ORIGINAL ARTICLE

Persistent and Developing Sleep Problems: A Prospective Cohort Study on the Relationship to Poor Outcome in Patients Attending a Pain Clinic with Chronic Low Back Pain

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■ **Abstract:** Sleep problems are common in people with low back pain (LBP); however, the mechanisms of how sleep influences pain are complex. To date there is a lack of prospective research on the timing and development of sleep problems in those who have LBP; such information would be useful to identify individuals at risk for poor outcomes. Our aims are to investigate the predictive role of sleep problems on self-report recovery and pain intensity using logistic regression reporting odds ratios (ORs). An observational cohort of 761 chronic LBP patients recruited from a pain management clinic participated, and they completed data at baseline and at 6-month follow-up (n = 682). Results show increased odds for reported nonrecovery (OR 1.52) and pain intensity (OR 2.69) among those who reported sleep problems at baseline. Further analysis on the experience of sleep problems through time showed that those with developing sleep problems (ie, no sleep problems at baseline but reported sleep problems at follow-up) were at increased odds for reporting nonrecovery (OR 2.17) and pain intensity (OR 2.95), as were those who reported sleep problems at both baseline and follow-up, for recovery (OR 2.88) and pain intensity (OR 3.45). Those with resolving sleep problems (ie, sleep problems present at baseline but not at follow-up) were at decreased odds for nonrecovery (OR 0.50) and pain intensity (0.49). Presenting, persistent, and developing sleep problems have a significant impact on recovery for those with LBP. Clinicians may wish to consider treatment options that can address sleep problems. ■

Key Words: low back pain, sleep, pain, recovery, prospective, cohort

INTRODUCTION

Low back pain (LBP) is a common condition affecting most people at some point in their lives. A recent review of 165 studies from 54 countries reported a point prevalence rate of 18%, a 1-year prevalence rate of 38%, and a lifetime prevalence range of 40% to 80%.[1] Recurrence of LBP is also common; a review of cohort studies reported an estimated 70% recurrence rate over 5 years for those with LBP.[2] This has led LBP to have a

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Submitted: August 15, 2016; Revised November 21, 2016; Revision accepted: March 9, 2017
DOI. 10.1111/papr.12584

significant global impact in terms of disability to the individual,[3,4] as well as a significant financial impact—LBP patients have higher direct and indirect costs compared to other patient groups.[5]

Recently there has been a growth of research attention on the role of sleep, particularly sleep problems, and on the effect this may have on outcomes for those with LBP. Sleep problems associated with back pain are common. A large epidemiological study reported that over half of those who reported back pain also reported sleep problems,[6] and a review of 13 LBP studies showed a prevalence rate of 58.9% for people ascribing sleep problems to their back pain.[7] The influence of pain on sleep, and vice versa, is complex and most likely reciprocal, with evidence of consistent associations between LBP and sleep initiation, sleep disturbance, sleep duration, sleep quality, electroencephalography and polysomnography output, and poor daytime functioning.[8–10] Studies have shown associations between increased poor sleep quality and increased pain intensity,[7] as well as experimental evidence of a lower pain threshold due to sleep disturbance,[11] and increased risk for psychological morbidity (eg, depression) due to sleep problems in those who report pain.[12] Current thought on the association between sleep disturbance and pain suggests a key link is the relationship between sleep, fatigue, and psychological morbidity (depression, anxiety), leading to a potential compounding effect on pain perception, function, and recovery.[7,8,10] Indeed, sleep problems are a diagnostic feature of depression, and therefore it is important to examine potential confounding effects.[12] There are also inflammatory processes associated with the sleep cycle that may modulate nociception.[8] Evidence shows more sleep disturbances are found within inflammatory populations (eg, rheumatology and fibromyalgia populations),[13,14] and recent evidence on chronic LBP participants has shown changes in proinflammatory markers (interleukin-6) linked to sleep disturbance.[15]

