SLEEP DISORDERS IN CHRONIC RENAL FAILURE PATIENTS

Thesis

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By

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ABBREVIATIONS

ABs	:	antibiotics.
AHI	:	Apnea hypopnea index.
AI	:	Apnea index.
ANCA	:	Antineutrophil cytoplasmic antibody.
BMI	:	Body mass index.
CA		Central apnea
C-ANCA	:	Cytoplasmic pattern antineutrophil cytoplasmic antibody.
CAP	:	Cyclic alternating pattern.
CAPD	:	Continuous ambulatory peritoneal dialysis
CIDP	:	Chronic inflammatory demyelinating polyneuropathy.
CKD	:	Chronic kidney disease.
CNI	:	Calcineurin inhibitors
CNS	:	Central Nervous System
CPAP	:	Continuous positive airway pressure
CRF	:	Chronic Renal Failure.
CRPS	:	Complex regional pain syndrome.
CSA	:	Central sleep apnea.
CSF	:	Cerebrospinal fluid.
CTS	:	Carpal tunnel syndrome.
CV	:	Cardiovascular
CVD	:	Cardiovascular disease.
DA	:	Dopamine
ECG	:	Electrocardiography.
EDS	:	Excessive daytime sleepiness.
EEG	:	Electroenchephalogram.
EMG	:	Electromyogram.
EOG	:	Electro-oculogram.
ESRD	:	End stage renal disease.
ESS	:	Epworth sleepiness scale.
FSGS	:	Focal and segmental glomerulosclerosis.
GFR	:	Glomerular filtration rate.
GNP	:	glomerulonephritis.
HD	:	Heamodialysis

HIV	:	Human immunodeficiency virus
HPA	:	Hypothalamic pituitary adrenal
HUS	:	Hemolytic-uremic syndrome.
ICSD-2	:	International calassification of sleep disorders
IgA	:	Immunoglobin A
K/DOQI	:	The Kidney Disease Outcomes Quality Intitiative
MM	:	Mononeuropathy multiplex.
MN	:	Mononeuropathy
MSLT	:	Multiple Sleep Latency Test.
MWT	:	Maintenance of wakefulness test.
NKF	:	National Kidney Foundation.
NREM	:	Non rapid eye movement
NOS		Not otherwise specified
OCR	:	Oculocrebrorenal
OSA	:	Obstructive sleep apnea.
P-ANCA	:	Perinuclear pattern antineutrophil cytoplasmic antibody
PD	:	Peritoneal dialysis
PKD	:	Polycystic kidney disease
PLMD	:	Periodic limb movement disorder
PLMI	:	Periodic limb movement index
PN	:	Polyneuropathy
PNS	:	Peripheral Nervous System
PRES	:	Posterior reversible encephalopathy syndrome
PTH	:	Parathormone
RDI	:	Respiratory disturbance index.
REM	:	Rapid eye movement
RLS	:	Restless leg syndrome.
RT	:	Renal transplantation.
SAH	:	Subarachnoid hemorrhage.
SAS	:	Sleep apnea syndrome.
SDB	:	Sleep disordered breathing.
TIA	:	Transient ischemic attacks.
TIB	:	Time in bed.
TNF	:	Tumor necrotic factor.
TST	:	Total sleep time.
TTP	:	Thrombotic thrombocytopenic purpura.

ABSTRACT

Purpose: This work aims to assess the prevalence and quality (type) of sleep disorders in chronic renal failure patients. **Subjects & Methods:** A prospective study was conducted on 40 patients with chronic renal failure and they were subdivided into two groups. Patients without heamodialysis HD (group I) (n=20), and patients on regular HD (group II) (n=20), and 20 sex and age matched control subjects. All subjects were subjected to through neurological and medical history taking and examination, Hamilton scale for depression, Epworth sleepiness scale ESS, laboratory work up, and polysomnography. **Results:** All patients had sleep complaints in the form of excessive daytime sleepiness, difficulty falling asleep, early morning awakening, jerking leg movements and fragmented sleep. Patients group had significant polysomnographic abnormalities when compared to control group while, only sleep efficiency was statistically significantly lower in group I compared to group II. Hb was positively correlated with sleep efficiency, and negatively correlated with AHI, AHI in nonREM, CA, hypopnea and number of awakening.FBS was negatively correlated with TST, sleep efficiency, lowest O_2 and average O_2 in REM and non REM, and was positively correlated with S1 sleep stage, AHI and hypopnea, Epworth sleepiness scale correlations: was positively correlated to central apnea. **Conclusion:** There is a high prevalence of sleep disorders in chronic renal failure CRF patients whether they are on regular heamodialysis HD or not and, proper management of these disorders will improve the morbidity and quality of life of those patients.

