Sleep Medicine Reviews 23 (2015) 68–82

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

Non-pharmacological interventions for improving sleep quality in patients on dialysis: systematic review and meta-analysis

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ARTICLE INFO

Article history:
Received 11 August 2014
Received in revised form
2 November 2014
Accepted 13 November 2014
Available online 10 December 2014

Keywords:
Renal insufficiency
Sleep disorders
Renal dialysis
Non-pharmacological therapy
Meta-analysis

SUMMARY

We conducted a meta-analysis to summarise and quantify the effects of non-pharmacological interventions on sleep quality improvement in uraemic patients on dialysis. We defined the primary outcome as the change of sleep quality before and after interventions (evaluated by polysomonography or subjective questionnaires such as Pittsburgh sleep quality index, PSQI). The change of fatigue scales, inflammatory cytokines and adverse events were analysed as secondary outcomes. Twelve eligible randomised controlled trials and one prospective cohort study were identified. All three identified non-pharmacological interventions could result in a greater PSQI score reduction compared to controls: 1) cognitive-behavioural therapy (CBT) versus sleep hygiene education (standardised mean difference (SMD) 0.85, 95% CI 0.37–1.34); 2) physical training versus no training (SMD 3.36, 95% CI 2.16–4.57) and 3) Acupressure (including other acupoints massages) versus control (SMD 1.77, 95% CI 0.80–2.73). In terms of subscores, we found that CBT may shorten sleep latency, alleviate sleep disturbance and reduce the use of sleep medications. The finding of the cohort study suggested that intradialytic aerobic exercise training improved sleep quality in haemodialysis patients with restless leg syndrome. In conclusion, in dialysis-dependent patients, CBT could shorten sleep latency, alleviate sleep disturbance and reduce the use of sleep medications. Acupressure (including other acupoints massages) and exercise training are promising interventions but the results in these subgroups should be interpreted cautiously due to the concern of methodological quality and potential confounding factors.

Introduction

Chronic kidney disease (CKD) is characterised by a reduced glomerular filtration rate, increased urinary albumin excretion, or both [1,2]. Globally, 8%–16% of general population are living with CKD. The number of CKD patients who progress to the end stage renal disease (ESRD) and need dialysis is expected to grow annually [3], which made CKD one of the leading health problems and socioeconomic concerns in developed and developing countries [4].

Sleep disorders, despite various definitions, are common in the dialysis-dependent CKD population [5–8]. The reasons of the high prevalence of sleep problems in patients on dialysis are not fully enucleated, and previous studies reported some potential intrinsic and environmental causes, e.g., large body mass index, inflammatory status [9], low nutritional indices, presence of depression [10], inadequate dialysis [11–13] and overnight rostral fluid shift (fluid displaced from the lower limbs into the neck overnight) [14,15]. The sleep disorders contributed to poor quality of life in dialysis-dependent patients, which further deteriorate the health status of dialysis patients [16].

Apart from the contributory effect on poor quality of life [16,17], sleep problems are suggested to promote the development of risk factors for CKD progression (hypertension, type 2 diabetes and obesity). Furthermore, sleep disturbances might have a direct effect on the deterioration of kidney function in patients on dialysis [18]. Therefore, proper management of sleep disorders in patients on dialysis may yield favourable outcomes. There is currently no specified pharmaceutical treatment guideline for dialysis

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http://dx.doi.org/10.1016/j.smrv.2014.11.005
1087-0792/

Abbreviations

CBT	cognitive-behavioural therapy
CIs	confidence intervals
CKD	chronic kidney disease
CRP	C-reactive protein
ESRD	end stage renal disease
ESS	Epworth sleepiness scale
HD	haemodialysis
HDL	high density lipoprotein
NNT/H	numbers needed to treat/harm
PD	peritoneal dialysis
PSG	polysomonography
PSQI	Pittsburgh Sleep Quality Index
QoL	quality of life
RCTs	randomised controlled trials
RLS	restless leg syndrome
RR	risk ratio
SMD	standardised mean difference
VAS	visual analogue scale

