Retrospective Review

Impact of Opioid Dose and Obstructive Sleep Apnea in Chronic Opioid Patients Using STOP-Bang Questionnaire

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Background: Obstructive sleep apnea (OSA) is the most common form of sleep-disordered breathing. While patients on chronic opioids are at increased risk of sleep-disordered breathing, there is a lack of data on the relationship between opioid dose and OSA risk in particular. The STOP-Bang Questionnaire (SBQ) is a common screening tool for OSA, but it has not been well studied in patients on chronic opioid therapy.

Objectives: This study uses the SBQ to examine the relationship between total daily opioid dose and the risk of OSA in patients on chronic opioid therapy.

Study Design: Retrospective chart review.

Setting: Academic medical center pain clinic.

Methods: Patients on stable doses of chronic opioids who completed the SBQ were grouped into 3 OSA risk categories, including low (SBQ score 0-2), medium (SBQ score 3-4), and high risk (SBQ score 5-8). Morphine equivalent daily dose (MEDD) was calculated and compared between the 3 risk groups. In a secondary analysis, patients were instead grouped into opioid dose categories, including low MEDD (≤ 20), medium MEDD (21-50), and high MEDD (> 50). The SBQ scores were then compared between the 3 MEDD groups.

Results: The charts of 190 patients on chronic opioid therapy were reviewed. One hundred forty-seven patients did not have a prior diagnosis of OSA. Of these, 92 (63%) patients completed the SBQ. Fifty-five percent were women and 45% men. The average age was 59. The average MEDD was 23.32. In the primary analysis based on the SBQ score, 39% were low risk for OSA, 42% medium risk, and 18% were high risk. There was no difference in total MEDD between the 3 groups ($P = 0.83$). In the secondary analysis based on total MEDD, 58% had low MEDD, 32% had medium MEDD, and 11% had high MEDD. There was no significant difference in SBQ scores between these groups ($P = 0.51$).

Limitations: This is a single center study, and only 63% of eligible patients completed the SBQ. The study did not attempt to control for potential confounders. The SBQ results were not confirmed with a polysomnogram.

Conclusion: We found no relationship between the opioid dose and the risk of OSA as measured by the SBQ score in this chronic opioid population. Opioids may be more associated with sleep apnea due to central rather than obstructive processes, and additional screening tools beyond the SBQ may be needed to better screen for sleep apnea in this population.

Key words: Stop-bang questionnaire, screening, sleep apnea, obstructive sleep apnea, chronic opioids, opioid dose

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Opioids and sleep have a complex relationship (1). At least 46% of patients on chronic opioids have been shown to have sleep-disordered breathing on polysomnogram (2). There are 2 primary subtypes of sleep-disordered breathing: central sleep apnea (CSA) and obstructive sleep apnea (OSA). CSA is caused by inadequate respiratory effort, while OSA is caused by upper airway obstruction. Many studies have evaluated the relationship between CSA and chronic opioid use, but less data exists on the relationship between chronic opioids and OSA.

Untreated OSA has been associated with serious adverse cardiovascular events (3). OSA has also been shown to cause irritability, increased fatigue, and non-refreshing sleep (4). Because chronic pain has also been associated with psychological stress and insomnia (5-6), it stands to reason that the symptoms of OSA may exacerbate chronic pain. Likewise, the overlap of symptoms between chronic pain and OSA may make the clinical diagnosis harder to establish. Thus, the identification and treatment of OSA in the chronic pain population may be important for a multidisciplinary approach to pain.

Depending on the stringency of criteria used, the prevalence of OSA in the general population ranges from 15-30% in males and 5-15% in females (7-9). Prior studies have estimated the prevalence of OSA in chronic opioid patients to be significantly higher, between 35-57% (10-12). Whether the chronic use of opioids is responsible for this difference has not been established. For example, there is evidence that individuals with OSA have a higher relative risk of receiving opioids than those without (13). Moreover, these studies found no association between the dose of opioids and OSA. A separate study found evidence of a relationship between opioid dose and obstructive events on a polysomnogram (14), but the effect was small, and the relationship between opioid dose and risk of OSA was not established.

