Author’s response to reviews

Title: The effect of brief pre-anesthetic exercise therapy of jaw and neck joints on mouth opening, neck extension, and intubation conditions during induction of general anesthesia: A randomized controlled trial

Authors:

Sue Young Lee (tndude49@hanmail.net)

Sung Il Bae (snugsoul@naver.com)

Sang-Hwan Do (shdo@snu.ac.kr)

Ju-Tae Sohn (jtsohn@gnu.ac.kr)

Jin-Woo Park (jinul8282@gmail.com)

Version: 1 Date: 29 Dec 2019

Author’s response to reviews:

Reviewer reports:
(Reviewer 1): the paper is original, the study well conducted, the topic interesting
I have just some comments:

1. Patients from 20 to 70 years are very different: were the exercises more effective in older patients? could you comment?
We appreciated your comment. The inclusion criteria of the patients’ age in this study ranged from 20 years to 70 years, however, the actual age range of the participants enrolled for the study was mostly in their 40’ s to mid 60’ s. In the age distribution, we could not find any statistically significant correlation between the patient’s age (or age group) and the effects of exercise therapy (Mallampati score and IDS). However, through the subgroup analysis for the patients with Mallampati score III or IV, we could suggest that the exercise therapy is more effective for improving intubation conditions in the patients who had a relatively small mouth aperture size. We already had presented the results and interpretation of the subgroup analysis in the manuscript. (Page 11, last paragraph)

2. How did you choose the exercise time (5 MIN)?
To prepare for the exercise regimen, we referred to previous studies regarding the effects of stretching or massage. In most studies (Phys Ther Sport 2006, 7(4):195-200., Phys Ther Sport 2008, 9(2):89-96., Arch Phys Med Rehabil 1996, 77(7):688-692., Scand J Med Sci Sports 2015, 25(5):e490-496., Scand J Med Sci Spor 2015, 25(1):32-40.), exercise treatments with a short time of around 5 to 10 minutes could reduce muscle stiffness. We thought that brief and simple exercise before the induction of anesthesia was clinically more feasible than complex and long-time regimen. We had to instruct the patients to focus on the exercise and to participate as hard as possible. However, the concentrativeness seemed to decrease slightly when exercise time got longer. During a pilot study, we found that the simple 5 min exercise is appropriate.

3. Please, I'm very purist, do not call Cricoid compression the BURP maneuver! for difference please
read Sellick's historical paper. Please correct cricoid compression with laryngeal compression (as in table 3) or BURP.

We apologize for using the misnomer. As you advised, we changed “cricoid compression” to “laryngeal compression” throughout the text.

4. Page 7 line 50: you describe the rescue plans in case of a difficult laryngoscopy. Please explain differences from your protocol and ASA/DAS guidelines in case of difficult intubation.

In this study, we followed DAS 2015 guidelines in case of difficult intubation. According to the DAS guidelines, anesthetist can use direct/video laryngoscopy, intubation stylet or bougie, and external laryngeal manipulation during tracheal intubation, like our protocol. The most important principle is that a maximum of three attempts is allowed at intubation and a fourth attempt should be performed by a more experienced colleague. We cited the reference “British journal of anaesthesia 2015;115(6): 827-48”.

5. Why didn't you cut the nasal surgery cases? They can confuse the data concerning oropharyngeal injury.

We completely agree with your comment. We had to exclude the patients undergoing nasal surgery as well as those undergoing oropharyngeal surgery. We had not anticipated that nasal surgery also could confuse soft tissue injury measurements. Fortunately, there weren't many cases of nasal surgery (4 cases in the control group and 9 cases in the exercise group) and there was no significant difference of the numbers between the two study groups.

6. If you used TOF monitoring please explain 2 cases of vocal cords mobility.

We appreciated your comment. Because we only visually assessed the response of TOF stimulus, the disappearance of T1 might not be accurately evaluated in the 2 cases. Therefore, in those cases, we assumed that intubations were attempted before sufficient muscle relaxation was achieved. In fact, in both cases, we confirmed that the vocal cords were fully opened immediately thereafter.

7. Did you explain to yourselves the high incidence of CL IIIb in your groups? IIIb is a very difficult intubation grade!

In our results, there were 12 patients with CL grade 3 among 138 patients, and 7 patients showed CL grade 3b. As you pointed out, the incidence of CL IIIb in our study was rather high, however we thought that it was not extremely high. When difficult intubation is defined as CL grade 3 or greater, the incidence of difficult intubation is known as 3 – 15.8%, depending on the patient population (Anesthesiology 2005;103(2): 429-37). Patients in our study also showed a higher proportion of Mallampati score IV, compared to previous studies. We believed that the distributions of these grades about airways could be variable somewhat depending on the patient population.

