Impact of Night Sleep Deprivation on Oxidative Stress and Blood Pressure in Adult Volunteers

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***Abstract*—This study was planned for investigate the effect of one-night sleep deprivation (SD) on blood pressure (BP), serum malondialdehyde (MDA), glucose, and renal function test. The volunteer persons were divided into two groups, each with 14 individuals 7 males with good sleeping (8 h) and 7 male with one-night deprivation. The same grouping was done on female volunteer. Mean BP (MBP) in females group of one-night SD exhibited high significant increases compared with good sleep, while in male group of SDs exhibited non-significant increase as compared with good sleep. Serum MDA exhibited a highly significant increase in both male and female groups after one-night SD as compared with good sleep groups. In conclusion, the results suggested that one-night SD increases BP and lipid peroxidation. Interestingly, the elevated BP mostly may be returned to high free radical production. According to the obtained results, the elevated BP may be due to vasoconstrictions, which highly increases diastolic BP rather than systolic BP; consequently, urine flow and glomerular filtration rate were changed in night sleep derivative persons. Hence, the main purpose of the present study is to investigate the possible effects of SD on these variables in both male and female volunteer students belonged to Biology Department/ College of Science/Salahaddin University-Erbil.**

***Index Terms*—Blood pressure, Glomerular filtration rate, Oxidative stress, Sleep deprivation.**

I. Introduction

Sleep deprivation (SD) has been shown to induce oxidative stress and cardiovascular disturbances that might increase cardiovascular risk. Sleep is a complicated and effective biological process that is required on a daily basis for all humans regardless of age, sex, or ethnic origin. Learning, memory mechanism, cellular repair, and nervous system development are among the most important functions of sleep [1-4]. In addition to maintaining normal brain functioning, sleep has important roles in controlling the functions of many other body systems, and this becomes very evident in states of SD [5]. SD is not limited to a special group of people, a nation, a gender or a particular age group. Rather, it is a new human behavior observed among millions of adults and children worldwide [6]. Sleep/wake disorders are common, underdiagnosed, and associated with serious consequences [7]. Sleep disorders are associated to a number of cardiovascular disturbances that might increase cardiovascular risk. SD, in particular, might, by inducing autonomic deregulation, raise arterial pressure, and hypertensive risk. Findings support the contention that one-night SD, in the absence of significant additional stress or disturbances, does not lead to increased arterial pressure values or to changes in autonomic or bar reflex profiles that could conceivably favor hypertension development, but induces the expected increase in tiredness and reduction in performance [8]. Accumulating evidence suggests that sleep disturbance is associated with inflammation and related disorders including cardiovascular disease, arthritis, and diabetes mellitus (DM) [9]. SD has been shown to induce oxidative stress which causes cognitive impairment the results revealed that SD impairs cognitive ability [10]. Quantitative understanding of the fundamental properties of the multi-oscillator circadian system in humans and their interaction with sleep/wake homeostasis has many applications to health and disease, including the development of treatments for circadian rhythm and sleep disorders [11]. The main feature of melatonin is the gating of its synthesis and release to the night whatever animals are diurnal or nocturnal. Because night length depends on seasons, the nocturnal peak of melatonin exhibits typical seasonal alterations, which are pivotal for the timing of annual functions, especially reproduction [12]. Melatonin decreases night-time blood pressure (BP) by increasing nitric oxide (NO) in endothelial cells. Whether serum asymmetric dimethylarginine (ADMA) attenuates the association of melatonin within night BP and dipping in humans is unclear. Melatonin increases endothelium-derived NO which decreases vascular tone and arterial BP [13] light exposure during night hours changes melatonin secretion and can disrupt the human circadian rhythm through melatonin secretion. In many animal experiments, it has been shown that expression and/ or activity of oxidative and antioxidative enzymes depend

