
Peer Review File

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Reviewer A

First of all, my major concern is the problematic clinical research design of this study, which was described as a cohort and observational study. However, the intervention, two sites of postoperative rehabilitation, was randomly assigned. So, the clinical research design should be a RCT and the paper should be reported according to CONSORT. Many methodological details of a RCT should also be provided in the revised version of this paper.

Reply 1: Thank you for your suggestion. We have to say this was indeed a cohort and observational study, because medical care that the children received was consistent and blinded until they were selected where to go after surgery. Before surgeries, neither the doctors nor the nurses knew where they planned to go. However, after surgery, one group was discharged home overnight and one group stayed in the hospital, which became a public event, and that's exactly the beginning of the data that we needed to observe. We could only ensure the consistency of children receiving surgery, but not the consistency of the postoperative environment, which is what we exactly want to observe, whether the different postoperative environment has an impact on the rehabilitation of children. After much discussion before the start of the study, we believed that this level could only be applied to cohort and observational study, but not a RCT.

Changes in the text: We added an explanation in Page 6, line 211-214.

Parents were given the same postoperative instructions, but one group went back home and the other stayed in the hospital overnight. We collected the effects of different postoperative environments on sleep diaries, melatonin secretion and OSA-18 scores.

Second, the title and elsewhere of this paper on the outcomes of this study seemed to be misleading, because OSA-18 and salivary melatonin level should be sleep-related measures, not recovery quality. The authors need to accurately describe the outcomes of interest of this study.

Reply 2: Thank you for your professional advice. For children with Obstructive Sleep Apnea Syndrome (OSAS), sleep problems are the biggest problem. Parents often come to hospitals because of snoring. OSA-18 is one of the gold standards to measure the recovery quality, it's easy to finish, particular to measure such low-aged-OSAS group recovery situation. Otherwise, the OSA-18 was originally developed for assessing

quality of life, not OSAS itself. Also, we consider several secondly outcomes to observe “home or hospital” different environments’ impacts. We consider sleep diaries, melatonin secretion to compare their differences. More and more, melatonin had been proofed not only related to sleep quality but also suppress inflammation and slow down stress responses, which is exactly a recovery quality indicator.

Changes in the text: We added the explanation in Page 8, Line 317-322.

For children with Obstructive Sleep Apnea Syndrome (OSAS), sleep problems are the biggest problem. Parents often come to hospitals because of snoring. OSA-18 is one of the gold standards to measure the recovery quality, it's easy to finish, particular to measure such low-aged-OSAS group recovery situation. Instead of OSAS itself, the OSA-18 was first created for evaluating quality of life.

Third, in the abstract, the authors did not describe the clinical significance of this research focus in the background, did not describe the method of randomization, measures of safety outcomes, and statistical methods for comparing the outcomes between the two groups in the methods, did not describe the baseline clinical characteristics of the two groups and quantify the findings on the outcomes of the two groups in the results, and did not have comments on the clinical implications of the findings.

Reply 3: Thank you for your constructive suggestions. 1. The background in abstract, we added a clinical significance of our research. 2. This was a cohort, non-randomized and exploratory observational study. Before the surgery, no one knew which group this child would be taken in, all children accept the same treatment. But after the surgery, we allocated them into two groups, then they went home or stayed in the ward, which was a public event, and all people knew that. So, this was a prospective cohort study. 3. We use many outcomes to guarantee children’s perioperative safe, please see anaesthesia and surgery part, we also record pain scales, and other adverse events (such as respiratory depression, sinus bradycardia, sinus tachycardia, hypertension, hypotension, nausea, and vomiting) between the two groups. Moreover, we guarantee children received same treatment before discharged to ward or back home after surgery. We use describe the baseline clinical characteristics of the two groups in table 1. We added description about quantify the findings on the outcomes of the two groups in the results, and added some content in conclusion part.

Changes in the text:

(1) We have modified our text as advised in Background (see Page 2, line 49-54);

Obstructive Sleep Apnea Syndrome (OSAS) Patient’s recovery in the hospital or at home after surgery may differ in terms of recovery quality and circadian rhythm status because of sleep disruption; however, this remains unknown. Pediatric

patients usually unable to explain their feelings effectively, and objective indicators to measure recovery situation in different environments are promising.

- (2) Added statistical methods in Methods part (see Page 2, line 58);

This was a cohort, non-randomized and exploratory observational study

- (3) Add guarantee children received same treatment peri-operation (see Page 5 line 194-195);

All patients received same treatment before discharged to ward or back home after surgery.

- (4) Added baseline clinical characteristics of the two groups (see Page 3 line 63-65);

There were no differences in the patient characteristics and perioperative variables between the Hospital and Home groups at baseline. They received the treatment and anesthesia in the same way.

- (5) Added description about quantify the findings on the outcomes (see Page 3 line 65);

They received the treatment and anesthesia in the same way.

- (6) Added some content in conclusion part (see Page 3 line 77).

...based on OSA-18 evaluation scale...

Fourth, in the introduction of the main text, the authors did not review the importance of the site of the postoperative rehabilitation, what has been known on the effect of site on the sleep of the patients, and importantly, what the potential clinical implications of this research focus are.

