โรคร่วมระหว่างภาวะซึมเศร้าและภาวะหยุดหายใจขณะหลับจากการอุดกั้น

โชติมันต์ ชินวรารักษ์*, Diego Garcia-Borreguero**
**คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช*
***Sleep Research Institute, Madrid, Spain*

บทคัดย่อ

ภาวะซึมเศร้าและภาวะหยุดหายใจขณะหลับจากการอุดกั้น เป็นความผิดปกติที่พบบ่อยในเวชปฏิบัติ อาการของภาวะซึมเศร้าและภาวะหยุดหายใจขณะหลับจากการอุดกั้น สามารถทับซ้อนกันได้หลายอาการ อาทิเช่น นอนไม่หลับ อ่อนเพลีย ง่วงนอนกลางวัน สมาธิไม่ดี ความผิดปกติแต่ละโรคสามารถส่งผลกระทบต่อกันทั้งสองทิศทาง แพทย์จึงจำเป็นต้องมีการประเมินที่ครอบคลุมซึ่งประกอบไปด้วยการซักประวัติ การตรวจประเมินทางเดินหายใจส่วนต้น และการตรวจการนอนหลับ เมื่อสงสัยว่ามีสองภาวะนี้ร่วมกันเพื่อการวินิจฉัยและวางแผนการรักษาอย่างเหมาะสม ปัจจุบันแม้ยังไม่มีคำแนะนำหรือแนวปฏิบัติการรักษาโรคร่วมระหว่างภาวะซึมเศร้าและภาวะหยุดหายใจขณะหลับจากการอุดกั้น อย่างไรก็ตามแพทย์ควรให้การรักษาควบคู่กันตามมาตรฐานของแต่ละความผิดปกติเพื่อให้ได้ผลลัพธ์ทางการรักษาที่ดียิ่งขึ้นแก่ผู้ป่วย

คำสำคัญ ภาวะซึมเศร้า ภาวะหยุดหายใจขณะหลับจากการอุดกั้น โรคร่วม

Corresponding author: โชติมันต์ ชินวรารักษ์
คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช
E-mail: chotimanchin@gmail.com
วันรับ : 13 มิถุนายน 2566 วันแก้ไข : 26 ตุลาคม 2566 วันตอบรับ : 30 ตุลาคม 2566

The Comorbid Between Depression and Obstructive Sleep Apnea

Chotiman Chinvararak*, Diego Garcia-Borreguero**
*Department of Psychiatry, Faculty of Medicine Vajira Hospital, Navamindradhiraj University
**Sleep Research Institute, Madrid, Spain

ABSTRACT

Depression and Obstructive sleep apnea (OSA) are common disorders in clinical practice. There are many overlapping symptoms of depression and OSA, such as insomnia, fatigue, daytime sleepiness, and poor concentration. Each disorder can affect the other bi-directionally. A comprehensive assessment, including history taking, upper airway evaluation and sleep test, is mandatory when physicians suspect these comorbid conditions. Currently, there is no treatment guideline for comorbid depression and OSA; however, parallel treatment with the standards of each disorder should be provided to patients to achieve better therapeutic outcomes.

Keywords: Depression, Obstructive sleep apnea, Comorbidity

Corresponding author: Chotiman Chinvararak
E-mail: chotimanchin@gmail.com
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Introduction

Depression is one of the most common mental disorders. The World Health Organisation (WHO) reports that the 12-month prevalence of major depressive disorder is approximately 6%.[1] In addition, a study by Read et al. (2017) found that having multimorbidity or chronic physical conditions increases the risk of depression by 2 - 3 times compared to those without multimorbidity.[2] Long duration of untreated depression is also associated with an increased risk of suicidality.[3]

Obstructive sleep apnea (OSA) is the most common sleep-related breathing disorder. Its cardinal characteristics are the repetitive, partial, or complete collapse of the upper airway during sleep associated with arousals with or without oxygen desaturations.[4] The prevalence of OSA in the general population when using the apnea-hypopnea index (AHI) higher or equal to 5 events per hour is 9 - 38%.[5] In addition, several studies revealed that OSA is associated with cardiovascular disease, metabolic disease, depression, and neurocognitive disorders higher.[6-8]

There are many overlapping symptoms of depression and OSA, such as insomnia, fatigue, daytime sleepiness, and poor concentration.[9-11] According to Gupta et al.'s study, the clinic-based prevalence of comorbid major depressive disorder (MDD) in OSA patients is 0 - 66%, and the population-based prevalence was 7.4 - 44%.[12] In addition, Tiensuntisook and Awiruthworakul found that the clinic-based prevalence of comorbid MDD in Thai OSA patients is 29.7%.[13] Although co-occurring depression and OSA mechanisms remain unclear, many studies have found bidirectional associations between them.[14-17] OSA results in greater depression severity. In turn, depression results in poor OSA treatment adherence. Therefore, it is crucial to tackle both conditions concurrently in clinical practice.

Bidirectional association

OSA may increase the risk of depression through the following mechanisms[14,15,18] 1) Sleep fragmentation and intermittent hypoxia lead to frequent nocturnal arousal and poor sleep quality 2) Intermittent hypoxia results in the production of pro-inflammatory cytokines, for example, interleukin 1 (IL-1), interleukin 6 (IL-6), and tumour necrosis factor (TNF). Hypoxia causes neuronal injury. Neuroimaging studies found structural and functional brain abnormalities among OSA patients in frontostriatal and limbic areas, which play a significant role in emotional regulation.