However, to date prospective evidence is limited on the relationship between LBP and sleep problems. Little is known about the timing and sequences on the development of sleep problems in those with back pain, or the impact they have on recovery, something that is reflected within the wider field of pain research.[9] Such information would be useful for clinicians to assist in the identification of individuals who may require additional interventions alongside usual pain management (eg, sleep hygiene treatment). The primary aim of the current study was to examine the prospective predictive role of sleep problems associated with LBP patient self-report recovery and pain intensity outcomes. Secondary aims were to examine differences over time between LBP patients who have no sleep problems and those with sleep problems, those who develop sleep problems over time, and those who have a reduction of sleep problems over time. In line with recent prospective evidence for the relationship between sleep and pain,[9] it is hypothesized that, compared to those who do not report sleep problems, those with developing sleep problems will be less likely to report a favorable recovery, and those with persistent sleep problems will have the worse outcomes overall.

METHODS

This was a prospective study of patients with LBP, carried out between February 2014 and December 2014. Full ethical approval was granted by the Medical Ethics Committee at Qazvin University of Medical Sciences, Qazvin, Iran.

The cohort was inclusive of a convenience sample of consecutive patients with LBP attending the Outpatient Chronic Pain Clinic, Department of Neurosurgery, Shahid Rajaee Hospital, Qazvin, Iran. Patients are referred to this chronic pain clinic by their primary care physicians, most often when pain persists beyond normal healing time or if pain is recurrent or persistent. Usual care at the chronic pain clinic involves patient education (pain management), prescriptions (nonsteroidal anti-inflammatory drugs), and physiotherapy (exercise, spa therapy). Patients are normally assessed for progress at 2-month intervals, and treatment usually lasts for 1 year. Patients were eligible to participate in the current study if they had a confirmed diagnosis of chronic LBP (ie, persistent LBP with or without referred leg pain for at least 3 months), were 18 years of age or older, and were able to speak and read Persian. Patients were excluded if they had any concurrent medical illness (eg, cardiopulmonary, central nervous system, diabetes, intellectual disorder, rheumatic diseases), serious spinal pathology (eg, fracture, metastasis), and/or had received spinal surgery. Patients scheduled to attend the outpatient chronic pain clinic were approached over a 3-month period (February 2014 to April 2014) and invited to take part. As this was a convenience sample of consecutive patients, the recruitment of patients to this study was not aligned to the beginning of treatment for each patient; variation existed on treatment type,

treatment stage, pain level, and pain impact of the participating patient population.

Patients were contacted by telephone and screened for eligibility by one of the authors (M.Y.). Eligible patients were invited to take part in the study at the same time as their scheduled appointment. Informed consent was obtained from patients at the time of their appointment, and patients were asked to complete a questionnaire. Subsequently patients were followed up at 6 months.

Measures

We used a single-item self-report global assessment of change question for the patients' perceived level of recovery at 6-month follow-up.[16,17] Such assessments of global recovery have clinical relevance, have been found to have high agreement with clinical assessment, and are suitable for research due to their brevity and simplicity.[18] The question consists of 6 categories (completely recovered, much better, better, no change, worse, much worse), and participants were asked to select 1 category. A cutoff was chosen for this measure on the basis of clinical utility (eg, identification of a subgroup of patients who may benefit from treatment due to no change or worsening outcome over time). This variable was collapsed to form 2 groups: a recovery group (completely recovered, much better, and better) and a nonrecovery group (no change, worse, much worse).

Pain intensity was measured using a visual analog scale (VAS), and patients were asked to rate their pain level when they filled out their baseline questionnaire and at 6-month follow-up.[6,19] For the logistic analysis we based the cutoff of 0 or 1 (0 to 10 mm) as an indication of patient recovery following previous methodology carried out to identify patient-perceived recovery from pain.[20,21] Information was also collected on the duration of LBP from patients at baseline. Patients were asked to signify "How long is it since you had a whole month without any pain?" We categorized the pain duration question into 2 groups for the analysis (6 months or less vs. 7 months or more) following previous methodology.[22,23]

