

Relationship between Pain Tolerance/ Sleep Disorders and Quality of Life in Elderly Diabetic Haemodialysis Patients

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Abstract

Background: Patients with sleep disorders report worse self-perceived quality of life than those without the disorders. In addition, it has recently been shown that poor quality of sleep is a predictive factor of near-term mortality in patients with end stage renal disease (ESRD).

The aim of this study was to evaluate possible relationships between sleep disorder, quality of life and chronic pain in elderly diabetic hemodialysis patients.

Methods: In the present study, the following groups were enrolled: 36 non-haemodialysis patients (group Non-HD) and 38 hemodialysis patients (group HD). The Pittsburgh Sleep Quality Index (PSQ-I) for sleep disturbances and health-related quality of life (HRQoL) questionnaires were administered in all the patients and their tolerability of pain was objectively evaluated with an algometer.

Results: In the HD group, a statistically significant positive correlation was observed between SF-36 and the maximum pain level ($r: 0.723$; $p < 0.05$). Similarly, a statistically significant negative correlation was reported between the PSQI and maximum pain level ($r: -0.795$; $p < 0.05$).

Conclusion: These data suggest the existence of a close relationship between pain tolerance with sleep disorders and health-related quality of life, in elderly diabetic patients with ESRD. Thus, the appropriate management of chronic pain in these patients could significantly improve the quality of life and ameliorate the sleep disorder.

Keywords: Elderly diabetics; Sleep disorders; Quality of life; Algometer

Introduction

Sleep disorders are present in 65% of dialysis patients [1]. These include delayed sleep onset, frequent awakening, restlessness and daytime sleepiness [2]. Patients with sleep disorders report worse self-perceived health-related quality of life than those without the disorders [1]. In addition, it has recently been shown that poor quality of sleep is a strong predictor of near-term mortality in patients with end stage renal disease (ESRD) [3].

Chronic pain represents a common health challenge experienced by patients with chronic kidney disease (CKD) and seems to be associated with poor quality of sleep [4,5]. Impaired pain threshold and sleeplessness are both frequent symptoms in patients CKD [6,7]. Although there are several studies in dialysis populations on the pain perception, its relationship with quality of life and quality of sleep is still unclear. In addition, objective pain evaluation with the Algometer was not previously evaluated in CKD patients.

Thus, the present study seeks to evaluate a possible relationship between threshold objective pain with sleep disorders and health-related quality of life, in both non-haemodialysis and haemodialysis patients.

Methods

Patient population

In the study protocol, a total of 74 elderly type 2 diabetic CKD (stage

G3b-4, G5) [8] subjects were enrolled in the study. All patients were clinically assessed by medical history, physical examination, and routine laboratory test and by comprehensive geriatric assessment. Diabetes was diagnosed in the last 20 years. Eligibility criteria of all patients include: age >65 years; no evidence of chronic pain, as evaluated by McGill questionnaire (McGill score =2), no evidence of depressive symptoms (GDS-15 <5), no evidence of malnutrition, as evaluated by albumin levels >3.5 g/dL; maintaining functional independence or loss of it in only one of the six basic activities of daily living (ADL); no evidence of significant cognitive impairment, as evaluated by Mini Mental State Examination (MMSE) >24; no evidence of severe diseases that might highly influence mood state (e.g.: cancer, symptomatic cerebro-vascular disease with residual deficit, schizophrenia and other psychoses); disease severity, as evaluated by Cumulative Illness Rating Scale for overall illness severity (CIRS) <3 (moderate). Since haemodialysis patients are characterized by an elevated comorbidity index (CIRS-CI) that has an impact on depressive symptoms, we compared them with elderly patients with a similar level of CIRS-CI such as the hospitalized group. The exclusion criteria are: oncology-related chronic pain disorder or the use of opioid analgesic, major anti-depressive or anxiolytic agents. The purpose of the study was explained to all subjects and their voluntary written consent was obtained before their participation. The study protocol was reviewed and approved by Ethical Committee of our Institution (121/2014).

Experimental protocol

For the present study, the following groups were enrolled: 36 non-haemodialysis patients (group Non-HD) with mean age of 75 ± 3 years, body mass index (BMI) of 26.5 ± 3 Kg/m², systolic blood pressure (SBP) of 125 ± 09 mmHg, diastolic blood pressure (DBP) of 80 ± 4 mmHg, HBA1c of $6.8 \pm 0.4\%$ and GDS-15 of 3 ± 1 , and 38 hemodialysis patients (group HD) with mean age of 76 ± 2 years, BMI of 26.1 ± 2 kg/m², SBP of 122 ± 08 mmHg, DBP of 81 ± 3 mmHg, HBA1c of $6.7 \pm 0.5\%$ and GDS-15 of 4 ± 2 . At the baseline, all patients had no chronic pain, as evaluated by McGill questionnaire. The clinical characteristics are reported in Table 1.

