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Review Article

Prevalence of obstructive sleep apnea in patients with posttraumatic stress disorder and its impact on adherence to continuous positive airway pressure therapy: a meta-analysis

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ABSTRACT

Objective: Although some authors have recently investigated the co-occurrence of posttraumatic stress disorder (PTSD) and obstructive sleep apnea (OSA), the topic remains insufficiently studied. The aim of this meta-analysis was to detect the pooled prevalence of OSA in PTSD and its impact on adherence to continuous positive airway pressure (CPAP) therapy.

Methods: We conducted a search for articles published until August 20, 2016, in PubMed, Embase, the Cochrane Library, and PsycINFO. The literature search identified 194 articles, and 12 studies were included in the meta-analysis.

Results: The pooled prevalence rates of OSA based on different apnea–hypopnea index (AHI) criteria in PTSD patients was 75.7% (95% confidence interval [CI] = 44.1–92.5%) (AHI ≥5) and 43.6% (95% CI = 20.6–69.7%) (AHI ≥10), respectively. Subgroup analysis showed that there was a significant difference between the prevalence of OSA in veterans with PTSD compared to nonveterans or mixed samples. Patients with PTSD and OSA demonstrated significantly lower adherence to CPAP therapy (regular use: $g = -0.658$, 95% CI = −0.856 to −0.460; time of average use per night: $g = -0.873$, 95% CI = −1.550 to −0.196) compared with those with OSA alone.

Conclusions: OSA is commonly seen in patients with PTSD. Given its negative impact on the adherence to CPAP therapy, the possibility of OSA should be monitored carefully in patients with PTSD.

1. Introduction

Disrupted sleep is an often intractable symptom in patients with posttraumatic stress disorder (PTSD) [1–3]. One of the most common sleep disturbances, obstructive sleep apnea (OSA), affecting between 5% and 10% of the American general population [4,5], has been given great attention in patients with PTSD [6,7]. In one study conducted among 264 veterans seeking PTSD treatment, the rate of OSA risk was 72.7% overall, 59.7% among women, and 77.2% among men [8]. Furthermore, the results of another study showed that the rate of high-risk status for OSA was 69.2% among 195 Iraq and Afghanistan war veterans with PTSD, and the severity of PTSD symptoms was positively correlated with the risk of screening positive for OSA [9]. Although some authors have recently investigated the co-occurrence of OSA and PTSD, the results of prevalence rates of OSA in patients with PTSD were varied in different studies [6,10–14]. This variation might have been associated with the differences in diagnostic criteria for OSA using the apnea–hypopnea index (AHI) (ie, AHI ≥5 or AHI ≥10), differences in sample size, and differences in ethnicity in different studies.

In patients with PTSD, comorbid OSA is associated with worsened symptoms, quality of life, and more somnolence compared with individuals with PTSD only [15]. Patients with PTSD and OSA showed significantly lower adherence and response to continuous positive airway pressure (CPAP) therapy compared with those with OSA only [15]. In a retrospective review of 15 patients with sleep disordered breathing and PTSD, patients who were adherent to CPAP therapy showed a 75% remission in PTSD symptoms

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compared with a 43% exacerbation in PTSD symptoms among those who were nonadherent [16]. Given the adverse impacts of the comorbidity of PTSD and OSA on clinical outcomes, the possibility of OSA should be considered carefully in patients with PTSD.

Clarifying the prevalence of OSA in patients with PTSD may raise awareness of the limitations in treatment facing this patient population and encourage development of new treatment modalities. Adopting a meta-analysis could provide the advantage of combining data from many published studies in a logical manner, accurately providing an effect size that is closer to the true value compared with considering individual studies separately [17]. Although Krakow et al. [7] have elaborated the mechanism of the co-occurrence of PTSD and OSA, there is no meta-analysis regarding the prevalence of OSA in patients with PTSD and its impact on the adherence to CPAP therapy. In this study, meta-analysis of previously published articles on the prevalence of OSA in patients with PTSD and its impact on adherence to CPAP therapy were performed based on the review by Krakow et al. [7].

2. Methods

2.1. Search strategy

Two independent authors (Y.Z. and R.R.) searched PubMed, Embase, the Cochrane Library, and PsycINFO from database inception to August 20, 2016. Key words used were PTSD (ie, PTSD or posttraumatic stress disorder or trauma or stress), and OSA (ie, obstructive sleep apneas, or other apneas or obstructive sleep apnea syndrome or OSAS). Manual searches were also conducted using the reference lists from two review articles by Gupta et al. [6] and Krakow et al. [7], respectively.

