MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2018; 24: 3084-3092
DOI: 10.12659/MSM.907565

Received: 2017.10.15
Accepted: 2017.11.03
Published: 2018.05.11

Comparison of the Efficacy, Side Effects, and Cost of Modafinil and Intranasal Mometasone Furoate in Obstructive Sleep Apnea-Hypopnea Syndrome: A Preliminary Clinical Study

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

CD 1 Shujia Zhang
AB 2 Jing Fu
EF 1 Zhongnin Duan

1 Department of Otolaryngology-Head and Neck Surgery, The First Peoples' Hospital of Lianyungang, Lianyungang, Jiangsu, P.R. China
2 Department of Respiratory Medicine, The First Peoples' Hospital of Lianyungang, Lianyungang, Jiangsu, P.R. China

Corresponding Author: Jing Fu, e-mail: FTolosashte@yahoo.com
Source of support: Departmental sources

Background: Obstructive sleep apnea-hypopnea syndrome (OSAHS) is characterized by repeated episodes of reduction in airflow due to the collapse of the upper airway during sleep. The aim of this study was to compare clinical outcome, side effects, and cost of treatment between modafinil and intranasal mometasone furoate in patients with OSAHS.

Material/Methods: Patients with OSAHS (N=250) were divided into two groups: the modafinil group (MG) (N=125) were treated with 100 mg modafinil twice a day; the intranasal mometasone furoate group (IMFG) (N=125) were treated with 100 µg of intranasal mometasone furoate in the evening. Quality of life, grading of OSAHS, plain-film radiography, the adenoidal-nasopharyngeal ratio (AN ratio), side effects, cost of treatment, and beneficial effects after discontinuation of treatment were evaluated for all patients.

Results: Duration of sleep apnea was significantly reduced in the IMFG compared with the MG (p=0.0145, q=9.262). Modafinil and intranasal mometasone furoate both had moderate effects on improvement of the OSAHS score. The IMFG showed a significantly greater beneficial effect on the AN ratio when compared with the MG (p=0.0001, q=6.584). No adverse events of treatment with modafinil and intranasal mometasone furoate were reported. Cost of treatment and beneficial effect after discontinuation were both significantly greater for the IMFG compared with the MG.

Conclusions: The findings of this preliminary clinical study were that for patients diagnosed with OSAHS, night-time treatment with intranasal mometasone furoate was more effective than modafinil.

MeSH Keywords: Autoradiography • Breath Holding • Mouth Breathing • Receptors, Steroid • Sleep Apnea, Obstructive

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/907565

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Background

The condition of obstructive sleep apnea-hypopnea syndrome (OSAHS) is characterized by repeated episodes of reduction in airflow due to the collapse of the upper airway during sleep and can lead to respiratory failure due to lack of nocturnal oxygen exchange [1]. The condition of OSAHS can lead to respiratory failure, pulmonary hypertension, and cardiac failure, and may require positive airway pressure ventilation during sleep [2]. Furthermore, during sleep apnea, nocturnal hypoxemia can exacerbate co-existing chronic or advanced pulmonary disease, including chronic obstructive pulmonary disease (COPD), and bronchial asthma [3].

Adenotonsillectomy is the most appropriate surgical treatment for OSAHS if the patient can tolerate surgery and general anesthesia [4]. However, adenotonsillectomy may not be an acceptable treatment option for all patients [5]. Studies have shown that patients who suffer from OSAHS can have elevated levels of serum inflammatory cytokines [6]. Therefore, corticosteroid treatment has been proposed as a possible effective treatment for patients with OSAHS [7].

Recent studies have shown that treatment with intranasal mometasone furoate can improve the symptoms of OSAHS [8]. Treatment with modafinil is also proposed for patients with OSAHS as modafinil acts as a mild selective dopamine reuptake inhibitor [9], and has an effect on neurotransmitter systems including histamine [10], γ-aminobutyric acid (GABA), noradrenergic, and serotonergic pathway, which explain the possible mode of action of modafinil in OSAHS [11].

The aim of this preliminary clinical study in a Chinese population was to compare the clinical outcome, quality of life, grade of OSAHS, X-ray findings, side effects, beneficial effects after discontinuation of treatment, and cost of treatment between twice daily modafinil and night-time treatment with intranasal mometasone furoate in patients with OSAHS.

Material and Methods

Ethical statement

The Clinical Practice Standards Committee of the Chinese Academy for Sleep Apnea-Hypopnea Medicines approved the study. The protocol of the study was in accordance with the current medical and medico-legal guidelines for the treatment of obstructive sleep apnea and snoring therapy of the Peoples' Republic of China [12]. All patients included in the study, or their parents or guardians, provided a signed informed consent before the study began, and provided consent for their findings to be included in a published form [12].

