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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 on how sleep influences pain are complex. To date there is a lack of prospective research on the timings and the development of sleep problems in those who have LBP, such information would be useful to identify individuals at risk of poor outcome. Aims are to investigate the predictive role of sleep problems on self-report recovery and pain intensity using logistic regression reporting Odds Ratios (OR). An observational cohort of 761 chronic LBP patients recruited from a pain management clinic participated, and completed data at baseline, and at 6 month follow-up (n = 682). Results show an increased odds of reported non-recovery (OR 1.52) and pain intensity (OR 2.69) for those who report sleep problems at baseline. Further analysis on the experience of sleep problems through time show that those with developing sleep problems (i.e. no sleep problems at baseline but reported sleep problems at follow-up) were at increased odds of reporting non-recovery (OR 2.17) and pain intensity (OR 2.95), as was 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 (i.e. sleep problems present at baseline but not at follow-up) were at a decreased odds of non-recovery (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.

Keywords

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 report a point prevalence rate at 18%, 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 report an estimated 70% recurrence rate over 5 years for those with LBP [2]. This has led LBP to have a significant global impact in terms of disability to the individual [3,4], and 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, in particular sleep problems, and the effect this may have on the outcomes for those with LBP. Sleep problems associated with back pain are common, a large epidemiological study reported that over half of those who report back pain also reported sleep problems [6], and a review of 13 LBP studies report a prevalence rate of 58.9% for people ascribing sleep problems related 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, EEG and polysomnography output, and poor daytime functioning [8-10]. Studies have shown associations between increases in 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 of psychological morbidity (e.g. 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 that associate with the sleep cycle that may modulate nociception [8]. Evidence shows higher sleep disturbance are found within inflammatory populations (e.g. rheumatology and fibromyalgia populations) [13,14], and recent evidence on chronic LBP participants has shown changes in pro-inflammatory markers (Interluekin-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 timings and sequences on the development of sleep problems in those with back pain, or the impact they have on recovery, something which 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 (e.g. sleep hygiene treatment). The primary aim of this 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 hypothesised that, compared to those who do not report sleep problems, those with developing sleep problems will be less likely to report a favourable recovery, and that those with persistent sleep problems will have the worse outcomes overall.

Methods

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

The cohort was inclusive of a convenience sample of consecutive patients with LBP attending the Outpatient Chronic Pain Clinic, Department of the 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 (NSAIDs), physiotherapy (exercise, spa therapy). Patients are normally assessed for progress at two month intervals, and treatment usually lasts for one year. Patients were eligible to participate in this current study if they had a confirmed diagnosis of CLBP (i.e. persistent LBP with or without referred leg pain for at least 3

months), were 18 years old or over, and be able to speak and read Persian. Patients were excluded if they had any concurrent medical illness (e.g. cardiopulmonary, central nervous system, diabetes, intellectual disorder, rheumatic diseases), serious spinal pathology (e.g. fracture, metastatic), and/or received spinal surgery. Patients scheduled to attend the outpatient chronic pain clinic were approached over a three month period (February 2014 to April 2014), and invited to take part. As this is a convenience sample of consecutive patients, the recruitment of patients to this study is not aligned to the beginning of treatment for each patient, variation exists 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 (MY). 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 the patient was 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 six categories (Completely Recovered, Much Better, Better, No Change, Worse, Much Worse) and participants were asked to indicate one category. A cut off was chosen for this measure on the basis of clinical utility (e.g. identification of subgroup who may benefit from treatment due to no change or worsening outcome over time). This variable was collapsed to form two groups: a recovery group (*Completely Recovered, Much Better, and Better)* and a non-recovery group (*No change, Worse, Much Worse*).

Pain intensity was measured using a visual analogue scale (VAS), and patients were asked to rate their pain level at the time of filling out their baseline questionnaire and at 6 month follow up [6,19]. For

the logistic analysis we based the cut off of 0 or 1 (0mm to 10mm) 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 categorised the pain duration question into two groups for the analysis (6 months or less *versus* 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 0-3 Likert scale with a global score of "5" or greater indicating clinically significant sleep problems; this global score was used as the cut off 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 two scales (depression, anxiety) and each scale comprises of 7 items. All items are rated on a Likert-type scale ranging from 0 to 3, with higher scores indicating higher symptom levels with scores ranging from 0-21 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, BMI score, and occupational status (working, sick leave, not in work, retired).

Analysis

Descriptive statistics of the percentage proportions, mean, median and inter quartile range were presented for all the measures. Initially a prospective model was tested using logistic regression producing Odds Ratios (OR) with 95% confidence intervals (95% CI). 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 two stage process was applied to each logistic regression model. Firstly 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 including 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. The use of an adjusted model gives important indication of the association whilst controlling for potential confounding (e.g. effect of depression on the sleep to pain pathway), and the use of both an unadjusted and adjusted model 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 (i.e. baseline and follow-up). The first category (no sleep problems), were participants who reported no sleep problems at baseline and at follow up (used as the reference category within the logistic regression). The second category (developing sleep problems) were those participants who reported no sleep problems at baseline, but did report sleep problems at follow up. The third category (persistent sleep problems) comprised of those participants who reported sleep problems at baseline and at follow up. The final category (resolving sleep problems) were 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.

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 were performed to statistically assess the difference in the patent's age, gender, BMI, depression, anxiety and pain intensity, occupation as well as sleep quality between those who responded at 6 months and those who did not respond at 6 month follow-up, and no differences were found.

