Research Progress of Chronic Rhinosinusitis Complicated with Sleep Disorders

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Abstract: Sleep is a functional state alternating with wakefulness. In light of the physiology, the main function of sleep is to promote mental and physical recovery. In general, sleep is very important for one's physical and mental health. As a chronic disease, sleep disorder has aroused universal concerns because of its impact on life quality. This paper summarized and analyzed the sleep disorders related data of patients with chronic rhinosinusitis and as follows.

***Keywords*:** chronic rhinosinusitis, sleep disorder, research progress

Studies have shown that non-rem sleep is mainly used for physical recovery, while rem is mainly used for mental recovery [1,2]. It has been reported that about 50% ~ 90% patients with chronic rhinosinusitis (CRS) developed sleep disorders[3]. Sleep impairment in CRS patients can be attributed to several factors, including nasal congestion and inflammatory processes. There is a close relationship between CRS and sleep disorders. Therefore, while performing treatment for CRS, it is also necessary to pay attention to the sleep health of patients, which is of great significance to improve the prognosis of the disease and the quality of life of patients. This paper discusses the relationship between CRS and sleep disorder and its treatment.

1. Epidemiological investigation

Chronic rhinosinusitis is a common clinical chronic disease with a disease course of more than 12 weeks. The main symptoms include nasal congestion, runny nose, head and face pain, loss or disappearance of sense of smell, dizziness, etc., which often leads to decreased immune function, weakened resistance, memory loss, etc., thus affecting individual work, learning and quality of life [4-8].

A cross-sectional survey found that the overall prevalence of CRS in China is about 8%, and the total number of patients has exceeded 100 million, with slightly higher prevalence of males (female: 7.28%, male: 8.79%). In addition, CRS is also found to be prevalent in patients with allergic rhinitis, chronic obstructive pulmonary disease, asthma and gout[9]. In clinical practice, many CRS patients complain of poor sleep quality and suffer from sleep disorders for a long time.

According to investigation, the prevalence of sleep disorders in CRS patients ranges from 50% to 90% [10]. Meanwhile, CRS patients are also prone to emotional disorders, among which the prevalence of anxiety disorders and depression is 13.22%-48.3% and 11%-76.2% respectively [11-18], which will lead to the deterioration of sleep quality. Therefore, there is a interactive relationship between CRS and sleep disorders, and we should not only reduce the clinical symptoms of patients with CRS, but also pay attention to their mental health and social functioning.

2. The relationship between CRS and sleep disorders

Sleep disorders are a kind of diseases related to breathing, including sleep apnea syndrome, restless leg syndrome, sleep shortening and sleep deprivation caused by insomnia, difficulty in falling asleep, early awakening, sleep deprivation and other diseases[19]. In clinical practice, there are many patients with CRS who complain about poor sleep quality and inability to concentrate, and thus their daily work and life are seriously affected. Therefore, sleep disorders related to CRS have become a hot research topic in recent years.

A large number of studies have shown that CRS is significantly associated with sleep disorders[11,20-21]. The association between CRS and sleep disorders was further confirmed by a study based on a large number of population conducted in Europe, which found that out of 26,647 subjects, there were 2,249 people with CRS. Patients with CRS were more vulnerable to sleep problems than those without CRS. The study also discovered that compared with patients without CRS, CRS patients show a higher risk of early rise, excessive daytime sleepiness, induced dyspnoea and snoring[22]. At the

same time, a 5-year follow-up study was conducted in Taiwan by choosing 971 patients with sleep disorders as the study cohort and 4855 patients without sleep disorders as the control cohort. The results showed that 161 patients (2.76%) were subsequently diagnosed with CRS, and the adjusted hazard ratio (HR) for subsequent CRS in patients with sleep disorders was 3.18(95% confidence interval:2.27 to 4.45) compared with those without sleep.

It was also found that patients with sleep disorders, regardless of gender, had a higher risk of CRS compared with patients without sleep disorders[23]. In addition, a foreign epidemiological survey also found that insomnia symptoms may be one of the risk factors for CRS [24], suggesting that patients with sleep disorders have a higher risk of developing CRS. In recent years, more and more studies have provided evidence that patients with CRS have poor subjective sleep quality compared with patients without CRS, and provided objective measures of sleep dysfunction [25,26]. A prospective study of sleep and CRS demonstrated an association between sleep and CRS by using objective indicators of sleep dysfunction.

