Impact of Exclusive Mouth Route and Lateral Position on the Efficacy of Oronasal CPAP to Treat OSA in Patients With OSA Adapted to Oronasal Mask

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BACKGROUND: Oronasal masks are used widely for treating OSA with CPAP. However, oronasal CPAP is associated with lower effectiveness and lower adherence than nasal CPAP.

RESEARCH QUESTION: What is the impact of oral route and lateral position in patients well adapted to oronasal CPAP? Can these patients be switched to nasal CPAP?

STUDY DESIGN AND METHODS: Patients with OSA receiving oronasal CPAP underwent two CPAP polysomnography titrations in random order using an oronasal mask with two independent sealed compartments connected to two separate pneumotachographs. One study was performed with the nasal and oral compartments opened and the other study was performed with only the oral compartment opened. CPAP titration was carried out in the supine and lateral positions. Finally, the patients were offered a nasal mask. A third polysomnography test was performed using nasal CPAP.

RESULTS: Twenty patients with OSA (baseline apnea-hypopnea index [AHI], 52 ± 21 events/h) adapted to oronasal CPAP were studied. Most patients (75%) were oronasal breathers with optimal CPAP. Oral CPAP was less effective to treat OSA than oronasal CPAP, evidenced by a higher residual AHI (median, 2 [interquartile range (IQR), 1-6.0] vs 12.5 [IQR, 1.8-28.3); P = .003), despite a significantly higher CPAP level (median, 10 cm H_2O [IQR, 9-10 cm H_2O] vs 11 cm H_2O [IQR, 10-12 cm H_2O]; P = .003). The residual AHI was significantly lower in the lateral position for both oronasal and oral CPAP. Finally, patients (75%) agreed to change and preferred to continue using a nasal mask, which resulted in lower CPAP and better OSA control.

INTERPRETATION: Our results indicate that the effectiveness of oronasal CPAP to abolish OSA is decreased significantly when patients are required to breathe exclusively through the mouth. Oronasal CPAP efficacy is significantly better in the lateral position. The transition to nasal mask results in higher CPAP effectiveness to treat OSA.

CLINICAL TRIAL REGISTRY: ClinicalTrials.gov; No.: NCT05272761; URL: www.clinicaltrials.gov

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KEY WORDS: breathing route; CPAP; oronasal mask; OSA

ABBREVIATIONS: AHI = apnea-hypopnea index; IQR = interquartile range; NOSE = Nasal Obstruction Symptom Assessment

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Take-home Points

Study Question: What is the impact of an exclusive oral route and of lateral position in patients with OSA well adapted to oronasal CPAP? Can these patients be transitioned to nasal CPAP?

Results: Oral CPAP resulted in lower CPAP effectiveness to treat OSA than oronasal CPAP, as evidenced by a higher residual apnea-hypopnea index and significantly higher CPAP level. In addition, CPAP effectiveness to treat OSA was significantly better in the lateral than in the supine position.

Interpretation: Oronasal CPAP is less effective at treating OSA when patients are forced to breathe through the mouth. Most patients using oronasal CPAP can transition to a nasal mask, resulting in good acceptance and better effectiveness in treating OSA.

OSA is characterized by recurrent episodes of partial or total airway obstructions during sleep, leading to hypopneas and apneas, respectively. OSA results in fragmented sleep and recurrent oxygen desaturations.[1,2] OSA is common in the general population, affecting almost 1 billion people worldwide,[3] and can lead to multiple consequences, such as worsening quality of life, increased risk of cardiovascular disease, and mortality.[4-6] Nasal CPAP is the gold standard treatment for moderate to severe OSA.[7] Nasal CPAP splints the airway open during sleep by projecting the tongue anteriorly and repositioning the soft structures of the airway.[7] Because mouth breathing is common among untreated patients with OSA,[8,9] the use of oronasal CPAP has increased steadily.[10] Data from the United States and France show that oronasal masks are used by 25% to 28% of patients with OSA receiving CPAP treatment in the United States and France.[10,11] However, as compared with nasal CPAP, oronasal CPAP often requires a higher pressure level and generates higher unintentional leak and residual apnea-hypopnea index (AHI), leading to lower adherence.[10,12,13] Consistent evidence indicates that oral positive pressure neutralizes the splinting effect of nasal positive pressure and may decrease or even abolish the beneficial effects of CPAP to treat OSA.[14-17] Therefore, exclusive mouth breathing may jeopardize the efficacy of CPAP to treat OSA.[10,12]

