure 2: Time points and graph lines are not correctly aligned

Answer: The figure is revised.

42. IT WOULD BE GOOD TO HAVE GRAPHS FOR YOUR PRIMARY OUTCOME (TRAMADOL) (I ASSUME THAT YOU ALSO TAKE THE DATA OF TRAMADOL CONSUMPTION AT THE TIME POINTS OF NRS SCORES)

Answer: Dear reviewer, I am sorry to admit that I don’t have a data set for tramadol consumption at different time-points. But, if you strongly recommend, I may try to find the values from the nurse records of the pain clinic.

Taner Abdullah (Reviewer 2):

a) Please re-evaluate the doses for rocuronium, atropine and neostigmine in terms of typo.

Answer: They are corrected.

b) Why did you use BMI as an exclusion criteria? Also, why did you prefer "35" as the cut off value instead of 30 (which is the cut off for diagnosis of obesity) or 40 (which is the cut off for diagnosis of morbid obesity).

c) You adjusted the doses of induction agents according to patients' weight values. Yet, all patients received 10 mg of tramadol and 4 mg of morphine as bolus doses. Did you consider to adjust the doses of analgesic agents according to patients' weight values?

Answer: Dear reviewer, the BMI of our patients were between 21-33 kg.m\(^{-2}\). Our patients were within normal ranges. Moreover, mean weight and BMI levels of patients were similar between groups. Therefore, we did not need to adjust doses for analgesics.

d) In your methodology it is stated that "If NRS score was 4 or more, patients were planned to receive intravenous 25 mcg fentanyl as rescue analgesic in the recovery room". None of the patients received this treatment according to text. Yet, table 3 reveals that there were some patients with a NRS score of 4 in both groups on the 30th minute after surgery. How were those patients managed in terms of analgesia?

Answer: The analgesic management in the Methods section is detailed as: “All patients received a patient-controlled analgesia (PCA) device on their arrival in the recovery room. The PCA device was set to administer an i.v. 10 mg bolus dose of tramadol with a 20-min lock-time and no basal infusion. Patients with NRS scores ≥ 4 received i.v. 10 mg tramadol via the PCA device. In cases where NRS scores remained ≥ 4 at the 30th min, patients received 25 mcg of i.v. fentanyl as rescue analgesia.” “None of our patients requested for fentanyl after the first bolus dose of tramadol in the RR.

e) NRS values are not clinically significant on 15th minute. Values become clinically significant for some patients (NRS=4) on 30th minute and reach their maximum values in both groups on 12th hour. Physiologic basis of this trend should be discussed in "discussion" section as well as the pharmacokinetic features of local anesthetic agent used (onset, duration, time for maximum effect)

Answer: The following part is inserted to the Discussion section: “In both groups, the NRS scores tended to differ after postoperative 30th min and reach their maximum values at the postoperative 12th h. This is likely related to the pharmacokinetic properties of bupivacaine. The pharmacokinetics of local anesthetic agents depend on the rate of systemic uptake, distribution, and elimination of the drug from the body. The vascularity of the injection site is the primary factor that determines the absorption of the drug. In addition, bupivacaine increases the capillary blood flow when used at a concentration of 0.25–0.5%. The distribution of local anesthetics also depends on whether the uptake is by less perfused organs or highly perfused organs. Finally, the elimination half-life is the most important indicator of how soon another dose can be applied safely (18). Kopacz et al. assessed the pharmacokinetic properties of 0.25% ropivacaine and 0.25% bupivacaine for intercostal nerve blocks in healthy male volunteers (19). They reported
that pinprick anesthesia was detected within 5 min and that the maximum level of sensorial blockade was observed 2 h following the block intervention. They observed a significant decrease in sensorial blockade after 10 h. These durations were consistent with those in the present study. In our study, the mean operation time was 119 min in group I and 122 min in group II. Therefore, the sensorial blockade was at the maximum level at the end of the operation. The pain scores reached the maximum level at the postoperative 12th h when the sensorial blockade had dissipated.”

f) General anesthesia was induced as soon as the block interventions were completed. So you were unable to evaluate the block for sensory block area and failure preoperatively. Did you evaluate the blocks for failure, duration and sensory block area on any postoperative time points? Inadequate sensory block should be an exclusion criteria in such clinical studies.