In this prospective multi-institution study, patients with CRS were compared with a non-disease control group. The Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (EpSS) were used to measure sleep subjectively. The objective indicators of sleep were determined by conducting a home based sleep study on all subjects. CRS patients were found to be significant in both subjective and objective sleep disorders.

In light of subjectivity, the total scores of PSQI and EpSS in CRS patients were significantly lower than those in CRS patients. In light of objectivity, even after confounding factors were regulated, there were more frequencies for CRS patients in snoring, significantly increased the times of waking-up, and thus the latency of REM sleep will increase accordingly. In addition, the mean oxygen saturation of patients at night and night decreased [27].

After adjusting variables (age, sex, family income, residence type, education, depression, alcohol, allergic rhinitis, chronic otitis media, angina OR myocardial infarction, asthma, chronic obstructive pulmonary disease, bronchiectasis and gastric ulcer), Jin Zhengwen and others demonstrated that 5-hour sleep duration was significantly associated with CRS (OR=1.502; 95%CI=1.164-1.938), and only the older subgroup (≥50 years old) was found to have a higher incidence of CRS with shorter sleep duration (≤5 hours) [28]. Notably, Jessica W et al found that African-American CRS patients had a higher risk of sleep disorders than white CRS patients [29].

In addition, CRS patients in Latin America have been found to be at increased risk of poor sleep quality and sleep disruption, and this study also found a significant shift to late sleep in CRS patients[30]. These studies have demonstrated a significant association between sleep disorders and CRS in systematic evaluations, cross-sectional studies, and prospective trials.

3. The importance of comorbid sleep disorders in CRS patients

3.1 Sleep disorders and quality of life in CRS patients

Comorbidities of sleep disorders in CRS lead to a significant reduction in quality of life. In one study, CRS patients with poor sleep quality obtained significantly lower scores on quality of life in both the naso-sinusitis disability index ($P<0.001$) and 22 sinus outcome tests ($P<0.001$). These two scores were significantly positively correlated with total sleep quality score and sleep quality-related variables, including sleep latency, sleep duration, sleep efficiency, sleep drug demand and daytime dysfunction[31]. These studies suggest that sleep deprivation may be the driving force for surgical treatment in patients with CRS, since patients with more severe sleep disturbances reported by CRS are more likely to choose FESS and continue medical management after surgery.

3.2 Sleep disorders and mental health in CRS patients

Studies have shown that CRS patients with sleep disorders will develop more severe anxiety[11]. Besides, depression is also discovered with frequent occurrence in CRS patients. The study adopted Patient Health Questionaire 2(PHQ2) to identify patients with potential risks for depression. Pain experience was measured using the Simple Scale of Pain Scale (BPI-SF) and the Simple Scale of McGill Pain Questionnaire (SF-MPQ), and sleep quality was assessed using the Pisburgh sleep Quality Index (PSQI)

3.3 Sleep disorders and cognitive function in CRS patients

Soler et al. showed that patients with CRS had significantly lower scores on the Cognitive Failure Questionnaire (CFQ) than that of healthy control group, and that CFQ score was significantly associated with sleep quality as measured by PSQI ($R=0.557$, $P<0.001$)[32]. These studies suggest that sleep deprivation in CRS may lead to a decline in cognitive dysfunction. However, the exact mechanism of sleep disorders in CRS patients leading to cognitive dysfunction remains to be studied.

4. Treatment of CRS combined with sleep disorders

Given the high prevalence of poor sleep quality and associated health problems in CRS patients, there is growing interest in the results of different treatments used for the disease. Treatment of CRS with sleep disorders includes medical and surgical treatment, also known as continuing medical management. One study was conducted to observe how CRS affects sleep. In this study, 64 patients with CRS who opted for continuing medical management were assessed for sleep quality using the PSQI before treatment and after 6 months of treatment. As a result, it showed that continuing medical management failed to improve subjectively reported sleep quality of CRS patients as measured by PSQI. It may even lead to deterioration of PSQI measurement scores in CRS patients [33].

