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# The effects of nasal decongestion on obstructive sleep apnoea

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ABSTRACT

*Background:* Many studies have indicated associations between impaired nasal breathing and sleep disorders. However, the precise nature of the relationship between nasal patency and sleep remains unclear.

*Purpose:* We analysed the effects of nasal patency on sleep architecture and breath in nasal obstruction-predominant obstructive sleep apnoea (NO-OSA) patients by applying nasal decongestant.

*Material and methods:* A randomized, placebo-controlled double-blind crossover study was performed in OSA patients with chronic nasal obstruction and without obvious pharyngeal narrowing. All OSA patients (confirmed by polysomnography) were recruited and completed 2 overnight studies (randomly applying oxymetazoline or placebo). Data collected after oxymetazoline or placebo treatments were compared. The ClinicalTrials.gov identifier is NCT03506178.

*Results:* Compared with placebo, oxymetazoline resulted in significant increase in rapid eye movement sleep ($p = 0.027$) and reduction of stage 1 sleep ($p = 0.004$), as well as arousal index ($p = 0.002$). Moreover, great improvements in apnoea/hypopnea index (AHI) were observed ($p < 0.001$); AHI in the supine position was significantly reduced ($p = 0.001$). Oxygen saturation during sleep was increased significantly [mean oxygen saturation ($p = 0.005$) and lowest oxygen saturation ($p = 0.024$)]. Oxygen desaturation index was significantly reduced ($p < 0.001$).

*Conclusions:* Improving nasal patency by decongestant could improve sleep quality, AHI, and oxygen saturation level during sleep.

## 1. Introduction

The pathophysiology of obstructive sleep apnoea (OSA) is complex and remains unclear. Current research has shown that OSA is a heterogeneous disorder [1]. Multiple risk factors contribute to the disorder in different proportions through varied pathogenesis among patients. Among the contributing factors, many studies have supported associations between impaired nasal breathing and sleep disorders [2,3]. Furthermore, in specific OSA patient populations, nasal surgery plays a key adjunctive role in management of the disorder [4].

However, the precise nature of the relationship between nasal patency and sleep has largely been unclear. The importance of nasal airflow in the pathogenesis of airway collapse in OSA patients remains controversial. Inconsistent improvement of the apnoea/hypopnea index (AHI) in OSA patients has been reported after nasal surgery. Some researchers reported that nasal surgery could significantly improve AHI [5,6]. However, other studies reported that nasal surgery could effectively improve subjective sleep quality, sleep architecture, snoring, and daytime sleepiness, but not AHI [7,8]. An explanation of the differences is complicated: it may be due to differences in the severity of nasal mucosal lesions associated with various surgical approaches; however, the results of these studies were measured among patients with different OSA phenotypes. The selection of OSA patients suitable for nasal surgery may be a key to obtaining satisfactory outcomes. Multilevel obstruction is common in OSA patients. It seems reasonable to assume that there will be greater benefit of surgery among patients for whom nasal obstruction is a major component in the pathophysiology of OSA. Notably, OSA patients with chronic nasal congestion and without obvious pharyngeal anatomy narrowing (with lower Friedman tongue position; without tonsillar hypertrophy) are considered to be nasal obstruction-predominant OSA (NO-OSA). The study of polysomnographic characteristics in NO-OSA patients before and after nasal

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decongestant usage will facilitate personalized treatment of OSA patients for whom nasal obstruction is the main factor.

In this study, we analysed the effects of nasal patency on sleep quality and breath in OSA patients by applying decongestant nasal spray. To reduce the interference of confounding factors and more clearly observe interactions between sleep disturbance and nasal obstruction in OSA patients, we performed a randomized, placebo-controlled double-blind crossover study about the effects of topically applied nasal decongestant on sleep architecture, respiratory events, body position, and subjective scores in NO-OSA patients.

## 2. Material and methods

### 2.1. Patients and physical examination

All patients participating in this study were diagnosed with OSA at our OSA Clinical Diagnosis and Therapy Centre and had not previously undergone treatment for OSA. In total, 15 OSA patients [14 males; 39 ± 9 years (25–54); body mass index 26.3 ± 3.4 $kg \cdot m^{-2}$ (22.8–31.4)] were included in this study. The conditions for enrolment were: (1) Typical symptoms (e.g. snoring, witnessed apnoea, and daytime sleepiness) and an AHI ≥ 5/h. (2) Subjective chronic impaired nasal breathing and objective nasal congestion, confirmed by nasal endoscopy examination (all patients had inferior turbinate hypertrophy). (3) Absence of obvious pharyngeal narrowing [without tonsillar hypertrophy and Friedman tongue position (FTP) grades I and II]. Exclusion criteria were previous upper airway surgery, nasal spray treatment within 3 months, and/or sleep disorders other than OSA.