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on the circadian rhythm, exposure to light-at-night results in altered endocrine functions, this is followed by generation of oxidative stress and many health disorders originating from shift work. This is followed by generation of oxidative stress and many health disorders, whose source originally is shift work [14]. One of the most remarkable effects of light with the blue wavelength (460–480 nm) is suppression of night-time melatonin production [15]. The antioxidant involves both direct scavenging of reactive oxygen species (ROS) exerted by melatonin or stimulation of the activity and expression of antioxidant enzymes. SD impairs neurocognitive functions and this effect is associated by reduced cerebral glucose supply due to prolonged wakefulness inducing a progressive depletion of cerebral glycogen stores [16]. Subsequent nights with partial sleep restriction result in impaired glucose tolerance, but the effects on insulin sensitivity have not been characterized [17]. There is evidence that sleep loss adversely affects glucose metabolism and increases the risk of developing Type 2 DM (T2DM) and some experimental studies have investigated the effects of severe sleep curtailment on glucose metabolism [18]. Due to little known about the effect of SD on renal function and oxidative stress which may strongly related with hemodynamic parameters like BP.

II. Materials and Methods

A. Experimental Design

The study was planned to investigate the influence of one-night SD on BP, serum malondialdehyde (MDA), glucose, and renal function tests. The volunteers (their ages were between 20 and 25) divided into two groups, each with 14 individuals. One group with good sleep and other was group night SD.

B. Blood Sample Collection

Blood samples were taken from peripheral veins by 5 ml syringe. Put into gel and clot-activator tubes for serum separation. The sera were separated by 3000 round per minute centrifugation for 20 min. They were frozen at −18°C in freezer for chemical assays.

C. Urine Sample Collection

The sample of urine was collected from all groups and the samples were preserved in clean bottles, then the amount of urine was measured by cylinders then urine flows were obtained in ml/hours.

D. BP Measurement

BP was measured using mercury column sphygmomanometer and calculated mean BP (MBP) obtained by this equation [19]

$$MBP = DBP+1/3\ (SBP-DBP)$$

E. Heart Rate and Breathing Rate Measurement

Heart rates were measured using finger feels the pulses beat the fingers tip on the wrist artery through 1 min. Whereas the numbers of the breathing rate were measured by counting the numbers of inspired and expired breath in 1 min assuming that each breath cycle is consist of one inspiration followed by expiration.

F. Chemical Analysis

Determination of MDA

The assessment of lipid peroxidation process is performed by determining the concentration of serum MDA which determined spectrophotometrically with TBA solution.

The concentration of MDA was calculated by the following equation [20]:

$$\mathrm{MDA}\left(\mu\mathrm{mol}/\mathrm{L}\right)=\frac{\mathrm{Absorbance}\,(532)}{\mathrm{L}*\mathrm{E0}}\times\mathrm{D}$$

Where:

L: Lightpath (1 cm)

E_0: Extinction coefficient = 1.56*105 $M^{-1}.Cm^{-1}$

D: Dilution factor (1 ml volume). Used in ref./0.15=6.7.

Blood glucose estimation

Blood glucose was estimated spectrophotometrically using glucose kit (ACCU-CHEK), Germany.

Determination of serum creatinine

For measuring creatinine in serum, 0.5 ml of serum was mixed with 0.5 ml of TCA, centrifugation at 2500 rmp for 10 min, then we take 0.5 ml of supernatant and mixed with 1 ml mixture (R1 + R2) in creatinine kit leave for 20 min in room temperature (37°C) and then read by spectrophotometer at 525 nm.

Glomerular filtration rate (GFR) estimation

A formula that allows an estimate of clearance in men that accounts for age-related decreases in GFR, body weight, and sex has been derived by Cockcroft-Gault [21]:

$$\frac{\text{Creatinine clearance}}{(\mathrm{ml}/\mathrm{min})}=\frac{\left(140-\mathrm{age}\right)*\text{lean body weight(kg)}}{\text{plasma creatinine}\ \left(\mathrm{mg}/\mathrm{dl}\right)*72}$$

This value should be multiplied 0.85 for women.

G. Statistical Analysis

Results are expressed as means ± SEM, and statistical analysis was performed by statistical software (SPSS version 22). The comparisons between groups were done by paired *t*-test. A Shapiro–Wilks, Kolmogorov –Smirnov tests, inspection of Skewness and Kurtosis, Q-Q plot and histogram showed that the measured parameters were approximately normally distributed except systolic BP (SBP) and MBP which they analyzed by Wilcoxon test because their data are not normally distributed according to Shapiro–Wilks test. The bar charts were made by GraphPad Prism (Version 5). Values were considered to be significantly different when $P < 0.05$.