However, there is a lack of criteria in this study for the strict control of drug therapy in CRS patients, thus the conclusion on the breadth can be confined. In addition, it is not known whether there are improvements on sleep quality in CRS patients who have just received medication. Therefore, future studies should be conducted on the impact of individual medications on sleep associated with CRS, especially those that target specific mechanisms.

More and more studies have proved that nasal endoscopic surgery can effectively improve the sleep quality of CRS patients. Previous studies have shown that patients with CRS after FESS, 22-item sino-nasal Outcome Test snot-22 or Rhinosinusitis Disability Index (RSDI) significantly improved sleep scores[34,35]. In recent years, increasing number of evidences have reconfirmed these results, suggesting that FESS therapy for CRS leads to significant improvement in sleep-related symptoms assessed by SNOT-22 [36].

To further study sleep quality in CRS patients, researchers adopted multiple sleep assessment questionnaires, including Epworth Sleepiness Scale (EpSS) and Pittsburgh Sleep Quality Index (PSQI). Among them, PSQI is the most widely used questionnaire, which is a standardized questionnaire used to evaluate the sleep breathing quality of patients in the recent 1 month with high sensitivity and specificity. The questionnaire is a measurement method composed of 19 project self assessment of sleep quality and duration, patients were asked to recall the sleep quality one month prior to the end of the survey.

PSQI produces an overall score (Range: 0-21) and seven component scores, including: sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disorders, sleep medication use, and daytime dysfunction (range: 0-3). The higher the PSQI score, the more severe the sleep disorder. A PSQI score of 5 or lower is considered to be the threshold for "good" sleep quality, while a score of more than 5 is considered to be "poor" sleep quality [37].

Multiple prospective studies have assessed sleep outcomes after FESS in patients with CRS, showing significant improvements in sleep quality in both PSQI and EpSS. In addition, a prospectively conducted study showed that postoperative nasal resistance in CRS patients was significantly reduced (P= 0.01), postoperative snoring score was significantly improved (P= 0.01), and postoperative mean daytime sleepiness score was significantly improved, but there was no significant difference between preoperative and postoperative mean apnea hypopnea index (P=0.55) [38].

The results of a systematic review showed that FESS had a statistically significant effect on two validated sleep instruments (i.e., EpSS and PSQI), but the AHI improvement was small after FESS, suggesting that nasal surgery may be a useful adadjuvant for the prevention and treatment of obstructive apnea in patients with CRS [39]. In a recent meta-analysis, it seems that FESS can possibly improve sleep quality and associated symptoms in CRS patients when sNOT-20 or SNOT-22 was used to analyze preoperative and postoperative outcomes. However, since SNOT-20 or SNOT-22 is only sued as sleep quality assessment tools in this conclusion, more comprehensive studies should be conducted to confirm the true impact of surgery on sleep quality [40].

Although the current literature suggests that FESS may lead to improvements in sleep quality, the mechanisms by which these improvements may occur remain unclear and further research is needed to elucidate the effects of FESS on sleep quality in patients with CRS.

5. Conclusion

At present, sleep disorders have become a major problem affecting public health. More and more evidence supports the relationship between sleep deficiency and CRS, which seriously affects the quality of life of patients and imposes a heavy burden on society and families. Therefore, top priority should be given in this regard. Multiple studies have shown that people with CRS are more likely to have poorer sleep quality than the general population. In addition, subjective measures of sleep quality in CRS patients improved after FESS.

However, there are limited studies on objective sleep quality outcomes based on FESS treatment. In addition, the pathogenesis of CRS with sleep disorders remains unclear, so more prospective studies are needed for investigation. Our understanding of the relationship between CRS and sleep dysfunction is still in its infancy. Further studies are needed to

assess objective outcomes after treatment so as to further explore the mechanisms leading to poor sleep quality in CRS patients. Finally, efforts were made to improve the sleep problems of patients, thus improving the prognosis and quality of life of patients.

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