The Pittsburgh Sleep Quality Index (PSQI) was used as a measure of overall sleep quality at baseline and at 6-month follow-up. The PSQI measures quality and sleep patterns using 7 domains: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, sleep medication, and daytime dysfunction over the previous month. Scoring uses a 0- to 3-point Likert scale, with a global score of 5 or greater indicating clinically significant sleep problems; this global score was used as the cutoff to identify those with sleep problems in this study.[24,25] The PSQI has been used previously in numerous pain population studies[26,27] and has validation in Persian.[28]

Depressive and anxiety symptoms were assessed using the Hospital Anxiety and Depression Scale (HADS) at baseline. The HADS includes 2 scales (depression and anxiety), and each scale comprises 7 items. All items are rated on a Likert-type scale ranging from 0 to 3 points, with higher scores indicating higher symptom levels, and with scores ranging from 0 to 21 for each scale.[29] The HADS has been translated into Iranian (Persian) and has been shown to be valid and reliable in this setting.[30]

Patients were asked to provide information regarding demographic characteristics at baseline: age, gender, body mass index (BMI), and occupational status (working, sick leave, not working, retired).

Analysis

Descriptive statistics of the percentage proportions, means, medians, and interquartile ranges were presented for all the measures. Initially a prospective model was tested using logistic regression producing odds ratios (ORs) with 95% confidence intervals (95% CIs). Those with sleep problems at baseline were tested against the reference category of those with no sleep problems at baseline, on both self-reported recovery status and pain intensity outcome, at 6-month follow-up. A 2-stage process was applied to each logistic regression model. First, an unadjusted model was created to assess the direct relationship between sleep problems and outcome (self-report recovery, pain intensity), and then a multivariable model was created that included adjustment for baseline depressive symptoms, baseline pain intensity (within the patient self-report recovery model only), baseline duration of pain, baseline anxiety symptoms, age, gender, BMI, and occupational status. An adjusted model may be used to demonstrate the relationship between sleep problems and outcome while controlling for potential confounding (eg, effect of depression on the sleep-to-pain pathway), and the use of both unadjusted and adjusted models allows for inspection of the difference in change due to adjustment, which may indicate potential mediation or suppression effects. Further exploratory analysis using logistic regression models was carried out to assess the full range of experience of sleep problems at both baseline and

follow-up (prospective and cross-sectional associations). Four categories of participants were created based on their sleep problem status at both time points (ie, baseline and follow-up). The first category (no sleep problems) was composed of participants who reported no sleep problems at baseline or follow-up (used as the reference category within the logistic regression). The second category (developing sleep problems) was composed of those participants who reported no sleep problems at baseline, but did report sleep problems at follow-up. The third category (persistent sleep problems) comprised those participants who reported sleep problems at baseline and at follow-up. The final category (resolving sleep problems) was composed of those who reported sleep problems at baseline but did not report sleep problems at follow-up. Data analysis was conducted using IBM SPSS version 20.0 (IBM Corp., Armonk, NY, U.S.A.).

RESULTS

In total, 807 participants were approached to take part and 761 agreed at baseline, representing a 94% baseline response rate. At 6-month follow-up, 682 participants responded, representing an 89% response rate. Independent *t*-tests or chi-square tests were performed to statistically assess the difference in the patient's age, gender, BMI, depression, anxiety and pain intensity, occupation, and sleep quality between those who responded at 6-month follow-up and those who did not respond at 6-month follow-up, and no differences were found.

Baseline characteristics showed a mean age of 41 years, with just over 55% of the cohort being male. Just over 37% ($n = 283$) reported their last pain-free month within the previous 6 months. At baseline, 48% of the cohort indicated they had experienced sleep problems in the previous month, and this rose to 67.6% at 6-month follow-up, with only 4.5% of participants reporting resolving sleep problems at follow-up. Self-reported recovery at follow-up showed that 58.2% of the cohort indicated they felt completely recovered, much better, or better compared to how they felt at baseline. For pain intensity, 38.3%% of the cohort reported VAS pain intensity levels at 10 mm or below at 6-month follow-up. Table 1 outlines the characteristics of the cohort.

