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Original Research Article

Inter-Relationship of Neurocognitive Dysfunction and Obstructive Sleep Apnea in Completely Edentulous Patients

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Abstract:

Purpose: To record the incidence of cognitive dysfunction in edentulous patients suffering from obstructive sleepapnea (OSA) and establish a plausible hypothesis to explain the correlation of cognitive dysfunction and OSA.

Materials and Methods: In this study, 315 edentulous patients (aged 60 to 65 years) visiting the outpatient department at Saraswati Dental College, Lucknow were recruited from January 2021 to October 2023. Prosthodontic Diagnostic Index (PDI) classification was used to assess the intraoral condition to relate it with the span of edentulousness. The BERLIN questionnaire and Epworth Sleepiness Scales were used to diagnose sleep-disordered breathing, following which the patients were put through all-night polysomnography. The apnea-hypopnea index (AHI) scores were derived. Mild and moderate OSA patients were classified into mild, moderate, and severe cognitive dysfunction based on SGRQ-C and SCD. Data were tabulated according to a new classification (Cognitive Dysfunction of Dental Sleep Medicine Patients [CDDSMP] Classification) designed specifically for this study. Data were analyzed using SPSS v15.0. Scores were tabulated as mean ± SD and median [IQR] values. Change from baseline was analyzed using Wilcoxon signed rank test.

Results: Mean scores at different time intervals were 3.03 ± 1.76 (3 months), 2.98 ± 1.80 (6 months), and 2.81 ± 1.84 (9 months). The median [IQR] values of scores at all time intervals except 9 months were 3 [1 to 5]. At 9 months, median [IQR] was 2 [1 to 5]. A significant change in scores was observed in the 3-month interval (p _ 0.001).

Conclusions: The severity of OSA and neurocognitive dysfunction could be directly related to the PDI classification and the span of edentulousness of the patient and modified mandibular advancement device treatment significantly improved the patients' condition, which was reflective from 3 months post-intervention itself.

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Introduction

Tooth loss has been correlated with a wide array of comorbid conditions (e.g., malnutrition, obesity, cardiovascular disease, rheumatoid arthritis, pulmonary diseases, cancer, and even mortality). [1] The oral cavity is virtually a reflection of the systemic health status of the patient. Complete tooth loss, also defined as edentulism, leads to a collapse of the vertical maxillomandibular relationship and a gross reduction in the volume of the oral cavity and the oropharynx due to reduction of lower facial height and mandibular rotation. [2,3] Previous studies have postulated that increased pharyngeal collapsibility is a major cause of obstructive sleep apnea (OSA).[4-6] It results from the combination of anatomical abnormalities of the upper airway with changes in neural activation mechanisms. Several structural changes in facial morphology (e.g., posteriorly located pharyngeal walls, retrognathic mandible, and enlarged tongue and soft palate morphology) have been implicated in OSA pathogenesis. [7,8,10-13] OSA is a sleep disorder characterized by interruptions in breathing or instances of shallow or infrequent breathing during sleep. [14-18,20] Each pause in breathing, called an apnea, can last from at least 10 seconds to several minutes, and may occur 5 to 30 times or more in an hour. Each abnormally shallow breathing event is called a hypopnea. Sleep apnea is often diagnosed using an overnight sleep test called a polysomnography (PSG), or "sleep study." This test measures various body functions including airflow, blood oxygen levels, breathing patterns, electrical activity of the brain, eye movements, heart rate, and muscle activity. [22-30] Earlier efforts at investigating the effects of OSA on cognitive functions [31-35,40-42] have demonstrated that

recurrent apnea, sleep fragmentation, and nocturnal hypoxemia may affect cognitive function and quality of life in these patients. Different stages of cognitive impairment have been found in OSA patients. [36-44]It is still controversial as to which factor, viz., sleep fragmentation, apnea-hypopnea index (AHI), or the degree of upper airway obstruction, would lead to cognitive impairment. The utility of a complete denture prosthesis modified for nocturnal use as a mandibular advancement device (MAD) has already been demonstrated.45,46 An increase in pharyngeal volume effected by this device has also been shown to effectively ameliorate OSA in edentulous patients.47 The present study was aimed at recording the incidence of cognitive dysfunction in edentulous OSA patients and establishing a plausible hypothesis to explain the correlation of cognitive dysfunction and OSA and period of edentulism.

