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Selective upper airway stimulation in older patients

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ABSTRACT

Objective: Selective stimulation of the hypoglossal nerve has proven to be an effective therapy for patients with obstructive sleep apnea (OSA). The aim of the study is to investigate the efficacy of selective upper airway stimulation (sUAS) in older adults.
Methods: All consecutive patients older than 64 years and who received an implant for sUAS were enrolled. As a control group, an equal number of patients younger than 65 years with matched apnea hypopnea index (AHI) and body-mass-index (BMI) were selected. Treatment outcome data were collected including daytime sleepiness as well as demographics with co-morbidities, BMI, adverse events and adherence to therapy.
Results: 62 patients were included. Both the control and study group did not differ significantly for AHI, BMI, and Epworth Sleepiness Scale (ESS) (28.7–28.4/h; 30.1 to 28.4 kg/m^2; 14.6 to 12.0 points); but co-morbidities were significantly higher in the study group. Our data showed no significant difference between the outcomes of study and control group for AHI, Oxygen desaturation index (ODI) and ESS (6.0–6.0/h; 7.9 to 5.5/h; 5.0 to 7.0 points). Serious adverse events did not occur in both groups and surgical implantation time did not differ.
Conclusion: sUAS leads to significant reductions of AHI, ODI and ESS in older patients. Despite higher age and more co-morbidities, surgical implantation time was not affected. Older patients showed higher usage of sUAS. Advanced age seems not to be a limiting factor for treatment outcomes of sUAS, thus indication for this treatment can also be applied to older people.

1. Introduction

Obstructive sleep apnea is the most common form of sleep-disordered breathing, characterized by frequent episodes of upper airway narrowing and collapsing during sleep, resulting in apneas and hypopneas terminated by sympathetic activation and arousals. OSA is also associated with increased likelihood of errors and accidents [1], cardiovascular morbidities such as systemic hypertension, coronary artery disease and cerebrovascular disease [2]. Further, prevalence of depression is higher in patients with OSA compared to patients without OSA [3] and OSA is regarded as a risk factor for dementia [4]. In subjects with dementia, OSA is highly prevalent and associated with functional impairment [5]. Continuous positive airway pressure (CPAP) is the first-line treatment for moderate to severe OSA even in older patients [6] or subjects with dementia. Patients with OSA who received CPAP therapy presented with a lower mortality rate compared to non-treated/non-compliant patients [7]. But the limiting factor of this treatment is a very heterogeneous adherence among patients [8]. Consequently, 40% of patients have a suboptimal usage of CPAP and 20–30% of patients quit CPAP usage during the first years of treatment [9]. The acceptance of CPAP among older subjects is reported to be even lower [10,11]. Therefore effective alternative treatments are needed to be evaluated in such patients.

Selective Upper Airway Stimulation (sUAS) is a novel stimulation therapy that has proven to be an effective alternative in the treatment of OSA [12]. Up to now the clinical outcome of sUAS has been investigated generally for all patients who fulfilled the criteria for surgical indication [12], but little is known concerning the outcome in older adults. An older person is defined as someone aged 65 years or more [13]. Structural changes of the upper airway (UAW) and an increase of pharyngeal resistance due to aging processes could explain the higher prevalence numbers in older people. The leading changes in aging patients are an increase of fat tissue around the upper airway and a reduced sensitivity of upper airway reflexes. Since advanced age is associated with more comorbidities, it is important to carefully examine all the other factors that come with advanced age when investigating

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the clinical outcome of sUAS in older people. It could be speculated that older patients may present less response to sUAS due to the decrease in genioglossus muscle strength, the key muscle for anterior tongue protrusion [14].

The aim of the study was to investigate the effectiveness of upper airway stimulation in the treatment of OSA and the persistence of effectiveness as well. Effectiveness was defined as a reduction of the AHI below 15 events per hour.

2. Material and methods

2.1. Patient selection

A consecutive cohort of all patients older than 64 years with moderate to severe OSA, who received an implant for sUAS since June 2014 at two departments of otorhinolaryngology at university hospital level, were enrolled. An AHI between 15/h and 65/h was qualifying for inclusion. There was no BMI cut-off in this cohort which explains the inclusion of patients even with a BMI above 35 kg/m [2] in contrast to the German- Postmarket study [15,16]. In addition, a control group of the same size consisting of non-geriatric patients who already received an implantation of a sUAS device with AHI matched were analyzed. Preoperative screening included home sleep tests (HST), clinical examination, and drug-induced sleep endoscopy (DISE) to rule out complete concentric collapse at the level of the soft palate [17,18]. The ESS was used for evaluation of daytime sleepiness. Patients were excluded if pronounced anatomical abnormalities preventing the effective use of sUAS were identified during clinical examination (e.g. enlarged tonsils). The Charlson index was used for better comparison of co-morbidities [19]. For qualifying as a control group, main aspect was to achieve a matching with study group for initial BMI and AHI. Similar group size was regarded as relevant for useful data interpretation. Informed consent was obtained for each patient.