The present study was designed to investigate the impact of breathing route on the efficacy of oronasal CPAP to treat OSA. Our primary hypothesis was that exclusive oral breathing compromises CPAP efficacy to treat OSA, as evaluated by the residual AHI. To this end, we compared the efficacy of oronasal CPAP to treat OSA during oronasal and exclusive oral breathing. Because the upper airway is less collapsible in the lateral than in the supine position,[18,19] we tested the secondary hypothesis that oronasal CPAP is more effective in the lateral position. To test these hypotheses, we studied patients well adapted to oronasal CPAP using an oronasal mask with two independent sealed compartments in the supine and lateral positions. Finally, based on the available evidence that nasal CPAP is the best treatment option for OSA, we offered a nasal mask to all patients.

Study Design and Methods

We included adult patients of both sexes with moderate to severe OSA who were well adapted to CPAP using an oronasal mask (use $>$ 3 months and $>$ 4 h/d). At study entry, patients provided a detailed clinical history and underwent physical examination. In addition, the Nasal Obstruction Symptom Assessment (NOSE) questionnaire was applied. The NOSE questionnaire quantifies the subjective perception of nasal patency.[20,21] A NOSE score of $>$ 50 is consistent with severe nose symptoms.[22] The local ethics committee approved the protocol (Identifier: CAAE 21338819.5.0000.0068), and informed consent was obtained from each participant. The study was registered at Clinicaltrials.gov (NCT05272761).

Sleep Studies

Patients were monitored with standard polysomnography (Embla N7000; Natus) and used CPAP (ResMed/VPAP Tx) with a dual port oronasal mask that had two independent sealed compartments (nasal and oral; Hans Rudolph) connected to two separate pressure transducers and two pneumotachographs (3700A; Hans Rudolph). A three-way stopcock valve (Hans Rudolph) was placed between the pneumotachs and the CPAP using hoses and was hung to a pole to provide comfort to the patient. Airflow was measured with differential pressure transducers (Validyne) attached to the pneumotachs. The mask was sealed to the skin with silicone (Silagum; DMG). A data acquisition system (Power 1401; Cambridge Electronic Design) was used to

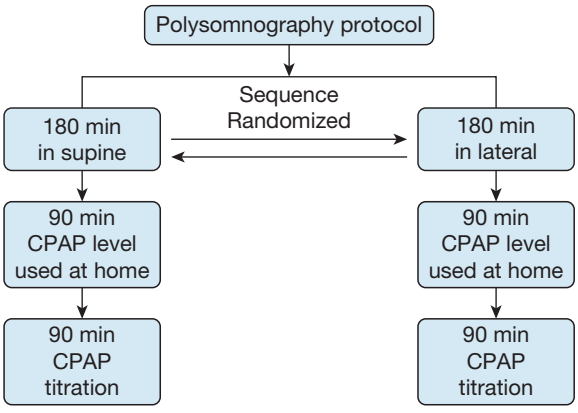

Figure 1 – *Flow diagram showing polysomnography protocol. Patients were positioned for 180 min in the supine position and 180 min in the lateral position in random order. CPAP was started at the same level used at home (90 min), followed by CPAP titration (90 min) during each 180-min period.*

capture and synchronize physiologic signals using Spike software (Cambridge Electronic Design). Zolpidem 10 mg was offered to all patients at the beginning of the sleep study. Patients were positioned during 180 min in the supine position and 180 min in the lateral position, in random order. The two periods of 180 min started at the CPAP level used at home (90 min) and was followed by CPAP titration (90 min) (Fig 1).