Materials and Methods

In this study, completely edentulous patients (aged 60 to 65 years) visiting the prosthodontic clinic at Saraswati Dental College, Lucknow were included. Of these, patients with systemic diseases and habits (e.g., hypertension, diabetes, COPD, asthma, endocrinal disorders, smokers, and alcoholics) were excluded. After applying the inclusion and exclusion criteria, 315 patients were recruited from January 2021 to October 2023. Each patient was provided a brief description of the study along with educational materials on OSA, after which an informed consent for participation was obtained. The protocol was approved by the Institutional Human Ethical Committee and Institutional Research & Development Committee and was in accordance with ethical principles of the World Medical Association Declaration of Helsinki.

All 315 edentulous patients were subjected to the Prosthodontic Diagnostic Index (PDI) classification to determine the degree of atrophy of oral tissues and to correlate this to the degree of collapsibility. This would help assess a possible relationship between the span of edentulousness and the severity of OSA at a later stage. Following this, all patients were subjected to the BERLIN Questionnaire and the Epworth Sleepiness Scale, to reconfirm

the affliction of disturbed sleep. Since these two subjective tests were positive for the entire patient study group, all 315patients were subsequently subjected to all-night polysomnography (PSG). Based on the Apnea-Hypopnea Index (AHI) score the patient cohort was divided into three groups: mild, moderate, and severe OSA.

The St. George's Respiratory Questionnaire – Concise version (SGRQ-C) and Subjective Cognitive Decline – Questionnaire (SCD-Q) were used to determine the degree of cognitive impairment in the three groups of edentulous OSA patients. To facilitate understanding of this study, the data obtained were tabulated according to a proposed new classification – Cognitive Dysfunction of Dental Sleep Medicine Patients (CDDSMP) Classification. The scoring criteria for the CDDSMP classification is as listed in Table 1.

Table 1 Scoring criteria for the CDDSMP classification

Normal OSA	0
Normal NCD (neurocognitive disorder)	0
Mild OSA	1
Mild NCD	1
Moderate OSA	2
Moderate NCD	2
Severe OSA	3
Severe NCD	3

Scoring scale was designed in the following manner:

Normal (Both Normal) – 0

Mild (Both mild/any 1 normal) – 1 to 2

Moderate (Both moderate/any 1 mild/normal) – 3 to 4

Severe (Both severe/any 1 moderate) – 5 to 6

All patients in this study were rehabilitated with complete dentures and provided detailed instructions on the use of the denture prosthesis as a MAD during sleep at night. The efficacy of the MAD in controlling OSA was assessed periodically (3-, 6-, and 9-month intervals), and the data recorded.

Statistical Analysis: Data were analyzed using SPSS v15.0. Scores were tabulated as mean ± SD and median interquartile range (IQR) values.

Distribution of severity grades has been shown as frequency and percentages. As the data were ordinal in nature, a nonparametric evaluation plan was followed. Change from baseline has been analyzed using Wilcoxon signed rank test. The confidence level of study was kept at 95%, and a '*p*' value less than 0.05 indicated a statistically significant change.

Results

At baseline, CDDSMP severity scores ranged from 1 to 6 with a mean value of 3.06 ± 1.73 and median value of 3 [IQR 1to 5]. At all the subsequent follow-up intervals the CDDSMP scores ranged from 0 to 6. Mean CDDSMP scores at different time intervals were 3.03 ± 1.76 (3 months), 2.98 ± 1.80 (6 months), and 2.81 ± 1.84 (9 months). The median [IQR] values of CDDSMP scores at all the time intervals except 9 months were 3 [1 to 5]. At 9 months, median [IQR] was 2 [1 to 5]. A significant change in scores was observed in the 3-month interval (p _ 0.001) (Table 2, Fig 1).