Medical histories of all patients were reviewed in detail and subjective perception of nasal congestion was measured by a visual analogue scale [VAS; 0 (no obvious nasal obstruction) to 10 (wholly obstructed nose)]. The upper airway was carefully assessed by endoscopic examination. Patients underwent physical examinations conducted by the same otorhinolaryngologist, including nasal endoscopy, active anterior rhinomanometry, and fibrolaryngoscopy.

The Ethics Committee of Beijing Tongren Hospital, Beijing, China, approved the protocol. A detailed explanation of the study was provided and written informed consent was obtained from all participating patients.

### 2.2. Design and protocol

A randomized placebo-controlled double-blind crossover study was designed. Each patient underwent 2 overnight polysomnographic studies, with placebo and treatment performed in random order on 2 different nights separated by a 48-hour washout period.

To avoid confounding by the “first-night effect” during sleep lab polysomnography (PSG), we randomly applied oxymetazoline on 1 night and placebo on another. During each night, patients applied either oxymetazoline (0.05% solution, 0.4 mL) or placebo (normal saline, 0.9% solution, 0.4 mL) in each nostril, in accordance with the randomization. To maintain the maximal pharmacologic efficacy, both nasal spray interventions were administered on sleep onset and at 3 h after sleep onset, respectively. Each patient was asked to perform a retrospective evaluation of the quality of sleep after each night to determine the degree of subjective sleep improvement. Subjective perception of sleep quality was assessed by VAS, from 0 (satisfied) to 10 (unsatisfied). Randomization was performed by using a computer-generated table of random numbers. Both subjects and technicians scoring the sleep study were blinded to the intervention. The ClinicalTrials.gov identifier is NCT03506178.

### 2.3. Polysomnography

Standard overnight PSG (Sandman Elite, Nellcor Puritan Bennett Ltd., Kanata, ON, Canada) was performed on all participants. The PSG system included 4-channel electroencephalography (EEG), 2-channel electrooculography (EOG), and 2-channel airflow measured with an oro-nasal thermistor and nasal pressure cannula, snoring sensor, respiratory (thoracic and abdominal) movements, body position sensor, submental and anterior tibial electromyography, electrocardiography, and pulse oximetry for oxygen saturation ($SpO_2$). Infrared video monitoring was also routinely performed.

The data were analysed in 30-second epochs and all PSG recordings were scored manually, in accordance with the American Academy of Sleep Medicine (AASM) guidelines. Apnoea was defined as a reduction in airflow of 90% or more, lasting for at least 10 s. Hypopnea was defined as a reduction in airflow of 30% or more, lasting for at least 10 s, with the presence of oxygen desaturation of at least 3%, or arousal. The oxygen desaturation index (ODI) was calculated as the total number of reductions of 3% or greater in oxygen saturation ($SpO_2$) per hour of sleep. The percentage of total sleep time with oxygen saturation below 90% was also calculated.

### 2.4. Data analysis and statistics

Statistical evaluations were performed by using SPSS version 21.0 (SPSS, Chicago, IL, USA). Data collected after oxymetazoline or placebo treatments were compared. Results were presented as means ± SD or median (P25, P75). Data collected after different treatments were compared by paired *t*-tests or Wilcoxon rank tests. A $P$ value of $< 0.05$ was considered statistically significant.

## 3. Results

### 3.1. Sleep architecture and quality

Table 1 shows changes in sleep architecture and subjective sleep quality with nasal decongestant treatment. There were significant improvements in sleep quality, including increased rapid eye movement (REM) sleep [20.3% (12.2%, 28%) vs. 25.1% (21.5%, 33.6%), $p = 0.027$], reduced stage 1 sleep [12% (7.8%, 21.8%) vs. 8 (3.4%, 13.0%), $p = 0.004$] and arousal index [19.3 (10.8, 31.1) vs. 10.4 (7, 16.0), $p = 0.002$]. Additionally, VAS on the morning after each sleep study were improved [6 (5, 7) vs. 5 (3, 6), $p = 0.011$].