Determination of Breathing Pattern During Oronasal Route

Breathing route was analyzed at the titrated CPAP level during at least 30 min of stable breathing. Based on the presence of flow (> 10% of the total flow in the nasal or oral compartment), each breath was classified as nasal (flow in the nasal compartment only), oronasal (flow in the nasal and oral compartment), or oral (flow in the nasal compartment only), as described previously.[17] Finally, each patient was classified as a nasal, oronasal, or oral breather based on the breathing pattern of most breaths (> 70%) during the titrated CPAP.[17]

Study Design

All patients were studied during two different nights within a 1-month interval. The two CPAP titration studies using the protocol described were conducted: (1) with both compartments (nasal and oral) opened (oronasal route) or (2) with the nasal compartment closed and the oral opened (oral route). The objective of CPAP titration was to abolish respiratory events and flow limitation. The sequence of the two studies (oronasal and oral route) was randomized. A sealed envelope containing the assigned sequence of positions was opened on the night of the first sleep study. The patients were assigned to the complementary mask route and complementary sequence of positions in the second sleep study. During the interval between sleep studies, patients were asked to continue CPAP as usual. After the two sleep studies, all patients were invited to switch from an oronasal to a nasal mask (Wisp/Philips Respironics). Patients who agreed had the CPAP level titrated with an auto-CPAP (ResMed S9) for 1 week. CPAP then was set at the 95th percentile. These patients were followed up by telephone once weekly for the first month and at the end of the second and third months. Patients experiencing difficulties underwent in-person assessments as necessary. After 3 months of nasal CPAP at home, patients were invited to undergo a new polysomnography examination with nasal CPAP set at the same level used at home. Patients slept 180 min in the supine and 180 min in the lateral position, in a random order.

Statistical Analysis

Data were expressed as mean ± SD or median (interquartile range [IQR]), when appropriate. A paired Student *t* test or Wilcoxon signed-rank test was used to compare polysomnographic variables between both CPAP routes studied and body position assessed in each breathing route (oronasal, oral, and nasal). The statistical software package used was SPSS version 20 (IBM). Statistical significance was set at $P < .05$.

Results

Of approximately 500 patients with OSA receiving CPAP identified in the Heart Institute Sleep Clinic electronic records, 34 patients were using oronasal masks. Twelve patients were excluded for different reasons. Seven patients declined to participate in the

TABLE 1] Demographic Features, Comorbidities, and Diagnostic Polysomnography Data of the Patients Studied (N = 20)

Variable	Data	Range
Male sex	15 (75%)	NA
Age, y	66 (10)	39-83
BMI, kg/m^2	34.4 (7.3)	24.5-50.3
Neck circumference, cm	46 (10)	40-84
Abdominal circumference	118 (14)	100-148
Comorbidities		
Arterial hypertension	20 (100%)	NA
Coronary artery disease	3 (15%)	NA
Cardiac arrhythmia	4 (20%)	NA
Diabetes mellitus	10 (50%)	NA
Asthma	1 (5%)	NA
Diagnostic polysomnography findings		
AHI, events/h	52 (21)	18-90
Minimum Spo_2, %	75 (9)	48-89
CPAP used at home		
Duration of oronasal CPAP, y	6.5 (6.3)	0.33-20
CPAP at home, cm H_2O	10 (2)	7-15
AHI (CPAP report), events/h	6 (4)	0-16

Data are presented as No. (%) or mean (SD), unless otherwise indicated. AHI = apnea-hypopnea index; NA = not applicable; Spo_2 = peripheral oxygen saturation.

study, two patients abandoned treatment, one patient had predominant central apnea, one patient was receiving supplemental oxygen, and one patient was using bilevel positive airway pressure. Among the 22 patients who agreed to participate, two patients were excluded from the final analysis because of unstable sleep throughout the night, resulting in low sleep efficiency (n = 1) and technical problems with the pneumotachograph signal (n = 1). The final sample (n = 20) consisted of predominantly overweight obese males with multiple comorbidities (Table 1). All patients identified themselves as oral breathers. However, the median NOSE score was 15 (IQR, 0-31; range, 0-100), indicating a relatively low level of nasal obstruction symptoms. Only one patient had severe symptoms of nasal obstruction (NOSE score, 75). All but one patient received 10 mg of zolpidem at the beginning of the study. No patient received an additional dose. However, zolpidem does not affect the severity of OSA.[23]