2.2. Inclusion and exclusion criteria

This meta-analysis was conducted in accordance with the Meta-analyses Of Observational Studies in Epidemiology (MOOSE) guidelines [18] and in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standard [19]. To estimate the aggregate effect-size of prevalence of OSA in PTSD, we included observational studies (cross-sectional, retrospective, and prospective studies) in adults that fulfilled the following criteria: (a) a diagnostic criterion of PTSD was specified; and (b) OSA diagnosis was present according to polysomnography (PSG). To estimate the aggregate effect-size of the differences of CPAP adherence between patients with PTSD and OSA and those with OSA alone, an additional criterion was that (c) studies reported regular use and time of average use per night. The excluded criteria included the following: (a) non-standardized diagnoses of OSA, (b) insufficient data for extraction of OSA frequencies and, for analysis of adherence to CPAP therapy, (c) including participants referred for sleep testing due to a high clinical suspicion for OSA, (d) home study, and (e) insufficient data for extraction of regular CPAP use and time of average use per night. All the included articles were published in English-language and peer-reviewed journals. In the case of multiple publications from the same study, only the most relevant paper or article was included.

2.3. Study selection and data extraction

After the removal of duplicates, both reviewers (Y.Z. and R.R.) screened the titles and abstracts of all potentially eligible articles. The two authors applied the eligibility criteria, and a list of full text articles was organized through consensus. Both reviewers then read the full texts of these articles and discussed the final list of included articles to reach consensus. A third reviewer (W.Z.) was available for mediation throughout this process. Data were extracted by one author (Y.Z.) and supervised by a second author (R.R.). The primary extracted data included the prevalence of OSA in patients with PTSD, total number of PTSD patients, and the potential predictors (ie, age, gender, and body mass index [BMI]). To estimate the aggregate effect-size of the impact of PTSD on CPAP adherence, the data of average use per night and regular use were also extracted.

2.4. Quality assessment

Two authors (Y.Z. and R.R.) independently reviewed all titles and abstracts identified by the search. Articles that met the inclusion criteria were selected for full-text review. Disagreements were resolved by discussion between both reviewers, and we invited a third author (W.Z.) who was available to determine eligibility if consensus could not be reached.

2.5. Statistical analyses

The meta-analysis was conducted using the program Comprehensive Meta-Analysis (CMA) version 2.0. The mean weighted event rate was estimated as proportions (percentage of OSA cases/PTSD sample size), and used to find effect sizes in the analyses. To estimate the aggregate effect-size (Hedges g) of the differences in adherence to CPAP therapy between patients with PTSD and OSA and those with OSA alone, the mean and standard deviation and sample size for each group were entered for calculation. For each global effect-size estimate, the Q statistic and I^2 were calculated to examine the presence and magnitude of heterogeneity, and to inform on the degree of overlap between different studies' 95% confidence intervals (CIs). It has been indicated that I^2 values of 75%, 50%, and 25% are considered as high, moderate, and low heterogeneity [20]. The random effect was performed if significant heterogeneity existed; otherwise, the fixed effects model was applied. Furthermore, we conducted subgroup analyses stratified by several categorical variables such as OSA diagnosis (AHI $\geq$5 and AHI $\geq$10), study sample (veterans and nonveterans), and country (United States [U.S.] and non-U.S.). As for continuous variables such as age, percentage of males, and BMI, a meta-regression analysis (if $N \geq 3$) was performed. Publication bias was tested using the Egger regression method [21] and Begg-Mazumdar test [22], with p values of <0.05 suggesting the presence of bias. In addition, a funnel plot was created, in which the study-specific effect estimates are showed in relation to the standard error to assess the potential presence of publication bias.

3. Results

3.1. OSA in PTSD

3.1.1. Search results and included participants

Our search yielded 194 publications, 10 of which met inclusion criteria to estimate the aggregate effect-size of prevalence of OSA in patients with PTSD (Fig. 1). The final sample comprised 632 unique patients with PTSD. Sample sizes of included studies ranged from 12 to 200 participants (Table 1). The mean age was 42.4 years (ages 18 and older). The majority of the studies [11,12,15,23–26] were conducted in the U.S. ($N = 7$; 70%) and most of the participants [11,12,14,15,23,25–28] were veterans ($N = 9$; 90%). As for the OSA diagnosis, three studies [11,15,26] of 10 (30%) used AHI $\geq$5 across PSG, six studies [12,14,24,25,27,28] of 10 (60%) used AHI $\geq$10, and one study [23] of 10 did not report the AHI criteria.