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Randomised controlled study of treatment for mild and moderate sleep apnoea

Key Messages

1. We have validated a Chinese version of the Sleep Apnoea Quality of Life Index, a disease-specific health-related quality of life (HRQOL) instrument, for use in health care research of obstructive sleep apnoea (OSA) in a Cantonese-speaking Chinese population. This instrument may be further adapted to suit Chinese populations whose main dialect is not Cantonese.
2. For treatment of mild and moderate OSA, using nasal continuous positive airway pressure or an oral appliance (OA) in addition to weight control will achieve improvements in terms of sleep parameters, daytime sleepiness, and HRQOL.
3. Continuous positive airway pressure is superior to OAs with respect to the first two parameters, but similar to OA in terms of HRQOL improvement.
4. For the treatments of mild and moderate OSA, lifestyle modification measures, in particular weight reduction, should be implemented for all overweight patients. However, only about half of them will achieve a degree of weight reduction over 10 weeks and associated reduction of sleep-disordered breathing events, and even then control of such events is usually incomplete.
5. Factors other than treatment effectiveness as demonstrated by physiological and neurobehavioural outcome measures affect the patient's choice of treatment modality; such factors include subjective considerations, convenience, and cost.

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Introduction

Obstructive sleep apnoea (OSA) affects 2 to 4% of the middle-aged Caucasian population as well as Chinese inhabitants of Hong Kong.¹ Criteria for treatment of OSA are based on symptoms and physiological severity. Various treatment options have their own benefits and limitations.² In severe OSA, application of nasal continuous positive airway pressure (CPAP) has been shown to be safe and effective as judged by various outcome measures, but the optimal management for those with milder OSA is more controversial. Apart from CPAP, other non-surgical options include oral appliances (OAs) and lifestyle modification.

Aims and objectives

This study aimed to produce a validated disease-specific health-related quality of life (HRQOL) instrument for use as an outcome measure in sleep apnoea in Chinese, and to evaluate the effectiveness of treatments (lifestyle modification alone vs addition of CPAP or an OA) in patients with mild or moderate sleep apnoea.

Methods

This study was conducted from September 1999 to March 2002.

Validation of the Chinese version of the Sleep Apnoea Quality of Life Index

The Sleep Apnoea Quality of Life Index (SAQLI) originally developed and validated in an English-speaking population,³ was translated into Chinese.⁴ The translated version was applied to OSA subjects for assessment of its acceptability, scaling assumptions, reliability, validity, and responsiveness.

Randomised controlled study of treatment of mild and moderate obstructive sleep apnoea

Patients were recruited from the Department of Medicine, Queen Mary Hospital and Department of Medicine, Pamela Youde Nethersole Eastern Hospital.⁵ Inclusion criteria were age >21 to 70 years, and the diagnosis of mild-to-moderate OSA was based on the following criteria: apnoea-hypopnoea index (AHI) ≥ 5 to 20 with Epworth sleepiness scale (ESS) score >9, or AHI >20 to 40. Exclusion criteria were other unstable medical diseases, 'dangerous' sleepiness, coexistence of sleep disorders other than OSA, previous surgery to the upper airway (excluding the nose), and pregnant women.

Patients were randomised to the following three arms of treatments for 10 weeks: (1) control group—only conservative measures (CM) of lifestyle-behavioural modification, (2) CPAP+CM group—use of nasal CPAP in addition to CM, and (3) OA+CM group—use of OA in addition to CM. Conservative management included advice on measures that help to decrease sleep apnoea. Those who were overweight were referred to a weight reduction programme. Those randomised to CPAP were advised to use it at a pre-titrated pressure every night during sleep; while those randomised to the OA were referred to an orthodontist in Prince Philip Dental Hospital for fabrication of the appliance and

to use it every night during sleep.