Polysomnographic Data

Of the 20 patients studied, 12 and eight underwent the first polysomnography with oronasal and oral CPAP, respectively. An overall trend was noted for worse sleep quality in the oral route than in the oronasal route, reaching a statistical difference for a higher arousal index and higher percentage of stage 1 sleep (Table 2). When analyzing the entire polysomnography results, oral CPAP was less effective to control OSA than oronasal CPAP, as evidenced by a higher residual AHI and lower minimal peripheral oxygen saturation (Table 2). The titrated CPAP level and residual AHI were significantly higher with oral CPAP than oronasal CPAP. A post hoc analysis showed a power of 0.9426 for our primary end point (AHI at titrated CPAP) (Fig 2). Intolerance to further increase in CPAP level was caused by awakenings. At titrated CPAP, residual OSA (AHI > 15 events/h) was present in two patients (10%) and nine patients (45%) receiving oronasal and oral CPAP, respectively (P = .013).

Supine vs Lateral CPAP

During the first 180 min at the CPAP level used at home (median, 10 cm H_2O [IQR, 9-10 cm H_2O]), residual AHI was higher significantly in the supine than in the lateral position with both oronasal CPAP (median, 21.5 events/h [IQR, 8.3-66.8 events/h] vs 1.5 events/h [IQR, 1-9.8 events/h], respectively; P = .005) and oral CPAP (median, 49 events/h [IQR, 27.5-68.5 events/h] vs 7.5 events/h [IQR, 5.3-26.8 events/h], respectively; P =

TABLE 2] Polysomnography CPAP Titration With Oronasal and Oral Routes of the Patients Studied (N = 20)

Variable	Oronasal Route	Oral Route	*P* Value[a]
All night			
TST, min	266 (245.9-299)	229.5 (152.6-264.8)	.17
Awake, %	26.6 (22.8-40.6)	35.8 (28.5-56.7)	.108
Sleep efficiency, %	69.1 (57.2-75.3)	61.6 (41.7-69.1)	.067
Arousal index, %	17.9 (14.2-22.2)	25.6 (21.2-32.8)	.001
S1	11.3 (7.9-14.6)	16.5 (11.7-20.2)	.028
S2	67.8 (53.8-78.6)	61.6 (53.5-72.3)	.627
S3	8.9 (1.9-19.7)	4.2 (0-23.8)	.811
REM, %	7 (5-13.6)	4.9 (0-9.9)	.12
AHI, events/h[b]	12.7 (6.2-31.2)	34.7 (22.5-40.1)	.002
Spo_2, minimum %	86 (82-88)	81 (79-86)	.013
Titrated CPAP			
Time-titrated CPAP, min	97.5 (70.7-110.5)	93.4 (60.5-117.2)	.30
Titrated CPAP, cm H_2O	10 (9-10)	11 (10-12)	.003
AHI, with titrated CPAP[c]	2 (1- 6.0)	12.5 (1.8-28.3)	.003
Spo_2, minimum %	90 (89-91)	87 (83-90)	.005

Data are expressed as median (interquartile range), unless otherwise noted. AHI = apnea-hypopnea index; REM = rapid eye movement; S1 = sleep stage 1 of nonrapid eye movement; Spo_2 = peripheral oxygen saturation; S3 = sleep stage 3 of nonrapid eye movement; S2 = sleep stage 2 of nonrapid eye movement; TST = total sleep time.
[a]Wilcoxon signed-rank test.
[b]All night AHI includes both supine and lateral position.
[c]AHI on titrated CPAP includes both supine and lateral position. Data expressed as median (25-75).

.006). This analysis included 14 patients who underwent at least 90 min in the supine position and 90 min in the lateral position (Fig 3A).

Better control of obstructive events in the lateral position also was evidenced in the second 180-min period, when CPAP was titrated in the oronasal and oral routes. This analysis included 16 patients who underwent at least 90 min in the supine position and 90 min in the lateral position (Fig 3B).