Of the screening questionnaires for OSA, one of the most useful is the STOP-Bang questionnaire (SBQ), which has been found to have an 88-93% sensitivity for mild to severe OSA (15). There have been few studies examining the relationship between the SBQ and chronic opioid use. In one study of relatively young individuals on buprenorphine, the average SBQ was 2.7, which corresponds to a low to intermediate-risk of OSA (16). However, there was no comparison in this study to non-opioid users and no distinction based on opioid dose. One study of chronic pain patients compared SBQ scores between opioid users and non-users and found no difference between the 2 groups (17), but it did not distinguish between different doses of opioids. This study aims to examine the relationship between the opioid dose and the risk of OSA as measured by the SBQ in patients on chronic opioids.

Methods

This was a retrospective chart review of patients in an academic pain center who were receiving chronic opioid therapy. The study was approved by the internal institutional review board.

Patients ≥ 18 years old receiving chronic opioid therapy for at least 3 months on a stable daily dose of at least 4 weeks were eligible for evaluation with the SBQ. We excluded patients with a prior diagnosis of OSA. For any patient evaluated with the SBQ, we gathered data including age, gender, SBQ score, and the daily opioid dose the patient was receiving at the time of evaluation. The daily opioid dose was reported as the morphine equivalent daily dose (MEDD) and was calculated using the conversion factors available on the Centers for Disease Control and Prevention website (18).

Patients were grouped based on SBQ score into risk categories for OSA, including low risk (SBQ score 0-2), medium risk (SBQ score 3-4), or high risk (SBQ score 5-8). The MEDDs of each risk category were then compared to determine if there was any relationship between the SBQ score and total MEDD. Significance was calculated using the analysis of variance test. Results were considered significant with a *P* value of less than or equal to 0.05.

Because the effect of opioid dose on the SBQ score may be hidden if a significant discrepancy exists between the number of patients on higher versus lower opioid doses, a secondary analysis was done in which patients were grouped by total MEDD and then compared based on the SBQ scores. Patients were grouped into 3 categories, including low MEDD (≤ 20), medium MEDD (21-50), and high MEDD (> 50). SBQ scores for each group were compared using the Kruskal-Wallis test. Results were considered significant with a *P* value of less than or equal to 0.05.

Results

The charts of 190 patients on chronic opioid therapy were reviewed. Forty-three (23%) had a prior diagnosis of OSA and were excluded. Of the remaining 147 patients without a prior diagnosis, 92 (63%) completed the SBQ and were included in the analysis (Fig.

1). Fifty-one (55%) were women, and 41 (45%) were men. The average age was 59.11 (Table 1).

For the primary analysis based on OSA risk categories, there were 36 (39%) patients in the low-risk group, 39 (42%) in the medium-risk group, and 17 (18%) in the high-risk group. Fifty-six (61%) of the patients were in either the medium or high-risk groups (SBQ ≥ 3). The average MEDD for all patients was 23.32 (range 5-90). There was no difference found in total MEDD between the 3 groups based on the SBQ score ($P = 0.83$) (Table 2).

As was anticipated, there was a larger discrepancy in the number of patients for each MEDD category in the secondary analysis. There were 53 (58%) patients in the low MEDD category versus 29 (32%) in the medium MEDD and only 10 (11%) in the high MEDD category. The overall average SBQ score was 2.98. The high MEDD group had the lowest average SBQ score of 2.5, but the difference between the 3 groups was not significant ($P = 0.51$) (Table 3).

Discussion

This study found no association between the MEDD and the risk of OSA as measured by the SBQ in patients on chronic opioid treatment. This would suggest that for patients on chronic opioids, adjusting the opioid dose, once stable, would have no effect on their risk of OSA, which may seem at odds with the established literature that supports an association between chronic opioid use and sleep-disordered breathing (2,10,11,14).