Keywords:

Sleep apnea – CRF – restless leg syndrome – heamodialysis – sleep disorders

INTRODUCTION

There is an increased prevalence of sleep disorders in patients with end-stage renal disease on heamodialysis treatment.Specific diagnostic and therapeutic regimen could improve quality of life and life expectancy, especially sleep apnea which is a disease that has a high prevalence in this patients group and which can be treated successfully **(Burmann** *et al.,* **1995).**

About 85% of patients on maintenance haemodialysis have sleep disorders that depend on co-morbidities, age, morning dialytic shift, and blood pressure. Some data exist on sleep disorders in chronic kidney disease (CKD) patients, and show that lack of refreshing sleep is present even at early stages of the disease and may affect 82% of patients without any relationship to co-morbidities **(De Santo** *et al.,* **2006).**

Excessive daytime sleepiness and sleep disorders, including sleep apnea syndrome, restless legs syndrome, and periodic limb movement disorder, occur with increased frequency in patients with end stage renal disease **(Perl** *et al.,* **2006).**

AIM OF WORK

The aim of this work is to assess the prevalence and quality (type) of sleep disorders in CRF patients.

Chapter One

CLASSIFICATIONS OF SLEEP DISORDERS

Normal Sleep:

Sleep is defined as "a reversible behavioral state of decreased responsiveness and interaction with the environment" ***(*Carskadon** *et al.,* **1983)** and it is considered a time in which the mind and body rest and recuperate **(Davis** *et al.,* **1999).**

***Two main processes are believed to regulate sleep and wakefulness*: (Davis** *et al.,* **1999).**

1) The circadian process: an internal rhythm or clock that dictates periods of activity (wakefulness) and inactivity (sleep) based on a light-dark cycle.
2) The homeostatic process: in which the requirement for sleep builds during waking hours and is relieved by sleep.

Stages of Normal Sleep:

Normal sleep is divided into non–rapid eye movement (NREM) and rapid eye movement (REM) sleep. NREM sleep is further divided into progressively deeper stages of sleep: stage N1, stage N2, and stage N3 (deep or delta-wave sleep). As NREM stages progress, stronger stimuli are required to result in an awakening. Stage (REM sleep) has tonic and phasic components. The phasic component is a sympathetically driven state characterized by rapid eye movements, muscle twitches, and respiratory variability. Tonic REM is a parasympathetically driven state with no eye movements. The REM period length and density of eye movements increases throughout the sleep cycle **(Iber et al., 2007).**

Waking usually transitions into light NREM sleep. NREM sleep typically begins in the lighter stages N1 and N2, and progressively deepens to slow wave sleep as evidenced by higher-voltage delta waves. N3 (slow wave sleep) is present when delta waves account for more than 20% of the sleep EEG. REM sleep follows NREM sleep and occurs 4-5 times during a normal 8-hour sleep period. The first REM period of the night may be less than 10 minutes in duration, while the last may exceed 60 minutes. The NREM-REM cycles vary in length from 70-100 minutes initially to 90-120 minutes later in the night.

Typically, N3 sleep is present more in the first third of the night, whereas REM sleep predominates in the last third of the night. This can be helpful clinically as NREM parasomnias such as sleep walking typically occur in the first third of the night with the presence of N3 sleep. This contrasts with REM sleep behavior disorder (RBD), which typically occurs in the last half of the night.