Breathing Route With Oronasal CPAP

During oronasal CPAP, a total of 37,105 breaths during best CPAP were analyzed and were classified as oronasal (n = 27,770 [79.1%]), exclusively nasal (n = 7,186

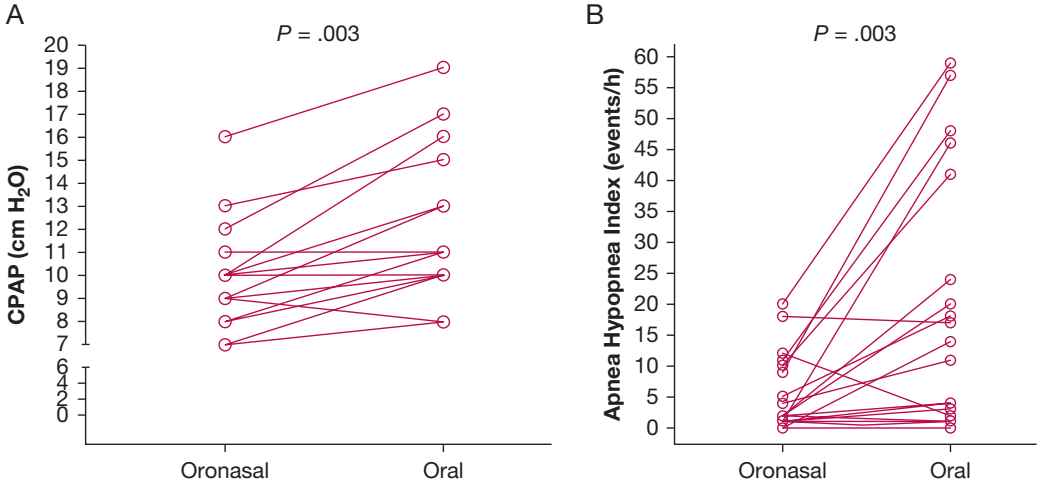

Figure 2 – *A, B, Graphs showing titrated CPAP (A) and residual AHI (B). Each pair of circles connected by a straight line represents one patient receiving oronasal CPAP and the same patient receiving oral CPAP. AHI = apnea-hypopnea index.*