Cognitive function was evaluated by a Mini Mental State Examination (MMSE), a widely used screening instrument for measuring global cognitive status [9]. It is composed of 30 items divided in two sections. The first section requires vocal responses and covers orientation, memory and attention. The second part focuses on the ability to name, to follow verbal and written commands, to write a sentence and a copy a complex polygon. Maximum total score is 30 and a score less than 24 indicate a significant cognitive impairment [9], although other rating scores have been employed. Screening tests to assess depressive symptoms include the Geriatric Depression Scale 15 items (GDS-15) [10]. The GDS was designed specifically assesses depressive symptoms in elderly patients [11]. GDS-15 represents a shortened version consisting of 15 questions [12] that has been found to correlate highly with the original 30-item instrument [13]. The GDS-15 is a reliable and well-validated measure of depression in elderly [10,14] and in CKD patients [15]. Responses were coded 1 = has symptom; vs. 0 = symptom not present. GDS-15 score >5 indicate depressive symptoms [10]. To assess physical illness we used the Cumulative Illness Rating Scale (CIRS) [16]. This measure evaluates the cumulative score derived from ratings of the degree of impairment in each of 13 major organ groups (cardiac; hypertension; vascular; respiratory; eye-ear-nose-throat-larynx; upper GI; lower GI; hepatic; renal; ureters-bladder-urethra-prostate-genitals; musculo-skeletal-integumentary; neurological; endocrine-metabolic) and impairment in the psychiatric-behavioral category [17]. In particular, the CIRS evaluates the clinical rating of impairment as follows: no impairment = 1; mild impairment = 2; moderate impairment = 3; severe impairment = 4 and extremely severe impairment = 5. Two CIRS summary measures were evaluated, each excluding the psychiatric/behavioural item to avoid confounding with mental health and cognitive functioning. First, overall illness severity is represented by the mean of the 13 CIRS items. Second, the comorbidity index (CIRS-CI), which reflects the diversity of severe illnesses, is the total number of the 13 categories in which moderate, severe or extremely severe impairment levels of disease are recorded. The functional status is evaluated by Activities of Daily Living (ADL) [18]. It consists of six items for evaluation of self-care, which measure the functional status as dependence in each of the six ADL. Dependence is defined as no ability to manage the following activities: bathing, toileting, transferring, continence, dressing and eating. One point was assigned for each of activities in which a subject was dependent, ranging from 0 (independent in all activities) to 6 (totally dependent).

The Pittsburgh Sleep Quality Index (PSQ-I) [19] screens for sleep disturbances over a 1-month period. There are 19 questions with seven component scores including 'subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, and sleep disturbance, use of sleeping medication and daytime dysfunction'. The seven component scores are summed to yield one global score [19]. A global score >5 has 89.6% sensitivity and 86.5% specificity for determining disturbance in sleep [19]. The PSQI has previously been used in CKD patients [20].

Participants were asked to complete a HRQoL questionnaire (SF-36v2 Health Survey) [21]. The SF-36 has been used extensively in patients with kidney disease and has sound psychometric characteristics in this patient

population to assess HRQoL [22]. The SF-36 is a well-validated 36-item questionnaire covering issues relating to physical, psychological and social functioning that generates scores from 0 (worst) to 100 (best) for eight sub-scales of HRQoL: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE) and mental health (MH). It is composed of two component summary scores, the Physical Component Summary (PCS) and Mental Component Summary (MCS). Higher scores indicate better HRQoL [23]. The McGill questionnaire was designed to provide quantitative measures of clinical pain. It consists primarily of major 3 classes of word descriptors-sensory, affective and evaluative- that are used by patients to specify subjective pain experience. It also contains an intensity scale and other items to determine the properties of pain experience. In addition the questionnaire comprised a top sheet to record necessary medical information (such as diagnosis and drug intake), line drawings of the body to indicate the spatial distribution of the pain, words that describe temporal properties of pain, and the overall present pain intensity (PPI). The PPI is recorded as a number from 1 to 5, in which each number is associated with the following words: 1, mild; 2, discomforting; 3, distressing; 4, horrible; 5, excruciating. This questionnaire initially requires 15-20 min, with increasing experience; it is completed in 5-10 min [24]. The pain threshold is evaluated with algometer [25]. This instrument consisted of a 0.8 mm needle with a round tip, fixed in a vertical position to a force transducer (FSG, Honeywell, Columbus, OH, USA). The signal from the sensor was amplified by an instrumental amplifier (INA 125, Burr Brown, Dallas TX, USA and digitized with an A/D converter (MAX 147, Maxim, Sunnyvale, CA, USA). This apparatus was encased in a small plastic box (10x15x3 cm) and connected to the parallel port of a personal computer. Custom software, written with LabView (National Instruments, Austin, TX USA), permitted the display, in real time, of the force applied to the transducer over time and the recording of the data for subsequent analysis. The system was calibrated before each use with two known loads (0 g and 220 g). The testing procedure required the subject to auto-administer increasing force on the testing needle until a pain sensation was realized (minimal test). This test was repeated eight times, respectively, on the tip and on the dorsal surface of the third phalanx of the second, third, fourth and fifth finger. These eight tests were then repeated, but the subjects were asked to push on the needle until the maximum tolerable sense of pain was reached (maximal test). For each test, the maximal applied force (in grams) was defined as "pain threshold" and used for statistical analysis. Thus, two pain thresholds were evaluated: one for the minimum pain level and the other for the maximum pain level. To evaluate the overall tolerability of the described protocol, and the end of every procedure, each subjects was asked to quantify on a 0 (no discomfort) to 10 (intolerable pain) scale, the overall discomfort as a result of the exam. All questionnaires and pain threshold are performed in the interdialytic day.

