Sleep Medicine 15 (2014) 329–335

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

The impact of weight reduction in the prevention of the progression of obstructive sleep apnea: an explanatory analysis of a 5-year observational follow-up trial

Henri Tuomilehto [a,b,*], Juha Seppä [c], Matti Uusitupa [b,d], Markku Peltonen [e], Tarja Martikainen [f], Johanna Sahlman [c], Jouko Kokkarinen [g], Jukka Randell [g], Matti Pukkila [c], Esko Vanninen [h], Jaakko Tuomilehto [i,j], Helena Gylling [d,k], on behalf of the Kuopio Sleep Apnea Group

[a] Oivauni Sleep Clinic, Kuopio, Finland
[b] Institute of Public Health and Clinical Nutrition, Department of Clinical Nutrition, University of Eastern Finland, Finland
[c] Department of Otorhinolaryngology, Kuopio University Hospital, Finland
[d] Clinical Research Center, Kuopio University Hospital, Kuopio, Finland
[e] Department of Health Promotion and Chronic Diseases Prevention, National Institute for Health and Welfare, Helsinki, Finland
[f] Clinical Nutrition and Obesity Center, Kuopio University Hospital, Kuopio, Finland
[g] Department of Respiratory Medicine, Kuopio University Hospital, Finland
[h] Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Finland
[i] Center for Vascular Prevention, Danube-University Krems, Krems, Austria
[j] South Ostrobothnia Central Hospital, Seinäjoki, Finland
[k] Department of Medicine, Division of Internal Medicine, University of Helsinki, Helsinki, Finland

ARTICLE INFO

Article history:
Received 8 September 2013
Received in revised form 22 October 2013
Accepted 1 November 2013
Available online 31 January 2014

Keywords:
Obstructive sleep apnea
Sleep-disordered breathing
Prevention
Progression
Weight loss
Long term
Follow-up

ABSTRACT

Background: Obstructive sleep apnea (OSA) is a chronic progressive disease, and it is well-documented that severe OSA is associated with an increased cardiovascular morbidity and mortality. Weight reduction has been shown to improve OSA; however, we need further evidence to determine if it may prevent the progression of OSA in the long term. The aim of our study was to assess the impact of weight change during a 5-year observational follow-up of an original 1-year randomized controlled trial.
Methods: The participants were divided into the two groups according to the weight change at 5-year follow-up using the 5% weight loss as a cutoff point, which was later referred to as the successful ($n = 20$) or unsuccessful groups ($n = 27$). The change in apnea–hypopnea index (AHI) was the main objective outcome variable.
Results: Fifty-seven patients participated in the 5-year follow-up. At 5 years from the baseline, the change in AHI between the groups was significant in the successful group (−3.5 [95% confidence interval {CI}, −6.1 to −0.9]) compared with the unsuccessful group (5.0 [95% CI, 2.0–8.5]) ($P = .002$). Successful weight reduction achieved an 80% reduction in the incidence of progression of OSA compared to the unsuccessful group (log-rank test, $P = .016$).
Conclusions: A moderate but sustained weight reduction can prevent the progression of the disease or even cure mild OSA in obese patients.

1. Introduction

Obesity has become an increasing health concern in recent decades. It is now well-known that obesity is associated with increased morbidity and mortality, in particular from cardiovascular and metabolic diseases [1,2]. Obesity also is the most important risk factor for obstructive sleep apnea (OSA); in fact, most OSA patients (at least 2 out of 3) are obese [3–5]. OSA is a chronic progressive disease and particularly the more severe stages of OSA have been linked to an increased risk for cardiovascular morbidity and mortality [6,7]. In the first randomized study conducted on the effects of weight loss on OSA, we demonstrated that a 1-year lifestyle intervention, which included an early weight reduction program, represented a feasible and effective treatment for overweight and obese participants with mild OSA [8]. These findings have been subsequently confirmed by two randomized studies, one conducted in obese OSA patients with type two diabetes mellitus (DM) and the

* Corresponding author at: Oivauni Sleep Clinic, Puijonkatu 12 B, 70100 Kuopio, Finland. Tel.: +358 40 5945068; fax: +358 17 3691121.
E-mail address: henri.tuomilehto@oivauni.fi (H. Tuomilehto).

1389-9457/$ - see front matter © 2014 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.sleep.2013.11.786

other in patients with moderate to severe OSA using continuous positive airway pressure therapy [9,10].

Furthermore, our 2-year follow-up study demonstrated that the favorable changes achieved by a supervised lifestyle intervention during the intervention could be sustained for at least 1 year after the discontinuation of the active intervention [11]. In a recent randomized, 5-year, observational, postintervention follow-up study [12], we revealed that supervised lifestyle intervention based weight reduction (i.e., a healthy diet, increased physical activity) represented an effective treatment to prevent the progression of OSA when initiated in early phases of the disorder. These findings were recently supported by another recent long-term follow-up of 3 years [13]. Although these data were encouraging and weight loss is now recommended in all clinical guidelines on OSA, the efficacy of weight reduction as a treatment of OSA may still be underrated by many clinicians. Clinicians commonly believe that any weight loss could be temporary and would return after stopping the active lifestyle counseling; they also believe that this change could result in a re-exacerbation or worsening of OSA in most patients.