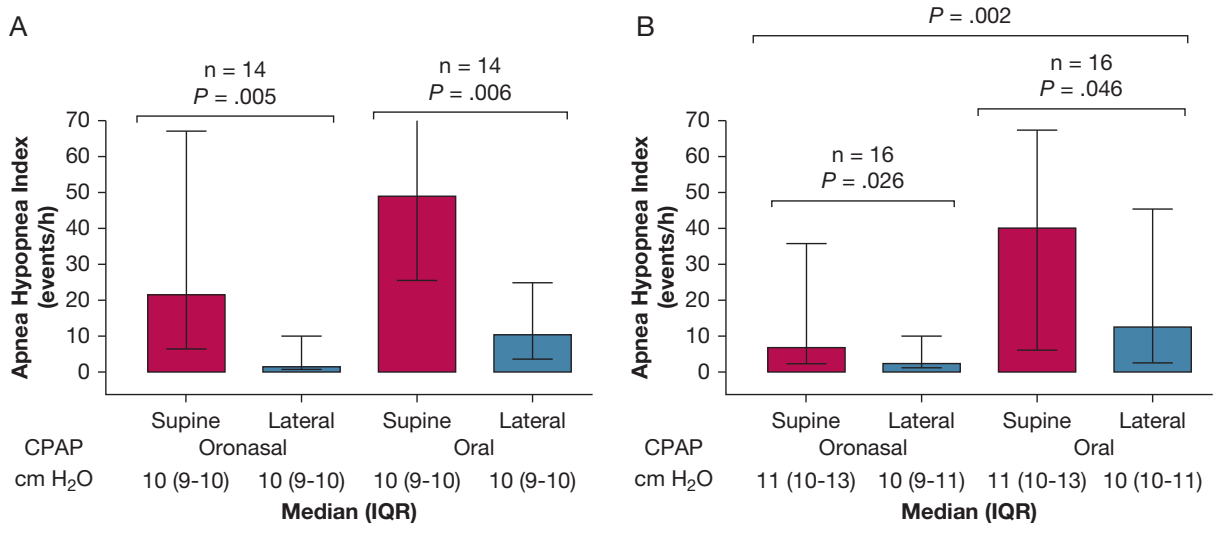

Figure 3 – *Graphs showing apnea-hypopnea index (AHI) comparison between oronasal and oral CPAP. A, Residual AHI during oronasal and oral CPAP in the supine and lateral positions with CPAP used at home (n = 14). Above the graphs are inserted the* P *values that are the result of: comparison between the oronasal route (supine and lateral;* P = *.005) and comparison between oral route (supine and lateral;* P = *.006). B, Residual AHI during oronasal and oral CPAP in the supine and lateral positions with titrated CPAP (n = 16). Above the graphs are inserted the* P *values that are the result of: comparison between oronasal CPAP (supine and lateral;* P = *.026) and comparison between oral CPAP (supine and lateral;* P = *.046). *Wilcoxon test. To compare oronasal and oral CPAP in all positions, the Friedman test* (P = *.002) was used. IQR = interquartile range.*

[20.5%]), and exclusively oral (n = 149 [0.4%]). Figure 4 describes the percentage of nasal, oronasal, and oral breaths of each patient.

Nasal CPAP Trial

Of the 20 patients studied, 15 agreed to exchange the oronasal mask for a nasal mask (Wisp-Philips). Nasal CPAP was titrated at home to 6.6 cm H_2O (IQR, 6.0-8.0 cm H_2O). The residual AHI taken from the CPAP device was 1.8 events/h (IQR, 1.2-3.9 events/h). Ten patients agreed to return for a third polysomnography

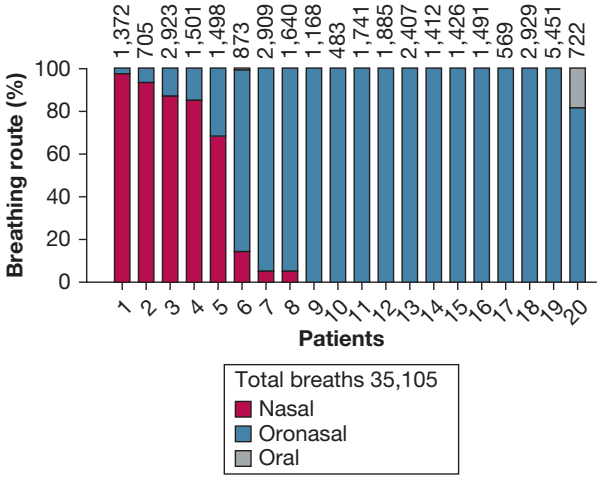

Figure 4 – *Bar graph showing patient breathing patterns (each bar represents a patient, identified from 1 through 20), expressed as a percentage of the total breaths analyzed during CPAP titration. The total number of breaths analyzed for each patient is shown at the top of each bar (total of 35,105 breaths analyzed).*

that was carried out with the same nasal mask. CPAP was fixed during the sleep study at the level used at home. The residual AHI determined during the sleep study was 4.3 events/h (IQR, events/h 2.2-11.1 events/h). Residual AHI in the supine and lateral positions was 6 events/h (IQR, events/h 2.5-17.3 events/h) and 2 events/h (IQR, 0.9-4.3 events/h), respectively. OSA (all night polysomnography AHI > 15 events/h) was abolished in all 10 patients receiving nasal CPAP. Finally, all 15 patients who switched to nasal CPAP opted to remain with nasal CPAP at the study termination. The CPAP level reduced from 10 cm H_2O (IQR, 8-10 cm H_2O) to 6.6 cm H_2O (IQR, 6-8 cm H_2O) with an oronasal and nasal mask, respectively (P = .002).

Discussion

Our study was designed to evaluate the impact of breathing route in patients with OSA treated with oronasal CPAP. Our main findings were the following. (1) Oral CPAP was worse than oronasal CPAP as evidenced by a higher residual AHI, despite a significantly higher CPAP level (Fig 2). Oral CPAP was associated with higher stage 1 sleep and higher arousal index than oronasal CPAP (Table 2). (2) Oronasal and oral CPAP efficacy was significantly better in the lateral position than in the supine position (Fig 3). (3) Objective flow evaluation using nasal and oral pneumotachographs showed that the patients studied predominantly were oronasal breathers during oronasal CPAP (Fig 4). (4) Finally, most patients agreed to

change and chose to remain with nasal CPAP after the study end. Nasal CPAP resulted in lower therapeutic levels and better OSA control than oronasal CPAP.