Study design

The primary aim of the study was to compare the clinical efficacy of modafinil with intranasal mometasone furoate in patients with obstructive sleep apnea-hypopnea syndrome (OSAHS). The secondary aims of the study were to compare the safety, quality of life, grade of OSAHS, X-ray findings, side effects, beneficial effects after discontinuation of treatment, and cost of treatment between twice daily modafinil and night-time treatment with intranasal mometasone furoate in patients with OSAHS. Intranasal mometasone furoate was purchased from Glenmark Pharmaceuticals, Hungary. Modafinil was purchased from Teva Pharma B.V., the Netherlands.

The study recruited 250 patients with obstructive sleep apnea-hypopnea syndrome (OSAHS) who were diagnosed and treated at the First Peoples' Hospital of Lianyungang, China between September 2015 to April 2016. Patients who were more than six years-of-age, and who had a history of OSAHS for at least three months, were included in the study.

Exclusion criteria included patients with sleep disorders other than OSAHS, including epilepsy, psychological and mental health problems, patients who were treated with central nervous system (CNS) stimulant drugs, who were on other drug treatments, who suffered from drug addiction, or who were enrolled in any other clinical studies were excluded from this study. Patients who had acute respiratory infections, who had planned adenotonsillectomy, who had OSAHS but also had genetic disorders, neuromuscular disorders, and who had craniofacial abnormalities were also excluded from this study.

Patient sample size calculation and allocation to treatment groups

OpenEpi 3.01-English, version 2013/04/06 (*www.OpenEpi.com*) was used to calculate the patient study sample size, which was determined to be 125 patients per group.

Patients with OSAHS (N=250) were divided into two groups. Patients in the modafinil group (MG) (N=125) were treated with 100 mg modafinil twice a day [13,14]. Patients in the intranasal mometasone furoate group (IMFG) (N=125) were treated with 100 µg of intranasal mometasone furoate in the evening [15]. The treatment interventions for both groups were continued for four weeks. During the study period, the enrolled patients did not receive any anti-allergy, anti-asthmatic, steroid, or antibiotic treatments.

Table 1 shows the baseline anatomic and physiological findings of the patients enrolled in the study. Figure 1 is a flowchart of the study design.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