While the precise mechanisms by which opioids contribute to sleep-disordered breathing have not been fully explained, opioids are thought to disturb the sleep-wake cycle through both central and peripheral mechanisms by inhibiting the respiratory drive and ventilatory response to CO_2 (19) and impairing motor control of upper airway tissues leading to obstructive events (20). However, several studies, including a systematic review and meta-analysis, suggest that the association between sleep-disordered breathing and chronic opioid use is largely driven by a higher rate of central events and thus increased risk of CSA rather than OSA (14,21,22). Although one study involving 60 patients on chronic opioids found a small dose-dependent increase in the obstructive apnea index on

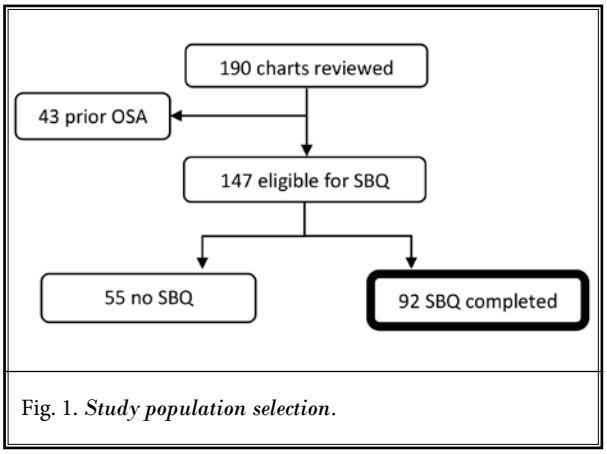

Fig. 1. *Study population selection.*

Table 1. *Patient demographics.*

	Female	Male	Average Age	Total
OSA risk category:				
Low (SBQ 0-2:)	27 (75%)	9 (25%)	57.89	36 (39.13%)
Medium (SBQ 3-4):	17 (43.59%)	22 (56.41%)	59	39 (42.39%)
High (SBQ 5-8):	7 (41.18%)	10 (58.82%)	61.94	17 (18.48%)
Total MEDD category:				
Low (MEDD ≤ 20)	31 (58.49)	22 (41.51%)	59.7	53 (57.61%)
Medium (MEDD 21-50)	15 (51.72%)	14 (48.28%)	56.83	29 (31.52%)
High (MEDD > 50)	5 (50%)	5 (50%)	62.6	10 (10.87%)
All groups	51 (55.43%)	41 (44.57%)	59.11	92

OSA, obstructive sleep apnea; SBQ, STOP-Bang questionnaire; MEDD, morphine equivalent daily dose.

Table 2. *Average MEDD per OSA risk category.*

OSA risk category	Average MEDD ($P = 0.83$)
Low (SBQ 0-2:)	24.83
Medium (SBQ 3-4):	22.40
High (SBQ 5-8):	22.21
All groups	23.32 [5-90]

OSA, obstructive sleep apnea; SBQ, STOP-Bang questionnaire; MEDD, morphine equivalent daily dose.

Table 3. *Average SBQ score per MEDD category.*

Total MEDD category	Average SBQ ($P = 0.51$)
Low (MEDD ≤ 20)	3.02
Medium (MEDD 21-50)	3.06
High (MEDD > 50)	2.5
All groups	2.98

SBQ, STOP-Bang questionnaire; MEDD, morphine equivalent daily dose.

polysomnogram, this was overshadowed by a much larger response in the central apnea index (14).

Since this study did not compare SBQ scores to non-opioid users, the data do not help clarify whether chronic opioid use is associated with an increased risk of OSA in a non-dose-dependent manner. Only one study has directly compared SBQ scores in chronic pain patients between opioid users and non-users. In a comparison of 196 opioid users to 101 opioid non-users, Tentindo et al found no difference in the rate of positive SBQ scores between the 2 groups, suggesting that opioid use alone is not related to an increased risk of OSA (17).