Statistical analysis

All values were expressed as the mean \pm standard error. Comparison between groups was performed using unpaired Student's "t" test. ANOVA was performed to evaluate the homogeneity of sample. Difference at the $p < 0.05$ level of probability were considered significant.

Results

Body Mass Index (BMI), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), HBA1c, serum creatinine, Blood Urea Nitrogen (BUN), Geriatrics Depression Scale (GDS-15), McGill Subjective Pain Questionnaires and SF-36 (SF-36v2 Health Survey), were all similar in both non haemodialysis (Non-HD) and in haemodialysis (HD) groups (p : ns), and the mean values are reported in Table 1.

Minimum pain level (an index of pain sensitivity) was of 456 ± 23 gin

	Non-HD (n= 36)	HD (n=38)
Age (yr)	75 ± 3	76 ± 2
BMI (kg/m ²)	26.5 ± 3	26.1 ± 2
SBP (mmHg)	12 ± 0.9	122 ± 0.8
DBP (mmHg)	80 ± 4	81 ± 3
FPG (mg/dL)	109 ± 7	112 ± 6
HBA1c (%)	6.8 ± 0.4	6.7 ± 0.5
Serum Albumin (g/dL)	4.1 ± 0.5	4.0 ± 0.6
Serum Creatinine (mg/dL)	3.1 ± 1.2	3.0 ± 1.0 (post HD)
Serum BUN (mg/dL)	75 ± 10	81 ± 12 (post HD)
GDS-15	3 ± 1	4 ± 2
McGill Pain Questionnaire	2 ± 0.3	2 ± 0.4
SF-36 (SF-36v2 Health Survey)	54 ± 3	58 ± 4

Table 1: Clinical characteristics of Non-Haemodialysis (Non-HD) and Haemodialysis (HD) groups.

Body mass index (BMI), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Fasting Plasma Glucose (FPG), Blood Urea Nitrogen (BUN), Geriatrics Depression Scale (GDS-15). Values are mean ± SEM.

the Non-HD group and it was significantly increased in the HD group to 615 ± 27 g (p<0.05).

Similarly, maximum pain level (an index of pain tolerance) was of 542 ± 24 g in the Non-HD group and it was significantly increased to 749 ± 31 g in the HD group (p<0.05).

PSQI (an index of sleep disorders) was 5 ± 1 in the Non-HD group and it was significantly increased to 23 ± 2 in the HD group (p<0.01).

In the HD group, a statistically significant positive correlation was observed between SF-36 and the maximum pain level (r: 0.723; p<0.05). In addition, a statistically significant negative correlation was reported between the PSQI and maximum pain level (r: -0.795; p<0.05) (Figure 1).

Discussion

In this study we observed in the HD group, a significant positive relationship between the quality of life (as evaluated by SF-36) and maximum pain level (an index of the pain tolerance). This observation highlights the crucial role of pain level in the quality of life in these patients. A recent study has in fact suggested that patients' perception of pain, may be more important than objective assessment in determining the quality of life of patients with ESRD [26]. Chronic pain represents a common disorder in CKD patients [27], especially in patients with end-stage renal disease (ESRD) [28]. In this regard, it has been reported that about 80% of ESRD patients undergoing dialysis had chronic pain [29] and 35-70% of patients had moderate to severe chronic pain [30]. There is evidence that symptoms (such as pain) are both under recognised [29] and under treated [31] in the dialysis population. Although there are several studies on sleep complaints and disorders and their relationship to pain level in chronic kidney disease (CKD) patients, the objective perception of pain, as evaluated by the algometer has not been studied in dialysis populations before. In our population, we did not observe significant differences in the subjective chronic pain, as reported by the use of McGill questionnaires. These data strongly suggest that subjective pain evaluation could under recognise the real pain in these subjects. Pain is a subjective feeling that is therefore particularly difficult to quantify and study [32]. For instance, different studies have reported that pain level, as evaluated by BPI questionnaire pain and McGill Pain Questionnaire (SF-