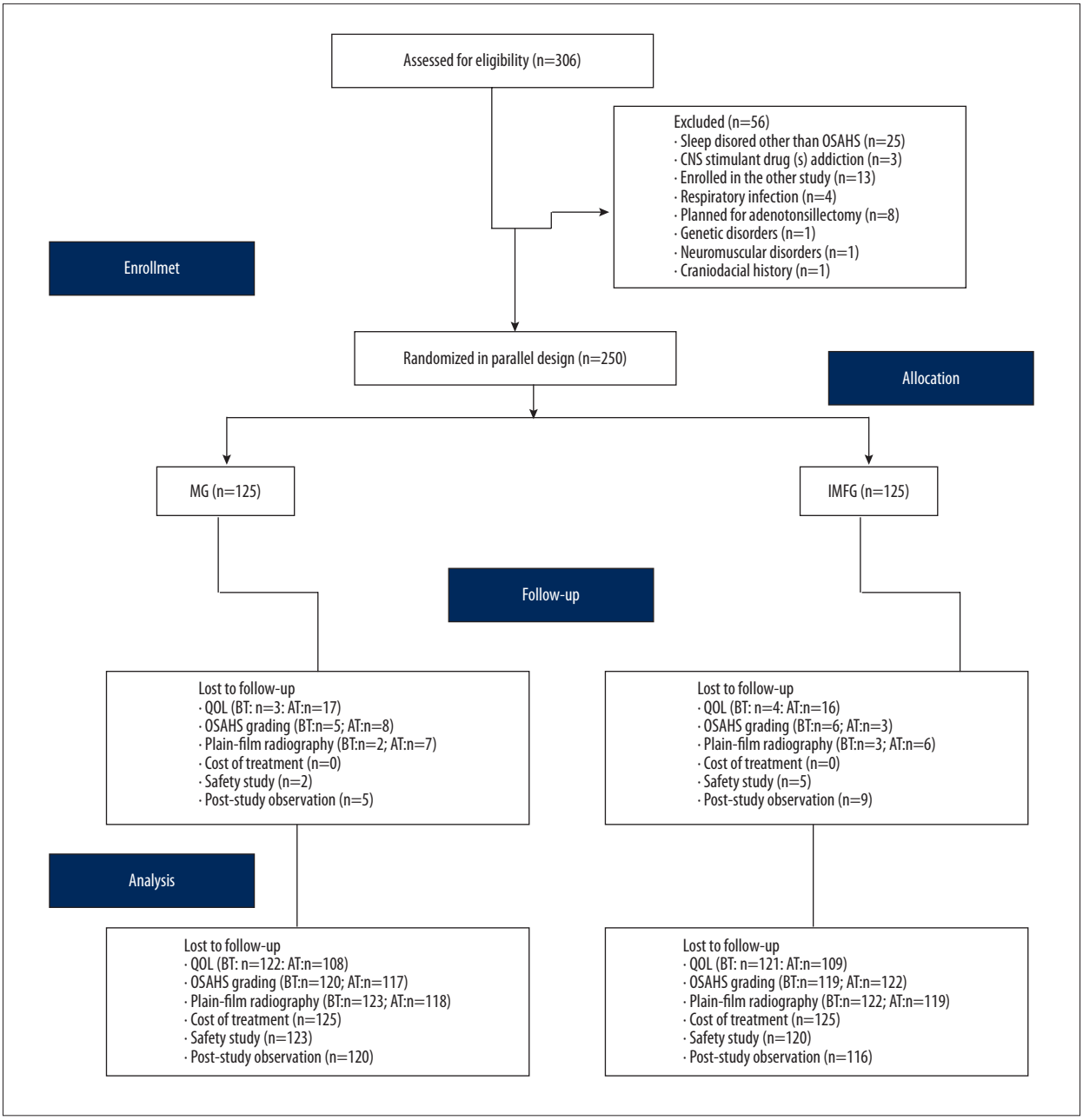

Figure 1. Flowchart diagram showing the study design of the clinical study on obstructive sleep apnea-hypopnea syndrome (OSAHS) including two patient treatment groups. Population size: 250. Hypothesized percentage frequency in population size: 80%. Confidence level: 95%. Design: randomized, parallel clinical study. QOL – quality of life; BT – before treatment; AT – four weeks after successful treatment; OSAHS – obstructive sleep apnea-hypopnea syndrome; IMFG – intranasal mometasone furoate group; MG – modafinil group.

Quality of life survey

Primary outcome measures were evaluated using a designed survey for discriminative quality of life for OSAHS patients. The survey was included 12 questions. The less frequent event was considered as an absent episode; mild to severe conditions were considered to be the presence of an episode [16].

Grading of obstructive sleep apnea-hypopnea syndrome (OSAHS)

The other primary outcome measure was recorded as grading for OSAHS before and after treatment. The grading system used for OSAHS was designed in-house and is shown in Table 2 [15].

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 1. The anatomical and physiological characteristics of enrolled patients at baseline.

Characteristics		Group		Comparisons between MG and IMFG, p-value
		MG	IMFG	
Sample size		125	125	
Age (Mean ±SD, years)		36.06±8.09	33.6±6.16	0.0004
Sex	Male	110 (88)	107 (86)	0.083
	Female	15 (12)	18 (14)	
BMI	≤20	8 (6)	9 (7)	0.019
	≥21 but <25	52 (42)	45 (36)	
	≥25 but <30	43 (34)	49 (39)	
	≥30 but <35	15 (12)	13 (10)	
	≥35	7 (6)	9 (8)	
Allergic rhinitis*		7 (6)	9 (7)	0.1581
Sinusitis		9 (7)	6 (5)	0.0833
COPD		3 (2)	8 (6)	0.0247
Asthma	Acute	23 (18)	25 (20)	0.1581
	Hereditary	1 (1)	0 (0)	0.3193
Nasal blockade		45 (36)	53 (42)	0.0012
Nasal discharge		52 (42)	62 (50)	0.0013
Eye discharge		33 (26)	37 (30)	0.0451

BMI – body mass index; COPD – chronic obstructive pulmonary disease; MG – modafinil group; IMFG – intranasal mometasone furoate group. * All patients were checked for allergy. All patients were of Chinese origin. All data were represented as Number (percentage). For statistical analysis presence of characteristic was considered as 1 and absent of that was considered as 0. A $p<0.01$ was considered as significant. Insignificant discrimination between groups.

Table 2. Grading for obstructive sleep apnea-hypopnea syndrome.