### 3.2. Sleep disorder breathing events

As shown in Table 2, after the application of nasal decongestants, the mean AHI (31.65 ± 16.98 vs. 22.64 ± 16.05, $p < 0.001$), REM sleep period AHI (36.59 ± 25.71 vs. 28.00 ± 22.08, $p = 0.035$) and NREM sleep period AHI (28.43 ± 17.52 vs. 20.75 ± 17.65, $p = 0.01$) were significantly reduced. The mean apnoea index (AI) also decreased (25.43 ± 18.22 vs. 18.25 ± 17.35, $p = 0.001$) (Fig. 1). However, mean hypopnea index (HI) did not show statistically significant

**Table 1**
Comparison of Sleep stage architecture and quality between groups.

| Variables | Placebo ($n = 15$) | Oxymetazoline (n = 15) | $p$ |
|---|---|---|---|
| Sleep architecture | | | |
| Stage 1 (%TST) | 12 (7.8, 21.8) | 8 (3.4, 13.0) | 0.004* |
| Stage 2 (%TST) | 59.07 (50.20, 67.40) | 60.9 (53.50, 64.20) | 0.426 |
| Stage 3 (%TST) | 0.3 (0, 10) | 3 (0, 6.7) | 0.575 |
| REM (%TST) | 20.3 (12.2, 28) | 25.1 (21.5, 33.6) | 0.027* |
| Sleep quality | | | |
| Subjective sleep quality | 6 (5, 7) | 5 (3, 6) | 0.011* |
| Arousal index | 19.3 (10.8, 31.1) | 10.4 (7, 16.0) | 0.002* |

Data was presented as median (P25, P75); comparisons were made using nonparametric test.
* $P < 0.05$.

**Table 2**
Comparison of the sleep disorder breathing events between groups.

| Variables | Placebo(n = 15) | Oxymetazoline (n = 15) | *p* |
|---|---|---|---|
| Respiratory events (events/h) | | | |
| AHI during TST | 31.65 ± 16.98 | 22.64 ± 16.05 | 0.000* |
| AHI during NREM sleep | 28.43 ± 17.52 | 20.75 ± 17.65 | 0.001* |
| AHI during REM sleep | 36.59 ± 25.71 | 28.00 ± 22.08 | 0.035* |
| Apnea Index | 25.43 ± 18.22 | 18.25 ± 17.35 | 0.001* |
| Hypopnea Index | 6.25 ± 5.02 | 4.4 ± 3.64 | 0.183 |
| Duration of respiratory events(s) | | | |
| Meantime of apnea | 25.51 ± 10.51 | 25.46 ± 11.25 | 0.975 |
| Longest time of apnea | 53.68 ± 23.00 | 53.75 ± 30.07 | 0.987 |
| Meantime of hypopnea | 27.48 ± 6.54 | 31.16 ± 9.08 | 0.026* |
| Longest time of hypopnea | 43.04 ± 11.41 | 54.02 ± 12.96 | 0.015* |

Data were presented as means ± SD. Comparisons were made using paired *t*-test.
* P < 0.05.

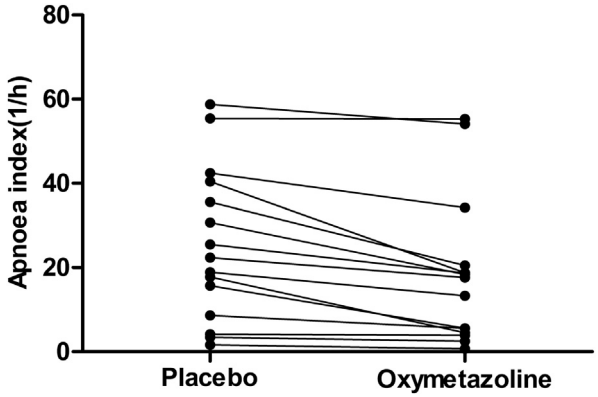


**Fig. 1.** The apnoea index for each subject on both placebo and oxymetazoline nights is shown. All subjects exhibited a reduced apnoea index after oxymetazoline administration.

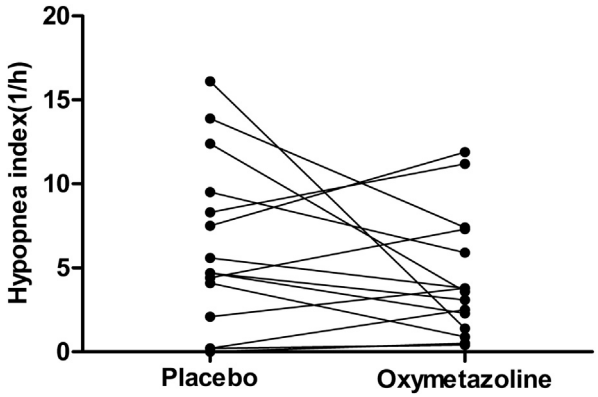


**Fig. 2.** The hypopnea index for each subject on both placebo and oxymetazoline nights is shown. Seven of 15 subjects exhibited an increased hypopnea index after oxymetazoline administration.