Baseline characteristics show 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 months 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 10mm or below at 6 month follow up. Table 1 outlines the characteristics of the cohort.

Patient self-report non recovery

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 (i.e. no reported sleep problems at baseline and at follow up) as the reference category within logistic regression analysis (see Table 2), show that those with developing sleep problems (i.e. no sleep problems at baseline, reported sleep problems at follow up) were almost over 3 times more likely to report non-recovery at 6 months (unadjusted OR 2.93, 95% CI 1.53, 5.61), and those with persistent sleep problems (i.e. sleep problems reported both at baseline and follow-up) were over 3 times more likely to report a non-recovery (unadjusted OR 3.24, 95% CI 1.63, 6.43), with those who have resolving sleep problems

(i.e. sleep problems reported at baseline but none reported at follow-up) having a reduced odds of non-recovery (unadjusted OR 0.49, 95% CI 0.31, 0.78). Within the fully adjusted model, results show that those with developing sleep problems are just over twice the increase in odds of non-recovery (adjusted OR 2.17 95% CI 1.04, 4.52), those with persistent sleep problems were just under 3 times the odds of non-recovery (adjusted OR 2.95 95% CI 1.48, 5.88), and those with resolving sleep problems were at a reduced odds of non-recovery (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 (cut off set at < 10mm on VAS to indicate recovery), show an increase in the odds of non-recovery 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 shows, that compared to those with no sleep problems reported at baseline and at follow-up, those with developing sleep problems had an increased risk of non-recovery for pain intensity by just under 3 times 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 is greater with almost 4 times the risk in the unadjusted model (OR 3.73 95% CI 1.92, 7.26) and just under 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 on perceived recovery and pain intensity on a cohort of LBP patients who attend a pain management clinic. This study tested the prospective relationship as well as examined the effect of persistent, developing and resolving sleep problems on outcomes. Our findings show support to the study hypotheses: the presence of sleep problems is a significant risk factor for non-recovery and pain intensity for those with LBP, also importantly this study reports the elevation of risk of poor outcome in those who develop sleep problems, the added

strength of risk if the person has persistent sleep problems, as well as a reduction of risk for those whose sleep problems resolve over the course of their back pain.

Comparison to the existing literature shows LBP prevalence is comparable within Iran to European countries, and other countries worldwide, with similar associated risk factors [1,31,32]. Whilst this current cohort reports a higher level of pain intensity compared to community based low back pain or chronic pain samples [23,33], it does report similar levels to population norms for patients seeking treatments for LBP or attending pain management clinics as is the case in this study [34,35]. The mean score for the PSQI within this current cohort (mean score, 10.5) is generally higher than community dwelling individuals (mean rages 4 to 6) [36,37], but this study's score is within the expected range for individuals with pain, comorbidity, sleep problems (e.g. insomnia), and poor health [38,39]. In terms of the effect of sleep problems, two recent longitudinal studies report similar significant effects to this study in terms of the role of the reduction in sleep problems in reducing the reports of pain at follow-up and 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 has been able to describe effects for those who present with sleep problems at baseline, those who subsequently develop sleep problems after baseline, and those where sleep problems have resolved at follow-up which gives a greater perspective on the timings 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 (i.e. chronic) have an increased risk of 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 (i.e. not every patient was at the beginning of their treatment) and so the trajectory or course of pain and sleep will differ with this case mix. This current study's results on the "developing sleep group" give some insight into these effects, however incidence cohort studies (i.e. onset of sleep problems within those 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 be likely to be higher within this current chronic pain clinic cohort, compared to general populations or primary care populations. Therefore the results in this current study may represent an overestimation of the association effects. Nevertheless both primary care and general population samples contain sub populations with high levels of pain and sleep problems [7,12], where particular individuals may be at similar or higher risk of poor outcome. Whilst 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 (e.g. 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 whilst there is clinical utility in the use of "cut points" (e.g. in this current 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 within individuals, within the sub group 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 of 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 treble the risk of non-recovery, and presence of pain intensity, due to the presence of sleep problems. Moreover the design of this study allowed an examination of the development of sleep problems, which showed that almost one quarter of patients develop sleep

problems that associate with poor outcome, whilst in comparison the proportion 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 of 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 report that their sleep problems have resolved are more likely to report recovery, compared to those who have 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 (2015) considered evidence of non-pharmacological Randomised Controlled Trial interventions targeted at sleep for adults who report long term pain [44]. Results show significant reductions in sleep problems, fatigue, and pain at post treatment.

Conclusion

This study of patients with LBP has shown an increase in risk of poor outcomes in those with LBP who report sleep problems. Clinicians may wish to consider treatment options that involve addressing sleep problems as part of their treatment.

Conflict of interest

No author has a conflict of interest

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Legends

Table 1 Cohort characteristics

Table 2. Logistic regression (LR) with 95% Confidence Intervals (95% CI) for relationship of sleep problems with non-recovery for those with low back pain.

Table 3.Logistic regression (LR) with 95% Confidence Intervals (95% CI) for relationship of sleep problems with pain intensity for those with low back pain.

Table 1 Cohort characteristics

Baseline			
Characteristic	**Number (%)**	**mean (SD)**	**Interquartile range**
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 < 10mm)	261 (38.3%)		
Non Recovery (VAS > 10mm)	421 (61.7%)		

Table 2. Logistic regression Odds Ratio (OR) with 95% Confidence Intervals (95% CI) for relationship of sleep problems with non-recovery 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

Table 3.Logistic regression (LR) 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		