Patient Self-Report Nonrecovery

Table 2 outlines the logistic regression analysis. Results show that the presence of sleep problems at baseline significantly increased the odds of poor recovery by approximately 50% at 6-month follow-up (unadjusted OR 1.52), and this result did not markedly change after adjustment for confounds (adjusted OR 1.50). Exploratory analysis using the no sleep problem category (ie, no reported sleep problems at baseline or follow-up) as the reference category within logistic regression analysis (see Table 2) showed that those with developing sleep problems (ie, no sleep problems at baseline, reported sleep problems at follow-up) were almost 3 times more likely to report nonrecovery at 6 months (unadjusted OR 2.93, 95% CI 1.53, 5.61), and those with persistent sleep problems (ie, sleep problems reported both at baseline and follow-up) were over 3 times more likely to report a nonrecovery (unadjusted OR 3.24, 95% CI 1.63, 6.43), with those who had resolving sleep

Table 1. Cohort Characteristics

Characteristic	*n* (%)	Mean (SD)	Interquartile Range
Baseline			
Age		41.15 (12.24)	16
Gender (male)	414 (55.4)		
PSQI sleep quality proportion (sleep problems) and scale score	365 (48.0)	10.5 (3.5)	5.0
VAS pain intensity		7.2 (2.31)	5.0
Depressive symptoms		7.8 (4.2)	5.0
Anxiety symptoms		11.8 (5.2)	8.0
BMI score		27.8 (6.3)	7.4
Last pain-free episode of back pain over 7 months	478 (62.8)		
Occupational status			
Working	285 (37.5)		
Sick leave	151 (19.8)		
Not employed	220 (28.9)		
Retired	105 (13.8)		
6-month follow-up			
PSQI sleep quality proportion (sleep problems) and scale score	461 (67.6)	9.32 (3.1)	5.0
Sleep problem categories			
No sleep problems	190 (27.9)		
Developing sleep problems	165 (24.2)		
Persistent sleep problems	296 (43.4)		
Resolved sleep problems	31 (4.5)		
Self-reported recovery			
Completely recovered	143 (18.8)		
Much better	91 (11.9)		
Better	209 (27.5)		
No change	58 (7.6)		
Worse	114 (15.0)		
Much worse	67 (8.8)		
Missing	79 (10.4)		
VAS pain intensity		5.1 (2.4)	5.0
Recovered (VAS $\leq$ 10 mm)	261 (38.3)		
Nonrecovery (VAS $>$ 10 mm)	421 (61.7)		

PSQI, Pittsburgh Sleep Quality Index; VAS, visual analog scale; BMI, body mass index.

Table 2. Logistic Regression Odds Ratio (OR) with 95% Confidence Intervals (95% CI) for Relationship of Sleep Problems with Nonrecovery for Those with Low Back Pain

Sleep Problem Status	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
No sleep problems	Reference category	Reference category
Sleep problems	1.52 (1.10, 2.08)	1.50 (1.09, 2.17)
Exploratory baseline and follow-up group analysis		
No sleep problems (none at baseline, none at follow-up)	Reference category	Reference category
Developing sleep problems (none at baseline, present at follow-up)	2.93 (1.53, 5.61)	2.17 (1.04, 4.52)
Persistent sleep problems (present at baseline and follow-up)	3.24 (1.63, 6.43)	2.95 (1.48, 5.88)
Resolving sleep problems (present at baseline, not present at follow-up)	0.49 (0.31, 0.78)	0.50 (0.31, 0.81)

*Baseline adjustment for: pain intensity, depressive and anxiety symptoms, age, gender, occupational status, and duration of back pain.

problems (ie, sleep problems reported at baseline but none reported at follow-up) having reduced odds for nonrecovery (unadjusted OR 0.49, 95% CI 0.31, 0.78). Within the fully adjusted model, results show that those with developing sleep problems had over twice the odds for nonrecovery (adjusted OR 2.17, 95% CI 1.04, 4.52), those with persistent sleep problems had under 3 times the odds for nonrecovery (adjusted OR 2.95, 95% CI 1.48, 5.88), and those with resolving sleep problems had reduced odds for nonrecovery (adjusted OR 0.50, 95% CI 0.31, 0.81) at 6 months.