For the purpose of evaluation, the primary outcome indicator was daytime sleepiness: ESS score, and the secondary outcome indicator was the HRQOL. These parameters were obtained at baseline and at 10 weeks. For those who were on CPAP and OA, polysomnography (PSG) was repeated after taking off the device for 1 week to assess for changes related to lifestyle modification rather than the device.

Evaluation instruments were: (1) PSG (Alice 3/4 system, Respironics, Atlanta, US) recording sleep stages, oxygen saturation, airflow, respiratory movements, etc; (2) symptoms—questionnaire on sleep apnoea symptoms and the ESS; (3) the HRQOL—Chinese version of short-form health survey questionnaire (SF-36) and SAQLI; and (4) blood pressure. Side-effects of treatment and adherence to therapy were also assessed at 10 weeks. On completion of study, patients were asked if they would choose to continue on the treatment to which they were randomised, and any reasons for discontinuation.

Results

Validation of the Chinese version of Sleep Apnoea Quality of Life Index

A cross-sectional sample of 106 Chinese OSA patients and a longitudinal sample of 51 patients in Hong Kong completed the Chinese (Cantonese) version of SAQLI.⁴ The instrument was understood and perceived as relevant by 97% of the subjects. Internal consistency, test-retest reliability, item-scale convergent validity and discriminatory validity, and construct validity were good to excellent. Construct validity was confirmed by significant correlations with SF-36 subscale scores. However, factor analysis showed that only items of daily functioning and symptom domains all loaded on the hypothesised scales. Longitudinal data showed that SAQLI was more responsive than SF-36 to changes after treatment.

Effectiveness of three treatment modalities

101 subjects were randomised to one of the three treatment groups. Ten subjects withdrew: four subjects in OA group had gum problems, one in the CPAP group had intolerance of the device, and five in the CM group refused to undergo PSG at 10 weeks. There was no significant difference between baseline parameters in those who completed the study and those who did not.

General advice on sleep hygiene was given to all subjects. Eighty-four subjects were overweight/obese and were referred for weight control programme. However, significant weight loss was only observed in the CPAP group. In all, 45 subjects had a decrease in body weight (15 subjects in each of the three groups) from a mean±standard deviation (SD) of 76±11 to 73±10 kg. Their AHI decreased from a mean±SD of 25±12 to 19±14.

Eight subjects (mean AHI=15 at baseline) had a mean AHI of <5 after weight reduction, while the others still had an AHI of ≥5.

Symptoms and physiological parameters

Regarding daytime sleepiness, compared with baseline values, ESS decreased significantly in all three treatment arms although the post-treatment ESS of the CM group was still above the norm (defined as >9). The differences between the mean change in ESS of the CM+CPAP and CM only groups, and between the CM+CPAP and CM+OA groups were statistically significant.

Regarding sleep study parameters, the AHI of subjects in both CPAP and OA groups decreased significantly compared to their baseline values, but only subjects assigned to CPAP achieved AHI values of <5, the commonly used threshold criterion for OSA. Subjects in the CM group did not yield any change in AHI after 10 weeks. Changes in AHI were significantly different among the three groups; the CPAP+CM group showed the largest decrease.

There was no statistically significant difference in changes in blood pressure among the three treatment groups, although there were reductions in post-treatment morning diastolic blood pressure compared to baseline in the CPAP and OA groups.

Health-related quality of life

At baseline, the scores of several SF-36 domains were lower than that of the local population norm. After the CPAP+CM treatment, all affected domains of the SF-36 were restored to normal, except for social functioning and mental health; while the scores for social functioning and bodily pain domains of the OA+CM group, as well as those for role-physical, social functioning, bodily pain and physical functioning of the CM group remained lower than the respective population norms. The CPAP was better than OA or CM in terms of the magnitude of the response in bodily pain, and better than CM with respect to the treatment response for physical functioning.

The SAQLI scores in both CPAP and OA groups increased significantly compared to their baseline values. The CPAP+CM group showed improvement in all four domains while OA+CM group improved in three domains, but not 'social interaction'; the CM group showed no significant change in any domain.