improvement after intervention. Conversely, in some patients (7/15), HI increased after treatment (Fig. 2). In addition, after nasal decongestant administration, significant prolongations of sleep hypopnea duration were observed. Both the average duration of sleep hypopnea (27.48 ± 6.54 s vs. 31.16 ± 9.08 s, $p = 0.026$) and the longest duration of sleep hypopnea (43.04 ± 11.41 s vs. 54.02 ± 12.96 s, $p = 0.015$) were increased.

**Table 3**
Comparison of the oxygen saturation changes between groups.

| Oxygen saturation | Placebo (*n* = 15) | Oxymetazoline (n = 15) | *p* |
|---|---|---|---|
| ODI | 26.92 ± 16.73 | 19.95 ± 18.24 | 0.000* |
| $MSaO_2$ (%) | 95.60 ± 1.23 | 96.00 ± 1.12 | 0.005* |
| $LSaO_2$ (%) | 82.93 ± 7.97 | 84.93 ± 8.52 | 0.024* |
| Time below 90% $SpO_2$ (%) | 1 (0.17, 3.76) | 0.26 (0.00, 2.15) | 0.002* |

Data was presented as means ± SD or median (P25, P75); comparisons were made using paired *t*-test or nonparametric test. Time below 90% SpO2: the percentage of total sleep time in the oxygen saturation below 90%.ODI: oxygen desaturation index, MSaO2: mean oxygen saturation during sleep, LSaO2: lowest oxygen saturation during sleep.
* $P < 0.05$.

### 3.3. Oxygen desaturation during sleep

As shown in Table 3, after the application of nasal decongestant to improve nasal patency, oxygen desaturation index decreased significantly (26.92 ± 16.73 vs. 19.95 ± 18.24, $p < 0.001$). The mean oxygen saturation (95.60 ± 1.23% vs. 96.00 ± 1.12%, $p = 0.005$) and lowest oxygen saturation during sleep period (82.93 ± 7.97% vs. 84.93 ± 8.52%, $p = 0.024$) significantly increased. Moreover, reduction in the percentage of total sleep time with oxygen saturation below 90% was observed in the treatment group [1% (0.17%, 3.76%) vs. 0.26% (0.00%, 2.15%), $p = 0.002$)]. All above results showed that with the improvement of nasal patency, blood oxygen saturation during sleep improved significantly.

### 3.4. Distribution and AHI of different sleep positions

As shown in Table 4, the AHI in supine position on placebo nights was 56.15 (36.40, 66.00), versus 34.25 (18.85, 49.14) on the treatment nights ($p = 0.001$). However, no significant improvement of AHI was observed in non-supine positions after the application of nasal decongestant. Additionally, regarding sleep position distribution, there were no significant effects on the percentage of total sleep time (TST) in the supine position (Supine position, % of TST) when nasal oxymetazoline was used.

## 4. Discussion

The relationship between nasal airway patency and OSA has consistently been controversial and exciting. As early as the 1980s, several studies revealed that experimentally induced nasal obstruction in healthy subjects caused a significant increase in the number of arousals and apnoeas during sleep [9,10]. The mechanism of nasal patency effects on sleep physiology is complex and remains unclear. Reduced nasal patency can generate greater negative intraluminal pressure

**Table 4**
Comparison of position related variables between groups.

| Variables | Placebo (*n* = 15) | Oxymetazoline (n = 15) | *p* |
|---|---|---|---|
| Supine position AHI | 56.15 (36.40, 66.00) | 34.25 (18.85, 49.14) | 0.001* |
| Non-supine position AHI | 15.00 (4.41, 46.10) | 9.59 (2.79, 9.59) | 0.093 |
| Supine position,% of TST | 42.34(27.84, 63.24) | 35.41 (24.50, 61.38) | 0.65 |

Data was presented as median (P25, P75); comparisons were made using nonparametric test. Supine position AHI: AHI in spine position; Non-supine position AHI: AHI in non-spine positions; Supine position, %, of TST: the percentage of total sleep time (TST) in the supine position.
* $P < 0.05$.