Patient Pain Intensity

Results for pain intensity at follow-up as the outcome (cutoff set at ≤ 10 mm on the VAS to indicate recovery) show an increase in the odds for nonrecovery and higher pain intensity for those with sleep problems at baseline, with an approximate 2.5 times elevated risk (adjusted OR 2.48, 95% CI 1.62, 3.70). Further exploratory analysis showed that compared to those with no sleep problems reported at baseline and follow-up, those with developing sleep problems had an increased risk (almost 3 times) for nonrecovery in terms of pain intensity in both unadjusted (OR 2.99, 95% CI 1.51, 5.92) and adjusted analyses (OR 2.88, 95% CI 1.32, 6.31). The effect for those with persistent sleep problems was greater, with almost 4 times the risk in the unadjusted model (OR 3.73 95% CI 1.92, 7.26) and almost 3.5 times the risk within the adjusted model (OR 3.45 95% CI 1.59, 7.46). However, those who have resolving sleep problems are more likely to recover compared to those with no sleep problems at baseline or follow-up (see Table 3).

DISCUSSION

This study tested the relationship of sleep problems to perceived recovery and pain intensity among a cohort of LBP patients who attended a pain management clinic. This study tested the prospective relationship and examined the effect of persistent, developing, and resolving sleep problems on outcomes. Our findings support the study hypotheses: the presence of sleep problems is a significant risk factor for nonrecovery and pain intensity for those with LBP; and the risk of poor outcome is elevated in those who develop sleep problems, with added risk if the person has persistent sleep problems, and reduced risk for those whose sleep problems resolve over the course of their back pain.

Comparison to the existing literature shows LBP prevalence in Iran is comparable to that in European countries and other countries worldwide, with similar associated risk factors.[1,31,32] While the current cohort

Table 3. Logistic Regression with 95% Confidence Intervals (95% CI) for Relationship of Sleep Problems with Pain Intensity for Those with Low Back Pain

Sleep Problem Status	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
No sleep problems	Reference category	Reference category
Sleep problems	2.69 (1.72, 4.11)	2.48 (1.62, 3.70)
Exploratory baseline and follow-up group analysis		
No sleep problems (none at baseline, none at follow-up)	Reference category	Reference category
Developing sleep problems (none at baseline, present at follow-up)	2.99 (1.51, 5.92)	2.88 (1.32, 6.31)
Persistent sleep problems (present at baseline and at follow-up)	3.73 (1.92, 7.26)	3.45 (1.59, 7.46)
Resolving sleep problems (present at baseline, not present at follow-up)	0.46 (0.25, 0.87)	0.49 (0.26, 0.93)

*Baseline adjustment for: pain intensity, depressive and anxiety symptoms, age, gender, occupational status, and duration of back pain.

reported a higher level of pain intensity compared to community-based LBP or chronic pain samples,[23,33] it reported similar levels to population norms for patients seeking treatment for LBP or attending pain management clinics, as was the case in this study.[34,35] The mean score for the PSQI within the current cohort (10.5) was generally higher than that for community-dwelling individuals (mean range 4 to 6),[36,37] but this study's score is within the expected range for individuals with pain, comorbidity, sleep problems (eg, insomnia), and poor health.[38,39] In terms of the effect of sleep problems, 2 recent longitudinal studies reported effects similar to those in this study of the role of the reduction in sleep problems in reducing reports of pain at follow-up and the effect sizes reported.[40,41]