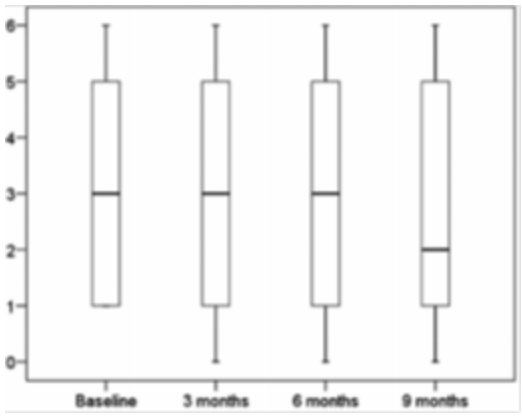

Figure 1: Box plot showing dispersion of scores at different time periods

CDDSMP severity grade scores are shown in Table 3. A statistically significant change from baseline was observed in the 3-month follow-up (p _ 0.001) (Table 3, Fig 2).

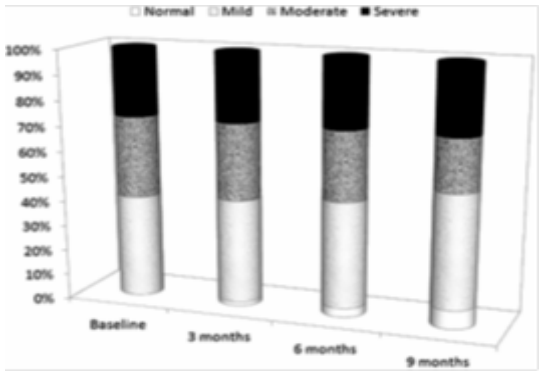

Figure 2 Severity levels at baseline and different follow-up periods

Discussion

Three hundred and fifteen (315) edentulous patients, aged 60 to 65 years, recruited for this study were chosen, based on the inclusion and exclusion criteria, at the prosthodontic clinic of Saraswati Dental College & Hospital, Lucknow, India between January 2021 and January 2023. These patients were then subjected to PDI classification to assess the span of edentulousness and the intraoral hard tissue and soft-tissue condition of the patients. Following this, BERLIN questionnaire and Epworth Sleepiness Scale were used to assess patients for sleep-disordered breathing. All 315 patients were diagnosed with sleep-disordered breathing and subjected to all night polysomnography. The AHI score varied with every patient, and they were categorized into mild, moderate, and severe OSA. The degree of cognitive dysfunction was then assessed using SGRQ-C and SCD. For ease of understanding, a new questionnaire-based classification called the Cognitive Dysfunction in Dental Sleep Medicine Patients (CDDSMP) was developed. The idea was to accrue data on PDI score, AHI, and SGRQ-C and SCD scores to classify edentulous OSA patients suffering from neurocognitive dysfunction. Until now, a questionnaire-based classification addressing these aspects had not been developed. This was an important aspect of the diagnosis and treatment plan. Earlier studies conducted on the incidence of OSA were either population based or specific to a particular race.[4,5,8,9] A hypothesis linking cognitive dysfunction to OSA and edentulism was put forth in this study. Essentially, OSA leads to disturbed sleep, which invariably has an effect on neurological functions. Lack of sleep results in homeostatic imbalance, causing abnormal motor

neuron activity.[17,19] The most convenient method of evaluating it was to assess the level of cognitive function or dysfunction. Recent epidemiologic data shows that sleep-disordered breathing is twice as frequent in men as in women.[22,26] It may be that women have fewer complaints, or are less often referred for further clinical evaluation. In this study, our finding was contradictory. Women exhibited a higher incidence of OSA, along with other systemic diseases. A plausible reason for this could be the anatomical difference between the sexes. The size of the mandible is smaller in women than in men. The upper airway diameter would also be smaller, and thus the risk of OSA markedly increased. In the present study cohort, the percentage of male subjects affected was 47.5%, whereas females constituted a larger sleep apnea group at 52.5%. Even as the precise pathogenesis of cognitive dysfunction in OSA patients remains unclear, OSA during sleep was shown to be dependent on the chemo-sensitive component of neuromuscular control of respiration and upper airway patency.