Common biological abnormalities found in OSA and depression are an abnormal function of serotoninergic neurotransmission and cortisol hyperarousal. 1) Reduced function of serotonin was found in both conditions. Serotonin is involved in mood regulation, sleep-wakefulness cycle, and controlling of upper airway motor dilator neurons. Decreased serotoninergic function links with depressed mood and a higher risk of upper airway collapsibility. 2) Hyperarousal of the cortical results in difficulty falling asleep and maintaining sleep. When insomnia symptoms worsen, depression will deteriorate as well. In addition, a low arousal threshold can worsen OSA severity from the destabilisation of ventilatory control or ventilatory overshoots.[10-11]

Depression can likewise affect the severity of OSA. According to studies of sleep architecture, depressed patients have an increase in REM sleep time. This phenomenon leads to a more extended period of REM-sleep muscle atonia, which intensifies OSA symptoms.[19-20] Additionally, loss of interest and reduced physical activity among depressed patients or hypersomnia and increased appetite among atypical-type depressed patients can lead to weight gain and obesity, which are the important risk factor of OSA.

Assessment

Since MDD and OSA occur together frequently, clinicians should always be aware of this. The main symptoms of OSA include snoring, witnessed apneas, gasping/choking at night, nocturia, unrefreshing sleep and morning headaches. Widely used OSA screening questionnaires include STOP-BANG, the Berlin questionnaire, and the Epworth sleepiness scale (ESS). Furthermore, systemic physical examination is mandatory

to assess a sign of upper airway narrowing and discover OSA risk factors such as obesity, hypertension, diabetes milieus, respiratory, cardiovascular, and neurological abnormality.[11,21] An objective test is required to confirm the OSA diagnosis. The test includes polysomnography (PSG), or home testing with portable monitors (PM), according to AASM guidelines.[21-22]

Core symptoms of major depressive disorder (MDD) are depressed mood, loss of interest or anhedonia, feelings of worthlessness and thought of death.[3,23] Comprehensive psychiatric evaluation based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) is required to diagnose MDD.[23] Assessments used to screen and track symptoms of depression in patients aged 18 and over include Patient Health Questionnaire (PHQ-9)[24], the Beck depression inventory (BDI)[25], the Hamilton rating scale for Depression (HRSD)[26] and Montgomery-Asberg Depression Rating Scale (MADRS).[27] However, there are still no specific questionnaires for assessing depression in OSA.

Overlapping symptoms of OSA and MDD include daytime sleepiness, fatigue/loss of energy, poor concentration, irritability, psychomotor retardation and weight gain.[10] Some cases of treatment-resistant depression may be caused by undiagnosed OSA.

Management

Currently, there are no standard practices for treating OSA patients with comorbid depression, but treating both conditions in parallel with the standards of each disorder certainly provides better therapeutic outcomes. Clinically interesting points in the treatment of the two conditions include:

1) Several studies found that treating OSA patients with comorbid depression with CPAP can improve mood, cognitive and insomnia symptoms.[28-31]

2) Effective treatment of depression may improve acceptance of OSA treatment and increase motivation for treatment, such as adherence to positive airway pressure (PAP) use.

3) Using sedative or hypnotic agents, especially benzodiazepines to aid sleep or reduce anxiety, can worsen OSA symptoms due to muscle relaxation and respiratory depression. These medications can also cause daytime drowsiness. Furthermore, long-term use of benzodiazepines also disturbs sleep architecture, particularly decreasing non-rapid eye movement stage 3 (NREM3) and rapid eye movement (REM) sleep.[32]

4) Insomnia is a common symptom that affects both depression and OSA. Insomnia is negatively correlated with CPAP adherence and improvement of depression. Although there is no standard guideline yet to treat both comorbidities, studies revealed that cognitive behavioral therapy (CBT-i), in addition to having an improved effect on insomnia symptoms, also improves mood symptoms.[10-11] Therefore, clinicians should consider CBT-i as one option of treatment if it is possible.

5) Non-benzodiazepine hypnotics or z-drugs, namely zolpidem, zaleplon and eszopiclone, have been found to help patients initiate sleep faster without affecting sleep architecture and AHI. A study by Wang et al. (2021) found that using eszopiclone increased CPAP usage time by 0.62 hour (95%CI=0.26-0.98) and increased consistency in CPAP use by 12.08% (95%CI=5.27-18.88). The pooled odds ratio of eszopiclone in increasing CPAP use was 2.48 compared to a placebo (95%CI=1.75-3.52). However, there is still no clear evidence that zolpidem and zaleplon support CPAP adherence. Well-designed studies are needed to prove the long-term effect of z-drug use.[33]

6) A PAP education with troubleshooting management remains the standard treatment to provide all OSA patients with PAP treatment to improve PAP adherence.[21-22]

7) The effects of the use of selective serotonin reuptake inhibitors (SSRIs) on OSA symptoms are unclear. Theoretically, SSRIs function through serotoninergic neurotransmission, resulting in the suppression of REM sleep and increasing the function of the upper airway dilator muscle, which may reduce upper airway collapsibility. Nonetheless, no study has demonstrated the significant efficiency of SSRIs on OSA treatment.[34]

Furthermore, clinicians should be careful when using antidepressants with high antihistaminergic effects because of the potential consequence of substantial weight gain. Weight and metabolic parameters should, therefore, be monitored regularly.

Conclusion

It is important to be aware that depression and OSA coexist very often. In addition, the two conditions are associated bidirectionally. Therefore, a comprehensive evaluation should be made to determine the diagnoses, and in-parallel treatments for both conditions are crucial to efficient patient outcomes. Future research should focus on how to improve the accuracy of diagnosis and develop standard treatment guidelines for comorbid MDD and OSA.

Conflict of Interest

None of the authors had conflicts of interest relevant to this study.

Authors' contributions:

Chotiman Chinvararak: study design, data synthesis, writing the manuscript; Diego Garcia-Borreguero: validation and editing of the manuscript.

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