2.2. Upper airway stimulation system

Qualified participants underwent surgical implantation of the sUAS system (Inspire II Upper Airway Stimulation System, Inspire Medical Systems, Maple Grove, Minnesota, USA) as previously described [20]. The sUAS system was implanted on the patient's right side under general anesthesia. Three surgical incisions are required for the placement of the components of the sUAS system. The stimulation lead is placed around selected hypoglossal nerve fibers responsible for tongue protrusion via a horizontal upper neck incision. A second incision is required inferior to the clavicle to create a pocket to accommodate the implanted pulse generator (IPG). The sensing lead, enabling detection of breathing efforts to generate synchronized hypoglossal nerve stimulation, is placed via a third incision on the right lateral chest wall. Proper functioning of the complete system was ascertained prior to closure. In general, the implantation is completed in about 90–120 min and always performed in general anesthesia. One month after surgery, the system is activated. This contains several technical checks including the sensing of the breathing cycle and the voltage thresholds the patient's tongue provides a clear protrusion. After several weeks of customization, a polysomnographic adjustment is done for appropriate voltage and sensing settings. Six and 12 months after implantation, an outpatient visit provides changes of daytime sleepiness and OSA using a HST. This appointment covers as well usage hours control and helps to identify difficulties in therapy use.

2.3. Follow-up

Follow-up visits were scheduled at months 1, 2, 6 and 12. At month 1 after surgery, the device was activated and patients were instructed in the use of the controller to initiate and terminate the therapy for nighttime home use. Patients were instructed to increase stimulation strength gradually from the initially programmed amplitude, and followed by a phone call one week later for the acclimatization status of therapy. After one month of sUAS therapy, a titration of the stimulation during an 18-channel inpatient polysomnography (PSG) according to the American Academy of Sleep Medicine (AASM) guidelines from 2012 was performed (month 2). An HST was performed at months 6 and 12. The same scoring criteria were used for all sleep studies: Hypopneas were scored based on a 30% reduction in airflow and 4% oxygen desaturation. Apneas were scored based on a 90% reduction in airflow. The outcome measurements and the classification of responders and non-responders were defined in dependence on the criteria postulated by Sher et al. [21]. Adverse events were recorded during the whole observation interval. Every telemetry read-out provides the total usage hours of activated therapy with a calculated weekly usage.

2.4. Statistical analysis

The reduction of the AHI below a value of 15 was determined as clinically relevant. Assuming a margin of error of 5% and a confidence level of 95% a response rate of 50% would require a sample size of 52 subjects. Variables were checked regarding assumptions underlying the use of parametric and non-parametric statistics, and analyzed accordingly. Results were summarized as means ± standard deviation. Statistical analysis is by chi square test for categorical data, and t-tests and Mann-Whitney *U* test for approximately normally distributed data, respectively. Paired t-tests were used for comparing paired observations within individuals. For group analyses, independent group-tests were used. The alpha-level of significance was set at 0.05 (two-tailed).

Analyses were performed using SPSS version 22.0 statistical software (SPSS Inc., Chicago, Il, USA).

2.5. Statement of ethics

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later revision.

3. Results

Overall 62 patients were included in this trial. For the study group describing the older subjects, every patient receiving an implantation

Table 1
Patients' characteristics at enrollment and implantation and comparison of study versus control group.

median ± standard deviation (range)	Study group n = 31	Control group n = 31	p value
Age (years)	70.0 ± 4.0 (65–80)	53.0 ± 9.1 (28–64)	
Gender (male/female)	24/7	28/3	
Body-Mass-Index (kg/m^2)	30.1 ± 3.5 (23.7–38.7)	28.4 ± 3.8 (21.4–37.0)	p = 0.042
Epworth Sleepiness Scale (points)	14.6 ± 5.1 (3–24)	12.0 ± 5.0 (4–21)	p = 0.159
Charlson Index (points)	1.0 ± 1.3 (0–4)	0.0 ± 0.8 (0–3)	p = 0.075
Apnea-Hypopnea-Index (events per hours)	28.7 ± 13.0 (16.2–64.9)	28.4 ± 10.6 (17.5–54.4)	p = 1.000
Oxygen-Desaturation-Index (events per hours)	27.0 ± 12.3 (12.1–62.0)	25.3 ± 13.2 (10.0–54.8)	p = 0.803