8. Page 13 line 31 "was performed at the beginning....." please explain better this sentence (therapy is the exercise?)

We apologized for the awkward expression. We reworded the sentence as follows.

“In our protocol, the patients in the exercise group performed masseter muscle massage at the beginning and at the end of the exercise therapy.” (Page 12, 1st paragraph)

9. Page 16 line 15: can you quantify how long the effect of the therapy last? it would be interesting in practical clinical routine.

Thank you for your comment. In fact, we did not test how long the effect of the therapy in this protocol lasted. However, in a previous study of knee joint exercise, 4 sets of stretching for 20 seconds each
produced a decrease in passive hamstring stiffness, and improved joint range of motion. The decrease in passive stiffness after the stretching lasted for 20 min (Phys Ther Sport 2006, 7(4):195-200.). Therefore, we assumed that the delay less than 5 minutes was clinically acceptable in the exercise protocol. We demonstrated the exercise regimen in our protocol significantly affected mouth opening and neck extension during anesthetic induction. We revised the text as follows.

“However, the delay did not extend over 5 minutes in both hospitals, and the exercise significantly affected mouth opening and neck extension during anesthetic induction. In a previous report, simple stretching less than 2 minutes alleviated passive hamstring stiffness for 20 minutes.” (Page 15, 1st paragraph)

(Reviewer 2): The authors attempt to evaluate the use of a brief exercise regimen to improve the opening and laryngoscopy of patients undergoing anaesthesia requiring intubation. The trial took place over two centres and was randomised as well as single blinded (observer blinded). It appears to be adequately powered based on a pilot study performed a priori. The results of the study showed an improvement in Mallampati scores and mouth opening, though no statistical significant difference in ease of intubation.

The trial has been well designed and executed. The results seem believable and robust. The statistical analysis was easy to follow. The trial was powered against the Mallampati scoring before and after exercise, that being a surrogate for ease of intubation. On this basis, the trial successfully demonstrated an intervention that improved outcome.

A few points I would ask to be modified:

1. Page 5, line 41: Capital 'P' please
   Thank you for the advice. As you recommended, we changed it to “P”.

2. Page 7 line 35 - 'raised it up' - please can you clarify what is meant by this?
   We appreciated your comment and apologized for the awkward expression. We changed the expression as follows.
   “During intubation, the anesthesiologist placed the laryngoscope into the mouth and raised the blade up and away from the patient to obtain a clear view of the glottis.” (Page 7, 1st paragraph)

3. Page 15, line 8 'The exercise intervention in our protocol was to increase' - I would edit this to read 'was intended to increase'
   Thank you for the comment. We reworded the text as you recommended.

4. Page 17, line 16 - I would suggest that the word 'would' is changed for 'may' as IDS scores haven't changed and the subgroup analysis is post-hoc, which while interesting, has not been independently validated.
   We appreciated your comment. We reworded the text as you advised.

5. Table 2 & 3 & 4: Explicit description of which statistical test was used (i.e. Student's t-test of Chi-square etc).
   As you pointed out, we added the description of which statistical test was used as follows.
   Table 2
   a Comparisons of baseline (before the intervention) mouth aperture, SMD, and Mallampati score between the two groups using Student’s t-test (mouth aperture and SMD) and linear-by-linear
association (Mallampati score).
b Comparisons of mouth aperture, SMD, and Mallampati score after the intervention, between the two groups using Student’s t-test (mouth aperture and SMD) and linear-by-linear association (Mallampati score).
c Comparison of the incidence of Mallampati score 1 after intervention between the two groups using chi-square test.
d Comparisons of mouth aperture and SMD between before and after the intervention within the exercise group using paired t-test.

Table 3

a Comparisons between the two groups using Student’s t-test (continuous variables), chi-square or Fisher’s exact test (categorical variables), and linear-by-linear association (Cormack-Lehane grade).

Table 4

a Comparisons between the two groups using linear-by-linear association (Cormack-Lehane grade) and chi-square test (IDS group).

6. I would suggest a line or two about further work: This could be to explore Grade III/IV MPS score patients to see if benefit from exercise much more significant. Also, I would be interested to see in future if regular pre-op exercise had a greater benefit (i.e. leaflet to patients to ask to start exercising 1 week before?)

We completely agree with your comment and suggested further studies in the discussion section as follows.

“………………. However, since this study was the first clinical trial demonstrating the effect of pre-anesthetic exercise, we excluded those patients to avoid condition where proper stretching was not possible due to joint pain, and to maintain uniformity in the 5 min intervention. Long-time and steady exercise program might be more helpful for them. Further studies would be necessary to identify the effect of preoperative exercise regimen on intubation conditions in the patients with a risk for difficult intubation.” (Page 14, 2nd paragraph)