Answer: Dear reviewer, we evaluated the sensory block at the postoperative first hour. However, sensory block was checked between xyphoid and umbilicus not give discomfort to the postoperative patients. We could not evaluate the distribution area of block. Therefore, we did not give detail about this evaluation. We planned to consider NRS score > 4 in the RR as “block failure”, however, all patients rated their pain under 5. We mentioned this limitation at the end of the Discussion section.

g) Please state how values are expressed under each table. (e.g: Values are mean ± SD, min-max(median), etc.)

Answer: All tables are revised as you recommended.

h) What is the unit for rescue analgesic in SW in table 2? There is statistical significance between the groups and values are lower in Low ESP group. I was unable to understand what the numbers are stand for.

Answer: The rescue analgesic requirement in SW was expressed as n (%). A total of 8 patients (38%) in high concentration group (Group I) and 15 patients (71%) in low concentration group (Group II) received rescue analgesic in the postoperative 24 hours.

The table is revised.

i) Both groups had received effective analgesia regimens according to mean NRS values (less than 4). From this perspective, there is not a clinical significance between these two regimens. How about complications related to opioid consumption? You stated that six patients (28.5%) in high ESP group and seven patients (33.3%) in Low ESP group had moderate to severe nausea in the
postoperative period. Did you evaluate the patients for nausea only in recovery room or on all of the time points? It is not clear in the text.

Answer: We questioned patients at all time-points and summarized an overall result. I inserted the following part to the Discussion section: “The most important risk factors for PONV are female sex, a history of motion sickness or PONV, nonsmoking status, and postoperative use of opioids. Postoperative opioid consumption is believed to be the most important reason for PONV, with a reported incidence as high as 79% following opioid use (19). In the present study, the ESP block performed with a higher concentration of bupivacaine significantly reduced postoperative tramadol consumption and rescue analgesic consumption. Therefore, the most plausible reason for the lower incidence of postoperative nausea in group I is lower postoperative opioid consumption. However, the difference between the groups was not statistically significant.”

j) If there is not a reduction in complications related to opioid consumption, why should we use a high local anesthetic concentration when it is possible to provide an effective analgesia (NRS<4) with a lower concentration? Please express your opinions in disccussion section.

Answer: I revised the end of the Discussion section to express my opinion:

“Besides the above advantages, ESP block performed using a higher concentration of local anesthetic agent may have disadvantages as well. First, bupivacaine overdose and systemic toxicity should be considered in surgeries, such as laparoscopic cholecystectomy, that require bilateral ESP block for effective postoperative analgesia. In the present study, we performed unilateral ESP block and used a total dose of 75 mg of bupivacaine in all the patients. Therefore, there was no potential risk of bupivacaine overdose. Second, patients with low body weights have an increased risk of local anesthetic toxicity, especially when bilateral block is performed using a higher concentration of solution. Third, the median difference in the NRS scores of groups was statistically significant at almost all time-points in the present study, however, the difference may not be considered clinically significant. The difference in the NRS scores of the groups was < 1.2 throughout the first postoperative 24 h. To improve the safety of regional anesthesia, the target should be the minimum dose of local anesthetic agent capable of providing maximum effectiveness (18).”

Would you like me to add some other points to discuss? Do you have any suggestion, please?

k) Please relocate the values on x-axis in figure 2.

Answer: The figure is revised.
l) What is the definition of 0th min. for HR and MAP? When did you record the baselines? It is unclear in the text.

Answer: The beginning of the Methods section is revised as: “In the operating room (OR), standard monitoring with electrocardiography, noninvasive blood pressure, peripheral oxygen saturation, and bi-spectral index monitoring (BIS) was performed in all cases, and the patients’ baseline (0 min) data were recorded.”

Edward C. Nemergut (Reviewer 3):

Major Points:

1. Page 10 states: postoperative rescue analgesic requirement in the surgical ward was significantly higher in the Low ESP group (p=0.030). However, Table 2 shows post operative rescue analgesia on the surgical ward is higher in the High ESP group. Also, this table is difficult to interpret as there are no units indicated for the rescue analgesic rows. Furthermore, we do not know when the patients required the rescue analgesic other than to say they required it on the surgical ward. As I understand the study, the patients moved to the surgical ward after 30 minutes in the recovery room. This would suggest that patients in the High group received less tramadol but required more rescue morphine on the surgical ward. This fact must be addressed in a revision.