The increase in SAQLI scores in both the CPAP+CM and OA+CM groups were significantly better than that of CM group. Only if treatment-related symptoms (domain E) were not included, did the CPAP group show more improvement than in the OA group.

Side-effects of treatment and compliance

All subjects in CPAP group reported some side-effects, including dryness of nose/mouth/throat, feeling of pressure,

noise from machine, and facial skin abrasion. The mean CPAP use was 4.4 nights per week and 4.2 hours per night. Side-effects experienced with the OA included excessive salivation, temporomandibular joint discomfort, dryness of throat, and teeth discomfort. All side-effects were considered as mild. Mean self-reported use of the device was 5.2 nights per week and 6.4 hours per night. No particular side-effects related to lifestyle modification measures were reported.

Patient choice of treatment

At the end of the study, 50% of the CPAP+CM group, 80% of OA+CM group, and 70% of CM group chose to continue with the assigned treatment instead of changing to another option. The reasons for doing so in CPAP and OA groups were perceived benefits from the treatment they were receiving, while the main reason for the CM group was the convenience.

Discussion

In patients with mild or moderate OSA, symptom relief and improving quality of life are important outcome measures as the long-term morbidity has not been established. Our study was designed to compare the three most commonly used treatment modalities regarding their effects on symptoms, health status, and physiological parameters in subjects with mild and moderate OSA.

Our study found that CPAP was more effective than OA in eliminating respiratory events during sleep, similar to that of previous studies, while patients on CM alone had no significant change in AHI. Subjective sleepiness measured by ESS improved in all three treatment arms, although those treated conservatively still had excessive daytime sleepiness as reflected by post-treatment ESS of >9. The improvement of ESS score was significantly greater in CPAP+CM group than OA+CM and CM groups, suggesting that only CPAP effectively improved the symptom of daytime sleepiness.

It is well-documented that the quality of life of severe OSA patients is impaired, and CPAP, compared with placebo, can improve their quality of life. For patients with milder disease, whether CPAP can improve quality of life is unclear. We found that both CPAP and OA can improve quality of life in these OSA subjects, while CM alone has no beneficial effect. Side-effects due to treatment were more common in the CPAP group, and this has an impact on HRQOL as evidenced by the SAQLI assessment which showed a nullification of the superiority of CPAP over OA when treatment-related symptoms were included.

Overweight OSA patients are usually advised to lose weight. No randomised controlled trial has been performed for this commonly used treatment in OSA, but several open

studies have shown improvement or deterioration of OSA with weight change. Although the CM group failed to show any significant change in body mass index or AHI, when we examined the entire study sample, subjects who could lose weight enjoyed an improvement in AHI. However, weight reduction was achieved in only about half of the overweight subjects, and less than 10% could achieve enough weight loss to result in a normal sleep breathing status of AHI <5. Addition of the device appeared to facilitate weight loss.

Although the CPAP+CM group showed the greatest improvement in physiological and neurobehavioural outcome measures, the lowest proportion of patients chose to continue this form of treatment suggesting that choice of treatment modality was not solely based on effectiveness of the treatment. Considerations of convenience, cost, and other factors may also influence choice. However, this study was not a cross-over study, so personal experience of all options in an individual was not available for decision-making.

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- (1) *Journal of Clinical Epidemiology*: Mok WY, Lam CL, Lam B, Cheung MT, Yam L, Ip MS. A Chinese version of the Sleep Apnea Quality of Life Index was evaluated for reliability, validity, and responsiveness. *J Clin Epidemiol* 2004;57:470-8. Copyright Elsevier.
- (2) *Thorax*: Lam B, Sam K, Mok WY, et al. Randomised study of three non-surgical treatments in mild to moderate obstructive sleep apnoea. *Thorax* 2007;62:354-9.

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