Reply 4: Thank you for your suggestion. As we have replied above, we have known that sleep disturb was the main symptom of OSAS children. So, we focused on sleep relative indicators, like OSA-18, melatonin, sleep diaries. The potential clinical implications are to detect whether different environment situation affect this kind of group's sleep situation and postoperative rehabilitation or not. (See Page 2, line 49-54)

Obstructive Sleep Apnea Syndrome (OSAS) Patients...because of sleep disruption... Pediatric patients usually unable to explain their feelings effectively, and objective indicators to measure recovery situation in different environments are promising.

Fifth, the methodology needs to be written according to CONSORT reporting guideline.

The authors need to describe the sample size estimation, randomization of the two treatments, whether and how blinding method was used, and details of assessments of secondary outcomes including safety outcomes. In statistics, please describe the data analytic subsets, such as ITT or PP, as well as the handling of missing data. It is also necessary to describe the test of baseline comparability. Please ensure $P < 0.05$ is two-sided.

Reply 5: Thank you for your reminder. This was a cohort, non-randomized and exploratory observational study. Since it was an exploratory clinical study, we did not perform sample size estimates. We recorded all the observation data and compared them. Data were expressed as the means (SD) for continuous variables conforming to a normal distribution, or as the medians and interquartile ranges (IQRs) for variables with a skewed distribution. The t-test or Mann-Whitney test was applied to analyse the control between the two groups using Stata 16.0 software (Statacorp, College Station TX, USA). $P < 0.05$ was considered statistically significant.

Changes in the text: We added an explain in the analysis part (Please see Page7 ling260-261).

This was a cohort, non-randomized and exploratory observational study. Since it was an exploratory clinical study, we did not perform sample size estimates...A box-plot was used to describe the changes of melatonin at different time points...

Reviewer B

The paper titled “Comparison of the postoperative in-hospital versus at-home recovery quality and circadian rhythm status in preschool kids after adenotonsillectomy: a cohort and observational study” is interesting. The postoperative recovery quality of preschool kids in the hospital is as good as at home. However, the clinical importance of the significant decrease in morning saliva melatonin levels with at-home postoperative recovery remains unknown and warrants further study. However, there are several minor issues that if addressed would significantly improve the manuscript.

The background did not indicate the clinical needs for this research focus, and needs further revisions.

Reply 1: Thank you for your professional advice. In the background in abstract, we added a clinical significance of our research.

Changes in the text: We have modified our text as advised in Background (see Page 2, line 49-54)

Obstructive Sleep Apnea Syndrome (OSAS) Patients...because of sleep disruption...

Pediatric patients usually unable to explain their feelings effectively, and objective indicators to measure recovery situation in different environments are promising.

What are the effects of adenotonsillectomy on the sleep structure of children? It is recommended to add relevant content.

Reply 2: Thank you for your suggestion. Obstructive sleep apnea is the main symptom of children with tonsil or adenoid hypertrophy. Sleep apnea affects the sleep structure of children and reduce melatonin secretion, which seriously hindering the growth and intellectual development of child.

Changes in the text: we added relevant content in Page 4, line 101-104.

Obstructive sleep apnea is the main symptom of children with tonsil or adenoid hypertrophy. Sleep apnea affects the sleep structure of children and abnormal melatonin secretion, which seriously affect the growth and intellectual development of child.

What are the risk factors for children undergoing adenotonsillectomy? What are the effects of circadian rhythm on postoperative complications? It is recommended to add relevant content.

Reply 3: Thank you for your suggestion. Sleep apnea affects the sleep structure of children and reduce melatonin secretion, which seriously affect the growth and intellectual development of child. We mentioned in discussion part (Page 4, line 101-104) to explain postoperative circadian rhythm. We also added a new quotation to discuss the relationship. (Page 9, line 348-350)

PLEASE SEE Page 9, line 348-350: *Older patients frequently experience postoperative circadian rhythm disorder; which may be a factor in the emergence of postoperative delirium (POD).*

The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “Characteristics of circadian rhythm-related genes and establishment of a prognostic scoring system for lung adenocarcinoma with experimental verification: a bioinformatics analysis, J Thorac Dis, PMID: 36389336”. It is recommended to quote the article.

Reply 4: Thank you for your constructive suggestions. It is true that circadian genes influence cancer treatment. We added this important article in Page4, line 112-113.

Circadian rhythm-related genes help to guide personalized cancer immunotherapy strategies

The number of patient samples in this study is too small, and a large sample study should be added for verification.

Reply 6: Thank you for your constructive suggestions. The sample of patients in our study is indeed flawed, because the project study was conducted during the COVID-19 pandemic, and the patient reception restrictions and patient care in our hospital affected the overall number of patients. It has been explained in lines 108-113 of the manuscript. We will expand the patient sample in future studies to ensure more accurate conclusions.

Whether the design of questionnaire content is authoritative? Is there a similar questionnaire? What is the author's next research plan? It is recommended to add relevant content.

Reply 7: Thank you for your suggestion. This questionnaire is authoritative and has been used to assess the symptoms of OSAS patients for many years. There are three main questionnaires Pediatric Sleep Questionnaire (PSQ), Obstructive Sleep Apnea Questionnaire (OSA-18), and pulse oximetry (PO) to evaluate OSAS severity. OSA-18 is the Optimized version and easy to operate.

Changes in the text: We added the OSA-18 content in Page 6 line 221-224.

It contains 18 questions scored on a Likert-type scale to collect data on 5 subscales: sleep disturbances, physical symptoms, emotional distress, daytime functions, and caregiver concerns. A score of ≥ 60 indicates the presence of OSAS in children.