Sleep in adults:

Stage N1 is considered a transition between wake and sleep. It occurs upon falling asleep and during brief arousal periods within sleep and usually accounts for 2-5% of total sleep time. Stage N2 occurs throughout the sleep period and represents 45-55% of total sleep time. Stage N3 (delta or slow wave sleep) occurs mostly in the first third of the night and constitutes 5-15% of total sleep time. REM represents 20-25% of total sleep time and occurs in 4-5 episodes throughout the night **(Kryger et al., 2005).**

Sleep in the elderly:

In elderly persons, the time spent in stage N3 sleep decreases, and the time in stage N2 compensatorily increases. Latency to fall asleep and the number and duration of overnight arousal periods increase. This often causes total time in bed to increase which can lead to complaints of insomnia**.**

Classification of Sleep Disorders:

Sleep Disorders are classified by DSM-IV:

1. **Primary Sleep Disorders:**
    a. **Dyssomnias**
        i. Primary insomnia
        ii. Primary hypersomnia
        iii. Narcolepsy
        iv. Breathing-related sleep disorder
        v. Circadian rhythm sleep disorder
        vi. Dyssomnia NOS
    b. **Parasomnias:**
        i. Nightmare disorder
        ii. Sleep terror disorder
        iii. Sleepwalking disorder
        iv. Parasomnia NOS

2. **Sleep Disorders Related to Another Mental Condition:**
    a. Insomnia related to an Axis I or II condition.
    b. Hypersomnia related to an Axis I or II condition

3. **Other Sleep Disorders:**
    a. Sleep disorder due to a general medical condition.
    b. Substance-induced sleep disorder.

To promote accurate diagnoses and improve treatment of sleep disorders, the *American sleep disorders association* has created a manual for diagnostic classification of sleep disorders (ICSD-2).

ICSD-2 Classification of Sleep Disorders (ICSD, 2005):

I. Insomnia:

- Adjustment Insomnia (acute insomnia)
- Psychophysiological insomnia
- Paradoxical insomnia
- Idiopathic insomnia
- Insomnia due to a mental disorder
- Inadequate sleep hygiene
- Behavioral insomnia of childhood
- Insomnia due to a drug or substance
- Insomnia due to a medical condition
- Insomnia not due to a substance or known physiological condition, unspecified (non-organic insomnia NOS)
- Physiological (organic) insomnia, unspecified

II. Sleep-related breathing disorders:

- Central sleep apnea syndromes:
    1. Primary central sleep apnea
    2. Central sleep apnea due to high-altitude periodic breathing
    3. Central sleep apnea due to a medical condition (not Cheyne-Stokes)
    4. Central sleep apnea due to a drug or substance
    5. Primary sleep apnea of infancy (formerly primary sleep apnea of newborn)

- Obstructive sleep apnea syndromes:
    1. Obstructive sleep apnea, adult.
    2. Obstructive sleep apnea, pediatric.

- **Sleep related hypoventilation /hypoxemic syndromes:**
    1. Sleep-related nonobstructive alveolar hypoventilation, idiopathic
    2. Congenital central alveolar hypoventilation syndrome
- **Sleep-related hypoventilation/hypoxemia due to a medical condition:**
    1. Sleep-related hypoventilation/hypoxemia due to pulmonary parenchymal or vascular pathology
    2. Sleep-related hypoventilation/hypoxemia due to lower airway obstruction
    3. Sleep-related hypoventilation/hypoxemia due to neuromuscular and chest wall disorders
- **Other sleep-related breathing disorder:** Sleep apnea/sleep-related breathing disorder, unspecified

III. Hypersomnias of central origin not due to a circadian rhythm sleep disorder, sleep related breathing disorder, or other cause of disturbed nocturnal sleep:

- Narcolepsy with cataplexy
- Narcolepsy without cataplexy
- Narcolepsy due to a medical condition
- Narcolepsy, unspecified
- Recurrent hypersomnia
    1. Kleine-Levin syndrome
    2. Menstrual-related hypersomnia
- Idiopathic hypersomnia with long sleep time
- Idiopathic hypersomnia without long sleep time
- Behaviorally induced insufficient sleep syndrome
- Hypersomnia due to a medical condition
- Hypersomnia due to a drug or substance
- Hypersomnia not due to a substance or known physiological condition (nonorganic hypersomnia NOS)