Conditions	Grade
Absent	0
Slight	1
Mild	2
Moderate	3
Moderate to severe	4
Severe	5
Requirement of positive airway pressure instrument	6

Plain-film radiography

Lateral plain-film radiography of each patient was performed. X-ray films of the lateral nasopharynx were measured using the China Hot Selling Medical ENT Treatment Unit with an ENT Chair (Vokodak Trade Co., Ltd., Guangdong, China) by maintaining the patient in the erect position to allow radiography to be performed at 70 kV with 0.8 s exposure time [8]. The distance between the anterior margin of the basi-occiput and the adenoid maximal convexity point (A), and the distance from the anterior-inferior edge of the spheno basal occipital synchondrosis to the posterior border of the hard palate (N), were recorded for each radiographic film, before and after treatment. The adenoidal-nasopharyngeal (AN) ratio was evaluated according to Eq. 1 [17]:

$$\text{Adenoidal – nasopharyngeal (AN) ratio} = A/N \quad (1)$$

Cost of treatment

The cost of treatment was evaluated for each patient and involved the diagnosis, intervention, and length of hospital stay during the treatment period [18.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 3. Quality of life survey of enrolled subjects.

Characteristics	Group								
	MG				IMFG				SA: MG *vs.* IMFG at AT (p-value)
	BT	AT	SA: BT *vs.* AT		BT	AT	SA: BT *vs.* AT		
Sample size	122	108	p Value	q Value	121	109	p Value	q Value	
Loud souring	27 (22)	21 (19)	0.0313	0.8759	25 (21)	11 (10)	0.0001	3.795	0.2141
Night time breath holding	65 (53)	42 (39)	<0.0001	3.86	69 (57)	22 (20)	<0.0001	10.545	0.0145
Night time frequent awaking	64 (52)	39 (36)	<0.0001	4.413	65 (54)	35 (32)	<0.0001	5.702	0.6035
Mouth breathing	77 (63)	38 (35)	<0.0001	7.702	72 (60)	36 (33)	<0.0001	7.051	0.7798
Respiratory obstruction	55 (45)	32 (30)	<0.0001	4.274	51 (42)	22 (20)	<0.0001	6.265	0.2156
Running nose	35 (28)	21 (19)	0.0001	2.869	36 (30)	11 (10)	<0.0001	6.535	0.2141
Dysphagia	12 (10)	1 (1)	0.001	5.207	9 (7)	1 (1)	0.0078	4.242	>0.9999
Hyper activeness	3 (2)	0 (0)	0.25	0.04842	4 (3)	0 (0)	0.0625	2.368	N/A
Mood disturbance	36 (30)	12 (11)	0.0006	6.154	32 (26)	2 (2)	<0.0001	9.792	0.2113
Drowsiness	12 (10)	1 (1)	0.001	5.207	11 (9)	1 (1)	0.002	4.954	>0.9999
Day time breath holding	43 (35)	3 (3)	<0.0001	11.756	39 (32)	4 (4)	<0.0001	10.428	0.9048
Frustration	4 (3)	0 (0)	0.125	2.348	3 (2)	0 (0)	0.25	0.04842	N/A

MG – modafinil group; IMFG – intranasal mometasone furoate group; SA – statistical analysis; BT – before treatment, AT: 4-weeks after successful treatment. All data were represented as number (percentage). For statistical analysis presence of episode was considered as 1 and absent of that was considered as 0. N/A – not applicable. A $p<0.05$, $q>3.33$ between BT and AT for both groups, and $q>3.32$ between groups were considered as significant.

Safety study

The Standard Practice Committee of the Chinese Academy for Sleep Apnea-Hypopnea Medicines approved the study protocol and analysis of the safety study. For access to the safety study, the interventions were continued for four months. The blood and urine sample of patients were collected after completion of the four months of treatment interventions [14]. The adverse drug reactions, including a headache, upper abdominal pain, loss of body weight, and palpitations, were recorded.

Laboratory testing of blood samples from each patient in the study was performed for serum γ-glutamyl transpeptidase (GGT), serum alkaline phosphatase (ALP), serum alanine aminotransferase (ALT), and serum thyroid stimulating hormone (TSH) levels. Urine glucose levels were measured, and blood white cell counts (WCC) were performed using standard clinical diagnostic kits (Shenzhen Zhonghe Headway Bio-Sci & Tech Co., Ltd. Guangdong, China) [19].

All patients who were enrolled in the study underwent safety evaluation that included an electrocardiogram (ECG), using an He-12A the Portable 12 Lead Digital Electrocardiogram Machine (Healicom Medical Equipment Co. Ltd, Jiangsu, China) at the end of four months.

Post-study observations

All patients discontinued treatment following the safety study, and they all were monitored for the sustained action of the drug after discontinuation of treatment [20].

Statistical analysis

The statistical analysis of the baseline anatomical and physiological characteristics of the patients enrolled in the study was performed using the Mann-Whitney U test with a 99% confidence interval (CI) [21]. The Wilcoxon matched pair test [22], following the Tukey-Kramer multiple comparisons test [23],

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 4. Effects of interventions grading for obstructive sleep apnea-hypopnea syndrome.