The main objective of our report was to extend the assessment of the postinterventional results conducted during the 5-year follow-up regarding the effect of weight loss and physical activity on OSA. To our knowledge, the effect of achieving the weight loss goal and sustaining it for years after the end of actual intervention has not been previously demonstrated. Percentage weight loss provides an easily measured goal for the intervention participants, and the number of participants who achieve a predetermined percentage of weight loss could offer a useful performance indicator for monitoring the efficacy of the intervention. Furthermore, the percentage also is an easily understood goal for the patients while aiming for weight loss. Thus weight loss $\geqslant$5% was the cutoff point we used in our study. We hypothesized that a successful and sustained weight reduction could prevent the progression of OSA.

2. Methods

Our paper is a detailed and extended secondary analysis of the original 5-year, controlled, randomized, follow-up trial examining the prevention of the progression of OSA [12]. Participants in the intervention group had received a 1-year lifestyle intervention including an initial weight reduction program with 12 weeks on a very low calorie diet. In the control group, only three general dietary and exercise counseling sessions were provided. The design of the study was previously reported in detail [8]. In our analysis on the association between weight change and OSA, the data on all participants were pooled and subdivided into two groups according to the body weight change at the 5-year follow-up using the 5% weight loss as a cutoff point, which was later referred to as successful or unsuccessful groups (Fig 1) [14,15]. The study protocol was approved by the Research Ethics Committee of the Hospital District of Northern Savo, Kuopio, Finland. The participants were given both oral and written information about the trial protocol and they provided a signed informed consent. The recruitment was planned for the previous 2 years and started in October 2004 and ended in December 2006.

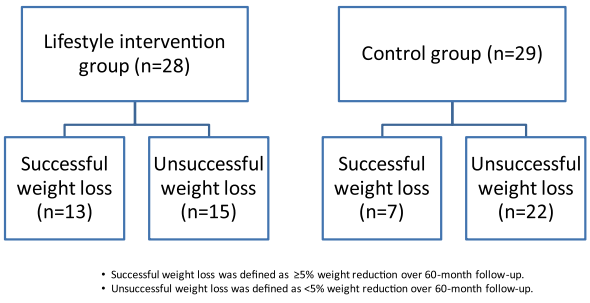

Fig. 1. Two groups according to the body weight change at 5-year follow-up using the 5% weight loss as the cutoff point (successful or unsuccessful group).

2.1. Participants

The study was conducted in Kuopio University Hospital, Finland. The study participants were consecutively recruited from the patients referred to the outpatient departments of Otorhinolaryngology and Respiratory Medicine of the Kuopio University Hospital due to a clinical suspicion of sleep-disordered breathing. They were assigned to undergo nocturnal cardiorespiratory monitoring. Weight and height were measured and the upper airways of the patients were inspected. The inclusion criteria for the initial trial were ages of 18–65 years, body mass index (BMI) of 26–40 kg/m^2, and apnea–hypopnea index (AHI) of 5–15 events per hour. The primary outcome measure was the magnitude of change in AHI during the follow-up period. The secondary outcome measures were changes in symptoms related to OSA and metabolic parameters. During the 5-year period, 24 patients dropped out of the study.

2.2. Intervention

In the original randomized study, the main goals of the dietary intervention were to reduce dietary fat to <30% of total energy and to increase the intake of fruits, vegetables, poultry, fish, and lean meat; they also needed to limit the consumption of dairy fats, fatty meats, and desserts. A detailed description of the implementation of the intervention has been previously reported [8]. In addition to the dietary counseling, the participants in the intervention group were recommended to increase their overall level of daily physical activity and endurance exercise, such as walking, skiing, jogging, or swimming. The frequency of physical activity of the participants was self-reported at the follow-up visits.

Based on the answers, the amount of physical activity was categorized to sufficient (i.e., 30 min or more exercise at least three times/week) or insufficient. The participants in the control group were only given standard care consisting of general verbal and written information about diet and physical activity at the baseline, 3-month, and 12-month follow-ups by the study nurse and physician without any specific individualized advice. During the next 4 years, no intervention or advice was offered to either of the randomization groups including at the 24-month follow-up. The study nurse regularly checked that the participants did not receive any co-intervention for OSA other than that specified in the study design.

2.3. Procedures and measurements

Nocturnal cardiorespiratory monitoring by Embletta® (Embla, Broomfield, CO) was conducted at the participants' homes in accordance with accepted guidelines for diagnosing OSA [16]. Recordings were manually evaluated and the two trained physicians (JKo, JRa) were blinded to clinical status and group. Apnea was defined as a cessation (more than 90%) of airflow for more than 10 s. Hypopnea was defined as a reduction (more than 30%) of airflow for more than 10 s with oxygen desaturation of $\geqslant$4%. AHI was defined as the number of apneas and hypopneas per hour; and mild OSA was defined as AHI of 5–15 events per hour, moderate as 15–30 events per hour, and severe as >30 events per hour [16]. The OSA was considered as objectively cured when AHI was <5 events per hour.

Validated questionnaires were used to screen for the intensity of snoring (Snore Outcomes Survey [SOS]) and daytime sleepiness (Epworth Sleepiness Scale [ESS]) [17,18]. The participants also