An effort has been made to hypothesize a possible correlation between OSA and cognitive dysfunction depending on the published literature and the present findings. Cognitive disorders lead to dyshomeostasis in the body, also known as cacostasis. This has a profound effect on the central nervous system as well as the peripheral organs. Various hormonal centers are affected (e.g., arginine vasopressin, corticotrophin-releasing hormone, pro-opiomelanocortin derived peptides, locus ceruleus, and autonomic norepinephrine centers).[40-44] The hormonal imbalance caused due to the activationof these centers affects growth, thyroid hormone level, the reward and fear system, wake-sleep centers of the brain, and the ventilator, metabolic, and cardiovascular systems. On the ventilator system, this hormonal imbalance leads to are duction in the reflexes (i.e., the neuromuscular control on the ventilatory system). This in turn leads to decreased genioglossal control causing pharyngeal collapse during sleep. This pathway finally causes OSA due to pharyngeal collapse (Fig 3).

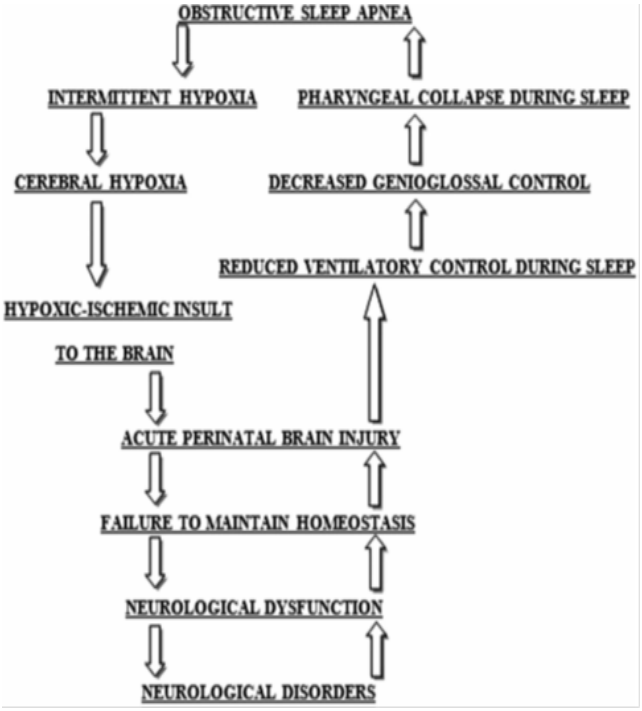

Figure 3 Hypothetical pathway to prove the increased incidence of OSA in patients with cognitive dysfunction.

Previous studies [29,30] have demonstrated that airway collapse leads to inhibition of function of the muscles of the upper airway, which in turn leads to progression in the passive collapse. The results of this study confirm the findings of a recent study by Lipford et al [43] in which OSA patients were found to have multifocal grey matter loss within specific memory centers in the hippocampus, and these changes were affected by neurotoxins (e.g., glutamate, which acts on the N-methyld- aspartate receptors) [43] and precipitated neurocognitive dysfunction. Relating this to this study, it can be stated that this damage causes perinatal brain injury and leads to neurological dysfunction which, in turn, alters the homeostasis of the body and brings about reduced ventilatory control during sleep and subsequent collapse of the pharyngeal airway. Thus, the relation between OSA and neurocognitive dysfunction found in the present study has strong support from previous research based on the

findings of earlier studies. [46,47] All patients of this study cohort were rehabilitated with complete dentures, which were used as MAD during sleep at night, and the reduction in severity of OSA and cognitive dysfunction was demonstrated.

Conclusion

This study found that the incidence of cognitive dysfunction in edentulous OSA patients was significant. A hypothetical correlation between neurocognitive dysfunction and OSA was derived with support from previously published literature. A novel method was developed for assessing prosthodontically rehabilitated OSA patients suffering from cognitive dysfunction by means of the Cognitive Dysfunction in Dental Sleep Medicine Patients (CDDSMP) questionnaire. Prosthodontic rehabilitation and use of MAD was shown to have a positive effect on the severity of OSA and cognitive dysfunction.

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