OSAHS score	Group								SA: MG *vs.* IMFG	
	MG				IMFG				At BT	at AT
	BT	AT	SA: BT *vs.* AT		BT	AT	SA: BT *vs.* AT		p Value	p Value
Sample size	120	117	p Value	q Value	119	122	p Value	q Value		
1	32 (25)	55 (47)	<0.0001	5.784	30 (25)	63 (52)	<0.0001	7.599	0.8421	0.53
2	8 (7)	7 (6)	>0.9999	N/A	12 (10)	8 (7)	0.125	1.726	0.6318	0.9361
3	13 (11)	9 (8)	0.125	1.452	15 (13)	11 (9)	0.125	1.561	0.8051	0.8529
4	33 (28)	25 (21)	0.0078	1.916	25 (21)	19 (16)	0.0313	1.9	0.3718	0.422
5	25 (21)	21 (18)	0.125	0.9777	27 (23)	21 (17)	0.0313	1.851	0.7987	N/A
6	9 (8)	0 (0)	0.0039	5.361	10 (8)	0 (0)	0.002	5.806	0.8996	N/A

All data were represented as Number (percentage). For statistical analysis presence of OSAHS score was considered as 1 and absent of that was considered as 0. N/A – not applicable. $p<0.05$ and $q>3.33$ between BT and AT for both groups were considered as significant. MG – modafinil group; IMFG – intranasal mometasone furoate group; SA – statistical analysis; BT – before treatment; AT – 4-weeks after successful treatment.

including a false discovery rate of q >3.33 as the level of significance, were performed between before treatment and after treatment.

The Mann-Whitney U test [21], following the Tukey-Kramer multiple comparisons test [23], including q>3.32 for the significance level, were used for statistical analysis between groups. A two-tailed paired t-test (β=0.1 and α=0.05, for both tails) was used [24], following the Tukey-Kramer multiple comparisons test [23], including q >3.328 for the level of significance, were performed between groups for the cost of therapy. GraphPad Instat (GraphPad Software Inc., San Diego, CA, USA) was used to perform the statistical analysis. The data were considered as significant with a 95% confidence interval (CI) for treatments.

Results

In this study of patients with obstructive sleep apnea-hypopnea syndrome (OSAHS), there were two treatment groups: the modafinil group (MG), treated with 100 mg modafinil twice a day, and the intranasal mometasone furoate group (IMFG), treated with 100 µg of intranasal mometasone furoate in the evening.

Quality of life surveys were not performed for three MG patients and four IMFG patients at the time before treatment, or baseline treatment (BT). There were 17 MG patients 16 IMFG patients who did not undergo have the quality of life survey data evaluated at four weeks after treatment.

There was no significant difference between the patients in the two treatment groups, the MG and IMFG, for loud snoring (p=0.8004,), night-time apnea (p=0.6980), night-time frequent waking (p=0.9586), mouth-breathing (p=0.5266), respiratory obstruction (p=0.6174), running nose (p=0.9366), dysphagia (p=0.7192), hyperactiveness (p=0.9096), mood disturbance (p=0.6267), drowsiness (p=0.8992), daytime apnea (p=0.6236), and sleep apnea discomfort (p=0.9041) at baseline.

Treatment with modafinil and intranasal mometasone furoate both resulted in a significant improvement in primary outcome measures for OSAHS patients in this study. However, night-time apnea was significantly reduced with treatment with intranasal mometasone furoate compared with modafinil (p=0.0145, q=9.262) (Table 3).

At baseline treatment, there was no difference between the two study groups for grading of OSAHS. The OSAHS grading data for five patients in the MG, and six patients in the IMFG at baseline treatment and eight patients in the MG and three patients of IMFG at the end of treatment could not be evaluated. Treatment with modafinil and intranasal mometasone furoate both resulted in moderate improvement in the OSAHS scores at the end of the treatment study (Table 4).

There were two patients in the MG, and three patients of IMFG at baseline treatment, seven patients in the MG and six patients of IMFG at the end of the treatment study did not undergo plain-film radiography because they were too old. There was no significant difference in the adenoidal-nasopharyngeal (AN) ratio at baseline treatment (p=0.8449). Modafinil (p<0.0001, q=17.766)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