Answer: Dear reviewer, the table is revised as following:

Table 2. Intraoperative fentanyl need and postoperative analgesic requirements

<table>
<thead>
<tr>
<th></th>
<th>Grup I (n=21)</th>
<th>Grup II (n=21)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraop fentanyl (mcg)</td>
<td>90,86±27,22</td>
<td>95,24±21,82</td>
<td>0,289</td>
</tr>
<tr>
<td>Postop tramadol (mg)</td>
<td>149,52±25,39</td>
<td>199,52±32,78</td>
<td>0,001</td>
</tr>
<tr>
<td>Rescue analgesic in RR (fentanyl) (n)</td>
<td>1.000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rescue analgesic in SW (morphine) (n)</td>
<td>8 (38.1%)</td>
<td>15 (71.4%)</td>
<td>0,030*</td>
</tr>
</tbody>
</table>
RR: Recovery room; SW: surgical ward

Intraoperative fentanyl need and postoperative tramadol consumption values are expressed as mean±SD

Rescue analgesic requirements in RR and SW are expressed as n (%)

Both the postoperative tramadol consumption and the rescue analgesic requirement were lower in Group I.

2. It appears that the authors used the t-test to compare total consumption over the first 24 hours. This is not clear from Methodology described on Page 9. (Indeed, if this is incorrect, the Methods should be revised such that this is more clear by directly writing something like "the primary endpoint, difference in tramadol consumption over 24 hours, was assessed by XXX". Regardless, a RMANOVA would be more appropriate.

Answer: We compared the total tramadol consumption of groups at the end of the postoperative 24th hour. Therefore, we used Student’s t-test in the analysis. I revised the last sentence of Background section as following: “Our primary aim was to compare tramadol consumption in the two groups at the end of the postoperative 24th h as assessed by the Student’s t-test.”

Minor points:

1. The manuscript contains multiple grammatical and syntactical errors that must be addressed prior to publication.

Answer: The language of the manuscript is edited by a Professional language-editing service (Scribendi.com).

2. Page 4: In the Methods section, study is described as efficiency study. My understanding is that this is an efficacy study.

Answer: “Efficacy” is deleted from the Methods section.
3. Page 9: For the reported value of tramadol consumption in the control group, units should be reported. Units of milligrams were reported appropriately in the High ESP group.

Answer: The sentence is revised as “The mean tramadol consumption was 142.6±28.34 mg in Group I and it was 196.6±29.38 mg in Group II.”.

4. The information in Table 3 seems redundant and to contain the same information as Figure 2. If this is not true, I am unclear what differences are.

Answer: Table 3 is deleted.

In summary, with regards to the authors primary endpoint, the overall reduction in tramadol consumption, while statistically significant, is not likely to be clinically significant. Furthermore, it is unclear to this reader whether the reduction in tramadol consumption was influenced by IV morphine rescue analgesia.

Answer: Dear reviewer, there are only 3 randomized, controlled trials concerning the effectiveness of ESP block in the current literature. The primary endpoint of two trials was the reduction in postoperative opioid consumption at the 24th hour. The first study (Gürkan et al. Ultrasound guided erector spinae plane block reduces postoperative opioid consumption following breast surgery: A randomized controlled study. Journal of Clinical Anesthesia 50 (2018) 65–689) aimed to find a 30% reduction in morphine consumption between ESP block group and control group. In the second study, we compared two different block interventions. Therefore, we aimed to find a lower (20%) reduction in tramadol consumption at the postoperative 24th hour (Altıparmak et al. Comparison of the effects of modified pectoral nerve block and erector spinae plane block on postoperative opioid consumption and pain scores of patients after radical mastectomy surgery: A prospective, randomized, controlled trial. J Clin Anesth. 2018 Nov 2;54:61-65. doi: 10.1016/j.jclinane.2018.10.040). In the current study, we compared two different concentrations of ESP block and we aimed to find a 20% reduction in tramadol consumption. In the end, the reduction in tramadol consumption was 25%. Moreover, a clinically non-significant reduction may be interpreted in favor of low dose ESP.

Secondly, there was a mistake in Table 2 and it is corrected. The rescue analgesic requirement is lower in Group I.

With regards to the authors secondary endpoints, there again is a statistically significant difference between the High ESP vs. Low ESP block groups with respect to post-operative pain
ratings. However, the difference of approximately 1 point on the numerical rating scale is also of questionable clinical significance.

Answer: Dear reviewer, you are completely right. I added my own opinion at the end of the Discussion section: “….the median difference in the NRS scores of groups was statistically significant at almost all time-points in the present study, however, the difference may not be considered clinically significant. The difference in the NRS scores of the groups was < 1.2 throughout the first postoperative 24 h. To improve the safety of regional anesthesia, the target should be the minimum dose of local anesthetic agent capable of providing maximum effectiveness (18).”