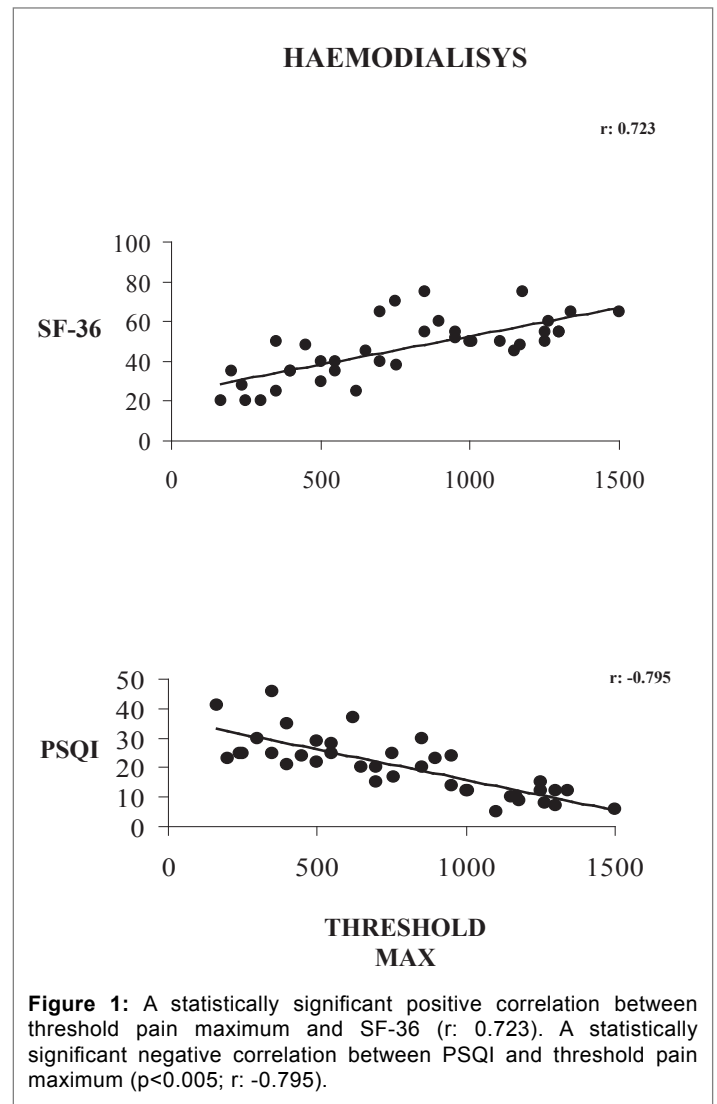


Figure 1: A statistically significant positive correlation between threshold pain maximum and SF-36 (r: 0.723). A statistically significant negative correlation between PSQI and threshold pain maximum (p<0.005; r: -0.795).

MPQ), could be under-recognized in these patients [29,33]. No studies have focused on the specific problem of pain in the dialysis population, using the algometer its evaluation. The algometer is quick and easy to execute and does not require complicated training for the examiner and is virtually free of any mechanical interference from the tester [25]. In the present study, we report the pain level, evaluated by an algometer, in elderly haemodialysis patients; demonstrating that an increased pain threshold characterizes ESRD patients.

Persistent pain may lead to sleep disorders. Sleep complaints and sleep-related disorders are common in dialysis patients [34]. In previous studies it has been observed that a substantial proportion of ESRD patients reported pain during off dialysis (44%) time and poor sleep (45% have a PSQI score of >5) [35,36]. Chronic pain and sleep disturbances each independently have profound detrimental effects on quality of life (QoL) in ESRD populations [37]. In particular, we observed, in HD patients, an increased maximal pain threshold (an index of increased tolerability) that is associated with a less sleep disorder, as evaluated by PSQI.

In conclusion the present study has demonstrated the utility of an algometer in the objective evaluation of pain tolerance, which may be underestimated by subjective methods of evaluation. The study has also shown that pain tolerance is directly related to quality of life (SF-36) and inversely related to sleep disorder (PSQI).

These data suggest the existence of a close relationship between chronic pain/pain tolerance with sleep disorders and health-related quality of life in ESRD patients. Thus, appropriate management of chronic pain in these patients could significantly improve their quality of life and ameliorate their sleep disorders.

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