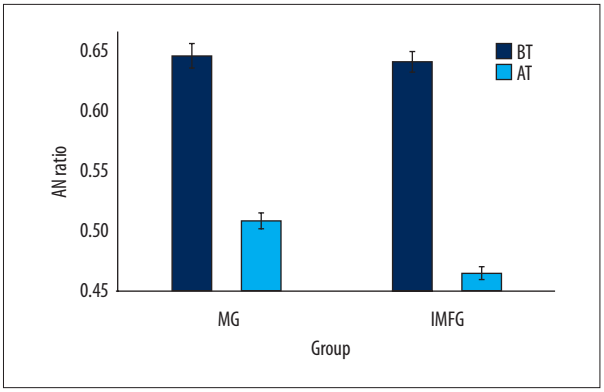

Figure 2. Effect of treatment interventions on the adenoidal-nasopharyngeal (AN) ratio. Patients in the modafinil group (MG) at BT (n=123) and at AT (n=118). Patients in the intranasal mometasone furoate group (IMFG) at BT (n=122) and at AT (n=119). At BT, comparison between the MG and the IMFG: p=0.8449; at AT, p=0.0001, q=6.584. Comparison between BT and AT for the MG, p<0.0001, q=17.766. Comparison between BT and AT for the IMFG, p<0.0001, q=21.561. p<0.05, q>3.329 between BT and AT for both groups, and q>3.3 between groups were considered to be significant. MG – modafinil group; IMFG – intranasal mometasone furoate group; BT – before treatment; AT – four weeks after successful treatment.

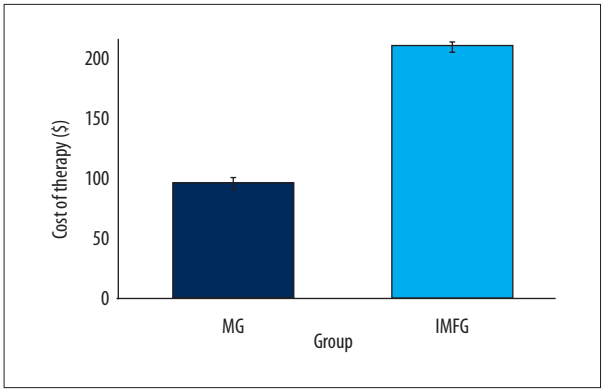

Figure 3. Comparison of the cost of the treatment with modafinil and intranasal mometasone furoate for patients with obstructive sleep apnea-hypopnea syndrome (OSAHS). Data are presented as mean ±SD. n=125 for both groups. p-value and q-value between MG and IMFG were <0.0001 and 405.62. MG – modafinil group; IMFG – intranasal mometasone furoate group. p<0.05 and q>3.328 were considered as statistically significant.

and IMF (p<0.0001, q=21.561) resulted in an improved AN ratio. However, treatment with intranasal mometasone furoate had a significantly greater effect on the AN ratio compared with modafinil (p=0.0001, q=6.584) (Figure 2). The cost of treatment for patients in the IMFG was significantly greater than for patients in the MG (p<0.0001, q=405.62) (Figure 3). Two patients from the MG and five patients from the IMFG did not take part in the safety study. Clinical and laboratory investigation data showed that there were no significant abnormalities or side effects during the safety study in both groups (Table 5).

The data from the post-study observations of five patients from the MG and nine patients from the IMFG were not collected. At the end of the study, patients in the MG had an average of six months of beneficial effects after discontinuation of the treatment. At the end of the study, patients in the IMFG had an average of 12 months of beneficial effect after discontinuation of the treatment (Figure 4).

Discussion

The findings of this preliminary clinical study, in a Chinese population of 250 patients with obstructive sleep apnea-hypopnea syndrome (OSAHS), showed that night-time treatment with intranasal mometasone furoate was more effective than modafinil. However, the cost of treatment with intranasal mometasone furoate was significantly greater when compared with modafinil.

Currently, intranasal mometasone furoate is the main treatment recommended for OSAHS, despite previous cost analysis supporting its increased cost [18]. Therefore, in this study, the selection this intranasal form of topical corticosteroid treatment for OSAHS patients was appropriate. In this study, the adenoidal-nasopharyngeal (AN) ratio was responsive to intranasal mometasone furoate treatment, which was supported by plain film radiography, which is routinely used for measurement of the AN ratio [17]. The AN ratio indicates enlargement of adenoids which can lead to OSAHS [25]. Mometasone furoate has previously been reported to reduce the size of adenoidal tissues [15].

In this study, OSAHS was defined as night-time apnea, frequent night-time sleeplessness, or night-time mouth-breathing. Modafinil has previously been reported to have strong wake-promoting activity because of its effect on several neurotransmitters [14]. In this study, although modafinil treatment had a beneficial effect in patients with OSAHS, an increased dose of 200 mg/day was required, compared with the dose of 100 µg/day for intranasal mometasone furoate.