population, and benzodiazepines, non benzodiazepine, anxiolytics and melatonin are all prescribed for these patients. As data on drug therapy effects in dialysis patients are limited, the existing recommendations are mainly based on expert opinions [19]. As a result, practitioners should be cautious when prescribe drugs for sleep disorders in dialysis patients. Take insomnia for example, the pharmacological approach remains the most widely used intervention [20,21], meanwhile, concerns about drug tolerance, habituation, complications and excessive accumulation (especially for renal insufficiency patients) are frequently raised [22]. Kidney transplantation is the most effective way to correct uremic abnormality and may have positive impacts on sleep quality of CKD patients. Previous studies showed a significant improvement in sleep apnea hypopnoea syndrome, restless legs syndrome and chronic insomnia after renal transplantation [23–26]. However, there are also emerging researches failed to find the improvement of general sleep quality after kidney transplantation [27,28]. When interpreting the results of these conflicting studies, we should be aware that fluid overload (mainly contributed to obstructive sleep apnea) remission and immune suppressive therapy after kidney transplantation are the main confounding factors. Besides, study designs on this topic could not be randomised, which weakened the validity of these studies. Recently, growing evidence indicates favourable effects and less adverse events of non-pharmacological interventions (such as cognitive-behavioural therapy (CBT), acupuncture, exercise, bright light therapy, etc.) on primary insomnia [29], which are potential effective methods to improve the sleep quality in dialysis-dependent population as well. But the results of available clinical researches in dialysis-dependent population were inconsistent and were not summarised. The present systematic review and meta-analysis aims at comprehensively summarising and quantifying the effects of non-pharmacological interventions for improving sleep quality in dialysis-dependent patients, which will be helpful for evidence-based clinical decision-making.

Methods

The protocol of this review has been registered in PROSPERO (CRD42014006949) (www.crd.york.ac.uk/PROSPERO).

Search strategy and study selection

We conducted a comprehensive search of the medical literature using PubMed (inception to June 2014), EMBASE (inception to June 2014), Cochrane controlled trials register (issue 5, 2014), Web of Science (inception to June 2014) and http://clinicaltrials.gov/(date of search: June 24th 2014). The PubMed search terms (both as medical subject headings and free text terms) were: (renal dialysis or renal replacement therapy or kidney disease) and (disorders of initiating and maintaining sleep or parasomnias or dyssomnias or intrinsic sleep disorder or insomnia or sleep apnea syndrome or nightmares or interrupted sleep or sleep disorders). Detailed PubMed search strategy was submitted as web extra material, and the search terms were adapted for the other electronic data sources. We additionally searched the reference lists of the original reports, reviews, letters to the editor, case reports, guidelines and meta-analyses retrieved through the electronic searches. There was no restriction on language of publications.

We selected the studies in two steps. Firstly, two review authors (Bo Yang and Jiaruo Xu) independently screened the titles and the abstracts. Secondly, the full text of potentially eligible studies was retrieved and assessed independently by the same two review authors. The pre-specified eligibility criteria are as follows: 1) randomised controlled trials (RCTs) or prospective cohort studies; 2) dialysis-dependent patients with end stage renal disease; 3) pharmacological interventions comparable in experimental groups and in control groups; 4) sleep quality evaluated before and after interventions; 5) the factors to be studied were non-pharmacological interventions; 6) placebo control (e.g., sham acupressure) or standard control (standard non-pharmacological interventions e.g., sleep hygiene education). Studies using other unrelated interventions were eligible, as long as these were administered to both the experimental and control groups. We excluded studies with the following properties: 1) patients with renal cell carcinoma; 2) patients with unstable or acute clinical situations; 3) presence of psychiatric disorders. If duplicate publication was identified, we used the one with the most relevant information. We abandoned all the retracted research. Any disagreement between review authors was resolved by consensus, adjudicated with the support of a third review author (Qiang Xue).

Data extraction

All data were extracted independently by two review authors (Tingting Wei and Jing Xu) into a predesigned data collection form (Microsoft Office Excel 2007; Microsoft Corp, Redmond, Washington, USA). All data extraction was then checked by a third review author (Chaoyang Ye). The following data were extracted for each study: study design; number of centres; geographical location of the study; patient characteristics (age; proportion of female patients; disease status; dialysis status and baseline sleep quality); sample size; duration of interventions; detailed relevant interventions; concomitant interventions allowed; and total number along with the detailed information about adverse events reported. We defined our primary outcome as the change of sleep quality before and after study (evaluated by polysomonography (PSG) or subjective questionnaires such as Pittsburgh sleep quality index (PSQI) [30] and its constituent components). As another common syndrome in patients on dialysis, change of fatigue scales was combined as secondary outcome; inflammatory cytokines and adverse events were also analysed as secondary outcomes. Domains used to evaluate the risk of bias for each study were also documented: methods used to generate the randomisation schedule; allocation concealment and blinding. We attempted to contact the original investigators in order to obtain further