Few studies have evaluated the impact of CPAP delivered exclusively by the oral route.[24,25] The only exception is an exclusively oral mask (oracle) that has been shown to be an effective OSA treatment.[24,26] However, the oracle mask has a unique design with a tongue positioner that helps maintain airway patency. We showed that oronasal CPAP is less effective in treating OSA when patients are required to breathe through the mouth (Table 2, Fig 1). This observation is in concert with the concept that for CPAP to be effective, it must be transmitted through the nose.[7,16] The transmission of CPAP through the oral cavity neutralizes pharyngeal splinting generated by nasal CPAP.[14-17,25] Supporting this concept, CPAP effectiveness to treat OSA improved when patients switched to a nasal mask. This observation suggests that even patients well adapted to oronasal CPAP should be offered a nasal interface.[10,13,27,28] Because the upper airway is less likely to close in the lateral position,[18,29] we also explored the impact of body position on oronasal CPAP effectiveness for treating OSA. Oronasal and oral CPAP efficacy to treat OSA were significantly better with patients in the lateral position (Fig 3). Our results are in line with a study that showed that positional therapy is an attractive add-on therapy for patients with CPAP titration difficulties.[30] However, mask model was not reported in the previous study. The choice of oronasal CPAP is based on the subjective perception that the patient is an oronasal breather. However, patients with OSA who perceive themselves as oronasal breathers frequently breathe through the nose.[8] In contrast to our previous investigation that showed that patients receiving oronasal CPAP predominantly were nasal breathers,[17] in the present study, most patients were oronasal breathers. One possible explanation is that the patients in the present study were older and more obese, factors associated with oral breathing among patients with OSA.[8,27] The relevant fact is that we studied oronasal breathers with a theoretical clear indication for an oronasal mask. We showed that even oronasal breathers can switch successfully to nasal CPAP, resulting in higher effectiveness in treating OSA. Moreover, our study is in line with previous studies[31,32] showing that mouth breathing is not a contraindication to nasal CPAP.

Our study has some limitations. We studied a relatively small number of patients. However, this was a physiologic study focusing on a specific group of patients with OSA well adapted to oronasal CPAP. Furthermore, the results were consistent with our primary hypothesis, and a post hoc analysis showed that the study had a power of 0.9426. Second, we studied patients with relatively few nasal symptoms, as evaluated by the NOSE score. However, the patients were not evaluated objectively for nasal obstruction. Switching from an oronasal to nasal mask may be not feasible among patients with severe nasal obstruction. Third, to document the breathing route, patients used a dual port oronasal mask with two sealed compartments. We have no means to exclude the hypothesis that the breathing route would be different if the patients were using a standard oronasal mask. Fourth, the comparison of AHI in the supine vs lateral position must be interpreted with caution because it was based on a short period (90 min). Finally, some patients did not agree to the mask change at the end of the protocol. Therefore, we cannot exclude a selection bias. However, it is remarkable that 75% of the patients well adapted to oronasal CPAP experienced a successful transition to nasal CPAP.

Interpretation

This study provided further evidence of the limitations of oronasal CPAP to treat OSA. Oronasal CPAP was less effective when oronasal breathers well adapted to an oronasal mask were required to breathe through the mouth. In addition, most patients with OSA previously receiving oronasal CPAP could be transitioned successfully to nasal CPAP, resulting in better treatment effectiveness. Therefore, the widespread use of oronasal masks is not justified by theoretical and empirical data.

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Author contributions: J. L. d. A. X. and G. L.-F. are guarantors of the content of the manuscript, including the data and analysis. J. L. d. A. X. and G. L.-F. had full access to all study data and assume responsibility for the integrity of the data and the accuracy of the data analysis, including and especially any adverse effects. J. L. d. A. X., M. D. F., R. G. S. s. A., P. R. G., and G. L.-F. contributed substantially to the study design, analysis, and interpretation of data and the writing of the manuscript.

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