In addition, this study does not clarify whether initiation of opioid therapy or escalation of the chronic opioid dose is associated with an increased risk of OSA in the short term. By design, this study only evaluated individuals already on chronic opioid therapy who were on a stable opioid dose for at least 4 weeks. While opioids can cause respiratory depression after either initiation of therapy or dose escalation, tolerance to this effect is known to develop early, and this should not impact our findings at 4 weeks of a stable dose (23). For a similar reason, it is unlikely that any decision by prescribers to avoid higher doses of opioids in patients who scored high on the SBQ affected our results. Because the opioid dose data reflected a stable dose over at least 4 weeks and were concurrent with the administration of the SBQ, any subsequent dose adjustments would not affect the results of this study.

The recent American Academy of Sleep Medicine position statement recommends appropriate screening and testing for sleep-disordered breathing in all chronic opioid patients (1). The results of this study, as well as other recent literature, call into question the usefulness of the SBQ in screening for sleep-disordered breathing in chronic opioid patients. The SBQ is a useful tool in screening for OSA, but this may be inadequate in the chronic opioid population where CSA is an important concern. While an increasing SBQ score has been found to correlate positively with OSA in the chronic opioid population (20), this would be expected since the OSA risk factors included in the SBQ are the same for both opioid users and non-users. There have been recent efforts to develop more robust screening models for sleep apnea in chronic opioid patients, including utilization of resting daytime oxyhemoglobin saturation and overnight home pulse oximetry (24), but no validated tools yet exist for this population.

Limitations

There are several important limitations to this study. The first limitation is that not all chronic opioid patients in the pain clinic were administered the SBQ. Only 63% of the patients without a prior diagnosis of OSA had completed the SBQ, and no data were collected on the patients who did not complete the SBQ, raising the possibility of selection bias. In addition, the entire study population is from an urban academic medical center which may not be generalizable to all chronic opioid patients. This study did not control for potential confounders such as patient demographics, comorbidities, and other sedating medications that may affect the study results. Finally, this study evaluated the relationship between opioid dose and OSA risk as measured by the SBQ, which has not been validated in the chronic pain population. The gold standard for diagnosing sleep apnea is the polysomnogram, which may have yielded different results in this population than what was suggested by the SBQ score.

Conclusion

In this study of chronic opioid patients who completed the SBQ to screen for OSA, we found no relationship between opioid dose as measured by MEDD and the SBQ score, which suggests that the association between sleep-disordered breathing and chronic opioid use may be the result of other factors such as central rather than obstructive processes. This is consistent with other related studies on the topic and underscores the need for additional screening mechanisms for sleep-disordered breathing in chronic opioid patients that can help identify at-risk individuals who may be missed by the SBQ.

References

1. Rosen IM, Aurora RN, Kirsch DB, et al. Chronic opioid therapy and sleep: An American Academy of Sleep Medicine position statement. *J Clin Sleep Med* 2019; 15:1671-1673.
2. Rose AR, Catcheside PG, McEvoy RD, et al. Sleep disordered breathing and chronic respiratory failure in patients with chronic pain on long term opioid therapy. *J Clin Sleep Med* 2014; 10:847-852.
3. Xie W, Zheng F, Song X. Obstructive sleep apnea and serious adverse outcomes in patients with cardiovascular or cerebrovascular disease: A PRISMA-compliant systematic review and meta-analysis. *Medicine (Baltimore)* 2014; 93:e336.