The findings of this study showed that intranasal mometasone furoate had a greater beneficial effect after discontinuation of intervention when compared with modafinil treatment. These study findings are supported by the findings of previously published studies of intranasal corticosteroid therapy for the treatment of sleep apnea in children [20]. In the post-study treatment findings of the present study, intranasal mometasone furoate treatment was preferred to modafinil by patients with OSAHS.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 5. Safety study of enrolled patients.

Parameters	Group		SA: Between MG and IMFG
	MG (n=123)	IMFG (n=120)	p Value
Headache	6 (5)	4 (3)	0.9199
Upper abdominal pain	0 (0)	2 (2)	0.9016
Loss of body weight	2 (2)	0 (0)	0.9085
Palpitation	2 (2)	0 (0)	0.9085
Abnormal GT	1 (1)	0 (0)	0.9992
Abnormal AP	1 (1)	0 (0)	0.9992
Abnormal AA	1 (1)	0 (0)	0.9992
Abnormal TSH	1 (1)	0 (0)	0.9992
Abnormal Urine glucose level	1 (1)	0 (0)	0.9992
Decreased WC	1 (1)	1 (1)	N/A
Sinus tachycardia	1 (1)	0 (0)	0.9992
Sinus bradycardia	1 (1)	0 (0)	0.9992
Ventricular extrasystole	0 (0)	1 (1)	0.9977

GT – serum γ-glutamyl transpeptidase level; AP – serum alkaline phosphatase level; AA – serum alanine aminotransferase level; TSH – serum thyroid-stimulating hormone level; WC – white cells count; MG – modafinil group; IMFG – intranasal mometasone furoate group. For statistical analysis presence of adverse effect was considered as 1 and absent of that was considered as 0. N/A – not applicable. A $p<0.05$ was considered as significant.

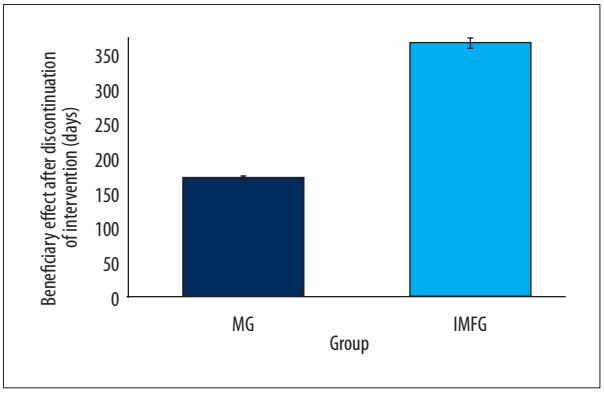

Figure 4. Post-study findings in patients treated with modafinil and intranasal mometasone furoate for obstructive sleep apnea-hypopnea syndrome (OSAHS). Patients in the IMFG had a high beneficial effect following discontinuation of the treatment intervention (p<0.0001, q=548.91). Data are presented as the mean ±SD. n=120 for MG and n=116 for IMFG. MG – modafinil group; IMFG – intranasal mometasone furoate group. p<0.05 and q>3.33 were considered as statistically significant.

This preliminary clinical study had several limitations. The study size was small and the enrolled study population consisted predominantly of male patients. This study limitation may be significant, as the pharmacokinetic profile of men and women may be different. There were significant differences between the mean age (p=0.0004), the presence of nasal discharge (p=0.0013), and nasal blockage (p=0.0012) between the two study treatment groups. Also, all patients were of Chinese origin, which may have been a study limitation because ethnicity may influence the metabolism of modafinil.

Conclusions

The findings of this preliminary clinical study showed that a four-week treatment period of topical intranasal corticosteroid treatment with mometasone furoate, was more effective than modafinil in obstructive sleep apnea-hypopnea syndrome (OSAHS). Future larger controlled multi-center and multi-ethnic clinical studies are recommended to include the evaluation of a combination of topical intranasal steroids

Acknowledgements

The authors thank all the study participants and the medical and non-medical staff of the First Peoples' Hospital of Lianyungang, China.

Conflicts of interest

None.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

References:

1. Voth AH, Catalan JC, Maanas PB et al: Obstructive sleep apnea-hypopnea syndrome in patients with severe chronic respiratory insufficiency. Med Clin (Barc), 2017; 148: 449–52
2. Stanchina ML, Welicky LM, Donat W et al: Impact of CPAP use and age on mortality in patients with combined COPD and obstructive sleep apnea: The overlap syndrome. J Clin Sleep Med, 2013; 9: 767–72
3. Nathan AM, de Bruyne JA, Eg KP, Thavagnanam S: Review: Quality of life in children with non-cystic fibrosis bronchiectasis. Front Pediatr, 2017; 5: 84
4. Marcus CL, Moore RH, Rosen CL et al: A randomized trial of adenotonsillectomy for childhood sleep apnea. N Engl J Med, 2013; 368: 2366–76
5. Marcus CL, Brooks LJ, Draper KA et al: Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics, 2012; 130: e714–55
6. Kim J, Bhattacharjee R, Dayyat E et al: Increased cellular proliferation and inflammatory cytokines in tonsils derived from children with obstructive sleep apnea. Pediatr Res, 2009; 66: 423–28
7. Rezaeetalab F, Rezaeitalab F, Dehestani V: Inhaled steroids reduce apnea-hypopnea index in overlap syndrome. Pneumologia, 2013; 62: 212–14
8. Jung YG, Kim HY, Min JY et al: Role of intranasal topical steroid in pediatric sleep-disordered breathing and influence of allergy, sinusitis, and obesity on treatment outcome. Clin Exp Otorhinolaryngol, 2011; 4: 27–32
9. Madras BK, Lin Z, Jassen A et al: Modafinil occupies dopamine and norepinephrine transporters *in vivo* and modulates the transporters and trace amine activity *in vitro*. J Pharmacol Exp Ther, 2006; 319: 561–69
10. Ishizuka T, Murakami M, Yamatodani A: Involvement of central histaminergic systems in modafinil-induced but not methylphenidate-induced increases in locomotor activity in rats. Eur J Pharmacol, 2008; 578: 209–15
11. Morgenthaler TI, Kapen S, Lee-Chiong T et al: Practice parameters for the medical therapy of obstructive sleep apnea. Sleep, 2006; 29: 1031–35
12. Ramar K, Dort LC, Katz SG et al: Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: An update for 2015. J Clin Sleep Med, 2015; 11: 773–827
13. Korat PS, Kapupara PP: Local infiltration of the surgical wound with levobupivacaine, ibuprofen, and epinephrine in postoperative pain: An experimental study. Biomed Pharmacother, 2017; 96: 104–11
14. Inoue Y, Takasaki Y, Yamashiro Y: Efficacy and safety of adjunctive modafinil treatment on residual excessive daytime sleepiness among nasal continuous positive airway pressure-treated Japanese patients with obstructive sleep apnea syndrome: A double-blind placebo-controlled study. J Clin Sleep Med, 2013; 9: 751–59
15. Chan CK, Au CT, Lam HS et al: Intranasal corticosteroids for mild childhood obstructive sleep apnea – a randomized, placebo-controlled study. Sleep Med, 2015; 16: 358–63
16. Walter LM, Biggs SN, Cikor N et al: The efficacy of the OSA-18 as a waiting list triage tool for OSA in children. Sleep Breath, 2016; 20: 837–44
17. Kolo ES, Ahmed AO, Kazeem MJ, Nwaorgu OG: Plain radiographic evaluation of children with obstructive adenoids. Eur J Radiol, 2011; 79: e38–41
18. Rodriguez-Martinez CE, Sossa-Briceno MP, Vladimir Lemos E: Cost-effectiveness analysis of mometasone furoate versus beclomethasone dipropionate for the treatment of pediatric allergic rhinitis in Colombia. Adv Ther, 2015; 32: 254–69
19. Sahreen S, Khan MR, Khan RA: Evaluation of *Rumex hastatus* leaves against hepatic fibrosis: A rat model. BMC Complement Altern Med, 2017; 17(1): 435
20. Kheirandish-Gozal L, Gozal D: Intranasal budesonide treatment for children with mild obstructive sleep apnea syndrome. Pediatrics, 2008; 122: 149–55
21. Schirinzi T, Di Lazzaro G, Sancesario GM et al: Levels of amyloid-beta-42 and CSF pressure are directly related in patients with Alzheimer's disease. J Neural Transm (Vienna), 2017; 124(12): 1621–25
22. Su P, Chang Y, Bai X, Wang R: Prevalence and association of mycoplasma infection in the development of coronary heart disease. Int J Clin Exp Pathol, 2017; 10: 979–87
23. Endharti AT, Wulandari A, Listyana A et al: Dendrophthoe pentandra (L) Miq extract effectively inhibits inflammation, proliferation and induces p53 expression on colitis-associated colon cancer. BMC Complement Altern Med, 2016; 16(1): 374
24. Gao Z, Cui F, Cao X et al: Local infiltration of the surgical wounds with levobupivacaine, dexibuprofen, and norepinephrine to reduce postoperative pain: A randomized, vehicle-controlled, and preclinical study. Biomed Pharmacother, 2017; 92: 459–67
25. Feng X, Li G, Qu Z et al: Comparative analysis of upper airway volume with lateral cephalograms and cone-beam computed tomography. Am J Orthod Dentofacial Orthop, 2015; 147: 197–204

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]