A major strength of this study is the prospective design, which enabled analysis of the predictive effects of sleep problems on outcomes in people with LBP. In addition, the study described effects for those who presented with sleep problems at baseline, those who subsequently developed sleep problems after baseline, and those whose sleep problems resolved at follow-up, which gives a better perspective on the timing and sequences of sleep problems and the effects they have on patient-reported recovery and pain intensity. Another strength of this study is the consideration of potential confounds within the analysis. For example, depression has a known reciprocal relationship with both pain and sleep, with sleep problems being a diagnostic feature of depression[12,42]; therefore, it was important to account for the potential effects of this within the analysis. Another important factor accounted for within the regression analysis was the duration of back pain prior to the patient entering the study. It was important to control for the effect of duration of back pain because research has shown that those with a longer duration of back pain (ie, chronic) have an increased risk for poor outcome in general.[43] However, this study did not account for other important confounds such as caffeine intake, comorbidity, and medication use (analgesia, sleep medication); any one, or all, of these may have influenced the effects reported. There are also limitations in terms of the sample. This study recruited a convenience sample of consecutive patients attending a chronic pain clinic. Firstly, recruitment was not aligned to the treatment stage of each patient (ie, not every patient was at the beginning stage of their treatment), and so the trajectory or course of pain and sleep will differ with this case mix. The current study's results on the "developing sleep group" give some insight into these effects; however, incidence cohort studies (ie, onset of sleep problems in patients with pain) will be better placed to give greater detail to the patterns and relationships over time. Secondly, severity of symptoms (sleep problems, pain, comorbidity) would likely be higher within the current chronic pain clinic cohort, compared to general populations or primary care populations. Therefore, the results in the current study may represent an overestimation of the association effects. Nevertheless, both primary care and general population samples contain subpopulations with high levels of pain and sleep problems,[7,12] where particular individuals may be at similar or higher risk for poor outcomes. While the measure of sleep problems used in this study is validated, and broadly used in epidemiological studies,[24,26] it still only captures a subjective rating of sleep quality. The use of objective measures (eg, polysomnography, actigraphy) may have improved the accuracy of our estimates, although this would have proved difficult to apply in large samples such as this one. Finally, while there is clinical utility in the use of "cut points" (eg, in this study the recovery measure, the pain intensity recovery measure, and the indication of significant sleep problems) to potentially identify groups of patients who may benefit from additional treatment, a limitation is that this study may have missed changes in individuals within the subgroup categories.

The key message derived from the results is that sleep problems significantly predict poor outcome for those with LBP who are seeking treatment. The effect sizes for those presenting with sleep problems at baseline indicate significant increased risk for poor outcome and pain intensity at follow-up, and examination of groups accounting for the presence of sleep problems through time show larger effects with roughly triple the risk for nonrecovery, and presence of pain intensity, due to the presence of sleep problems. Moreover, the design of this study allowed examination of the development of sleep problems, which showed that almost one-fourth of patients developed sleep problems that were associated with poor outcome, while in comparison the proportion of sleep problems that resolved was relatively small. This finding highlights not only a need to evaluate and perhaps address sleep problems in the presenting patient, but also to be aware of the potential risk to patients for developing sleep problems, and so monitoring and assessment of sleep problems may be beneficial. A further noticeable finding, albeit in a small proportion, is that those who reported that their

sleep problems had resolved were more likely to report recovery, compared to those who had not reported sleep problems at all. This may reflect the intrinsic link between pain and sleep,[10] and may suggest that to address both within treatment may have an additive positive effect on recovery, over and above targeting pain or sleep independently. Indeed, early evidence is now emerging on the benefits of targeting sleep problems in those with pain. A recent meta-analysis by Tang et al.[44] considered evidence of nonpharmacological randomized controlled trial interventions targeted at sleep for adults who reported long-term pain. Results showed significant reductions in sleep problems, fatigue, and pain at post-treatment.

CONCLUSION

This study of patients with LBP showed increased risk for poor outcomes in those with LBP who reported sleep problems. Clinicians may wish to consider treatment options that involve addressing sleep problems as part of their treatment.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

FUNDING

No funding sources were provided.

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