4. Osman AM, Carter SG, Carberry JC, Eckert DJ. Obstructive sleep apnea: Current perspectives. *Nat Sci Sleep* 2018; 10:21-34.
5. Ortego G, Villafañe JH, Doménech-García V, Berjano P, Bertozzi L, Herrero P. Is there a relationship between psychological stress or anxiety and chronic nonspecific neck-arm pain in adults? A systematic review and meta-analysis. *J Psychosom Res* 2016; 90:70-81.
6. Mathias JL, Cant ML, Burke ALJ. Sleep disturbances and sleep disorders in adults living with chronic pain: A meta-analysis. *Sleep Med* 2018; 52:198-210.
7. Young T, Palta M, Dempsey J, Peppard PE, Nieto FJ, Hla KM. Burden of sleep apnea: Rationale, design, and major findings of the Wisconsin Sleep Cohort study. *WMJ* 2009; 108:246-249.
8. Dempsey JA, Veasey SC, Morgan BJ, O'Donnell CP. Pathophysiology of sleep apnea. *Physiol Rev* 2010; 90:47-112.
9. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol* 2013; 177:1006-1014.
10. Webster LR, Choi Y, Desai H, Webster L, Grant BJ. Sleep-disordered breathing and chronic opioid therapy. *Pain Med* 2008; 9:425-432.
11. Mogri M, Desai H, Webster L, Grant BJ, Mador MJ. Hypoxemia in patients on chronic opiate therapy with and without sleep apnea. *Sleep Breath* 2009; 13:49-57.
12. Sharkey KM, Kurth ME, Anderson BJ, Corso RP, Millman RP, Stein MD. Obstructive sleep apnea is more common than central sleep apnea in methadone maintenance patients with subjective sleep complaints. *Drug Alcohol Depend* 2010; 108:77-83.
13. Chen K, Yaggi HK, Fiellin DA, et al. Associations between obstructive sleep apnea and prescribed opioids among veterans. *Pain* 2020; 161:2035-2040.
14. Walker JM, Farney RJ, Rhondeau SM, et al. Chronic opioid use is a risk factor for the development of central sleep apnea and ataxic breathing. *J Clin Sleep Med* 2007; 3:455-461.
15. Chiu HY, Chen PY, Chuang LP, et al. Diagnostic accuracy of the Berlin questionnaire, STOP-BANG, STOP, and Epworth sleepiness scale in detecting obstructive sleep apnea: A bivariate meta-analysis. *Sleep Med Rev.* 2017; 36:57-70.
16. Farney RJ, McDonald AM, Boyle KM, et al. Sleep disordered breathing in patients receiving therapy with buprenorphine/naloxone. *Eur Respir J.* 2013; 42:394-403.
17. Tentindo GS, Fishman SM, Li CS, Wang Q, Brass SD. The prevalence and awareness of sleep apnea in patients suffering chronic pain: An assessment using the STOP-Bang sleep apnea questionnaire. *Nat Sci Sleep* 2018; 10:217-224.
18. Calculating total daily dose of opioids for safer dosage. Centers for Disease Control and Prevention. Accessed March 24, 2022. www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf
19. Correa D, Farney RJ, Chung F, Prasad A, Lam D, Wong J. Chronic opioid use and central sleep apnea: A review of the prevalence, mechanisms, and perioperative considerations. *Anesth Analg* 2015; 120:1273-1285.
20. Lam KK, Kunder S, Wong J, Doufas AG, Chung F. Obstructive sleep apnea, pain, and opioids: Is the riddle solved? *Curr Opin Anaesthesiol* 2016; 29:134-140.
21. Chung F, Wong J, Bellingham G, et al. Predictive factors for sleep apnoea in patients on opioids for chronic pain. *BMJ Open Respir Res* 2019; 6:e000523.
22. Mubashir T, Nagappa M, Esfahanian N, et al. Prevalence of sleep-disordered breathing in opioid users with chronic pain: A systematic review and meta-analysis. *J Clin Sleep Med* 2020; 16:961-969.
23. Algera MH, Olofsen E, Moss L, et al. Tolerance to opioid-induced respiratory depression in chronic high-dose opioid users: A model-based comparison with opioid-naïve individuals. *Clin Pharmacol Ther* 2021; 109:637-645.
24. Selvanathan J, Waseem R, Peng P, Wong J, Ryan CM, Chung F. Simple screening model for identifying the risk of sleep apnea in patients on opioids for chronic pain. *Reg Anesth Pain Med* 2021; 46:886-891.