within the upper airway and cause greater downstream suction forces that lead to inspiratory collapse at the pharyngeal level [11]. Moreover, with higher nasal resistance, oral breathing occurs more frequently during sleep. Oral breathing associated with reduction of the retropalatal and retroglossal areas renders the upper airway more collapsible and increases OSA severity [12]. Furthermore, nasal mucosa receptors, which are sensitive to airflow, may have a reflex effect on ventilation and muscle tone in the upper airways, thus affecting OSA severity. White et al. demonstrated that, despite good nasal patency, nasal anaesthesia induced disordered breathing during sleep and produced an effect similar to that of complete obstruction [13]. Several studies showed that the normal function of the nasal mucosa influenced the patency of the upper airway and ventilation, which may contribute to the frequency and severity of apnoea during sleep [14,15]. Therefore, different nasal surgeries were applied by several clinical centres, with the goal of improving nasal patency in OSA patients. However, different nasal surgical approaches led to varying degrees of nasal mucosa damage, which may have at least partly affected the outcomes of nasal surgeries performed to treat OSA. In this study, to diminish the confounding factor of differences in degrees of nasal mucosa damage, nasal decongestion was performed to investigate the effects of improving nasal patency on sleep, while preserving nasal mucosa.

Because impaired nasal breathing contributes to OSA in different proportions through a variety of aetiologies among individuals, selecting OSA patients who would benefit most from nasal airway improvement therapy is key to achieving satisfactory outcomes from nasal treatment. Many studies have been performed on the anatomical and physiological factors associated with outcomes of nasal treatments. Ikoutsourelakis et al. found that baseline nasal breathing epochs in PSG can predict surgery outcome [16]. Park et al. reported that nasal surgery could reduce OSA severity in 56% of OSA patients with complaints of nasal obstruction, but without tonsillar hypertrophy [5]. Li et al. reported that OSA patients who had the lower Friedman tongue position achieved a better success rate after nasal surgery [17]. Similarly, our previous study found that a satisfactory cure rate after nasal surgery treatment could be achieved by screening for patients who exhibited severely obstructed nasal cavities and ensuring favourable oropharynx anatomy [18–20]. Based on the results of these previous studies, this study used absence of tonsillar hypertrophy, lower Friedman tongue position (FTP), and upper airway endoscopic examination to select a subset of patients whose significant nasal obstruction appeared to be a more dominant aspect of OSA pathophysiology. We studied the polysomnographic characteristics and individual scores of this group of patients before and after application of nasal topical decongestant.

The data indicated that both subjective and objective sleep quality, as well as oxygen saturation level, improved after nasal decongestion. AHI in both REM and non-REM sleep periods decreased. However, after improving nasal breathing of the patients by decongestant administration, the AI significantly decreased, while the HI did not significantly improve. A possible explanation could be that, after the improvement of nasal patency, some apnoea events may have decreased in severity, thus becoming hypopnea events. As a result, the HI did not significantly decrease. However, significant prolongations of sleep hypopnea duration were observed. Both the average and longest durations of hypopnea events were significantly prolonged. These results, particularly the prolongations of sleep hypopnea duration, indicated that application of nasal decongestant could clearly improve apnoea events, but not hypopnea events. OSA patients in whom apnoea was the dominant respiratory event during sleep could be more sensitive to nasal patency improvement therapy. Furthermore, our data also showed that AHI in the supine position was significantly lowered after improving nasal breathing by administration of nasal decongestant. Thus, supine AHI-predominant OSA patients, especially positional OSA patients (PPs, supine AHI/non-supine AHI $\geq 2$) may attain better outcomes from nasal patency improvement.

Overall, the observational results from the application of topical nasal decongestant in OSA patients could provide clues regarding the role of nasal patency in the pathophysiology of OSA, as well as further guidance in terms of patient selection for nasal therapy. This investigation suggests that patients with PSG characteristics of AI and supine AHI predominance may experience greater benefits from nasal treatment. Variables related to anatomy and sleep parameters could be combined to facilitate screening for OSA patients who should undergo nasal breathing improvement therapy.

Our investigation was limited in that we did not consider functional assessment of the upper airway, especially the collapsibility of the pharyngeal airway. Further studies, including drug-induced sleep endoscopy are needed to investigate upper airway collapsibility in OSA patients. By including functional assessments, further information could be gathered for an improved assessment of patients, supporting provision of more appropriate therapy.

## 5. Conclusion

Improving nasal patency by topical decongestant administration could improve sleep quality, AHI, and oxygen saturation level during sleep. There were significant improvements in apnoea events, but no significant change in HI. Notably, AHI in the supine position was significantly reduced after nasal decongestion.

## Conflict of interest

No potential conflict of interest was reported by the authors.

## Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

## Informed consent

Informed consent was obtained from all individual participants included in the study.

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