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III. Results

In group of one-night SD increased SBP as compared with good sleep, as shown in Fig. 1.

In females group of one-night SD exhibited high significant increase diastolic BP (DBP) (86.642 ± 3.585) when compared with good sleep (72.071 ± 3.164), while in males group of one-night SD did not increase when compared with good sleep as shown in Fig. 2.

MBP in females group of one-night SD exhibited high significant increased ($P < 0.01$) (95.585 ± 3.542) as compared with good sleep (84.035 ± 2.559), while in males group of one-night SD nonsignificantly increased when compared with good sleep as shown in Fig. 3.

Heart rates in females group of one-night SD exhibited high significant decreased (68.714 ± 2.409) when compared with good sleep (75.357 ± 1.903), while in males group of one-night SD did not significant when compared with good sleep as shown in Fig. 4.

Breathing rates in females group of one-night SD did not significant but slightly increased where compared with good sleep, while in males group of one-night SD did not significant but slightly decreased where compared with good sleep, as shown in Fig. 5.

MDA as indicator of the oxidative stress, and lipid peroxidation, exhibited high significant increase (3.711 ± 0.285), (4.317 ± 0.374) in both male and female groups after one-night SD as compared with good sleep groups (3.030 ± 0.129), (3.432 ± 0.217), respectively, as shown in Fig. 6.

Serum glucose in females group also in males group of one-night SD nonsignificantly increased when compared with good sleep as shown in Fig. 7.

Statistical analysis revealed that serum creatinine was significantly P decreased in one-night SD of females from 0.81 ± 0.05 to 0.73 ± 0.016 mg/dl, whereas serum creatinine of males nonsignificantly slightly reduced as shown in Fig. 8.

GFR in females group also in males group of one-night SD increased nonsignificantly when compared with good sleep (Fig. 9).

IV. Discussion

In the present study, female volunteers with one-night SD, MBP increased, while such elevation in BP did not observe in male volunteers. Sleep disorders are associated to a number of cardiovascular disturbances that might increase cardiovascular risk. SD, in particular, might, by inducing autonomic deregulation, raise arterial pressure, and hypertensive risk. Available evidence, however, is contradictory. One night SD in 24 volunteers might alter hemodynamics heart rate and arterial pressure [8]. Furthermore, SD reduces melatonin levels, work schedules involve exposure to light-at-night, which may reduce normal nocturnal melatonin production, create circadian rhythm disruptions and unhealthy lifestyle [22]. There is well established that melatonin may reduce BP, particularly nocturnal BP [23]. Therefore, when the level of melatonin reduces in SD persons, consequently the BP will rise. Melatonin decreases night-time BP by increasing NO in endothelial cells. Whether serum asymmetric ADMA, a major endogenous competitive inhibitor of endothelial NO

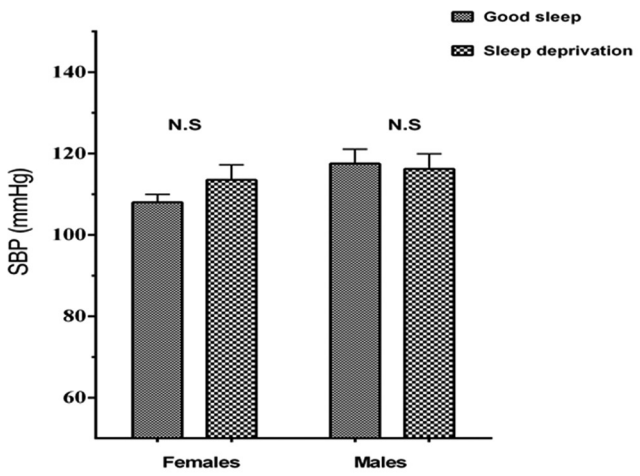

Fig. 1. Effect of one-night sleep deprivation on systolic blood pressure in female and male volunteers.

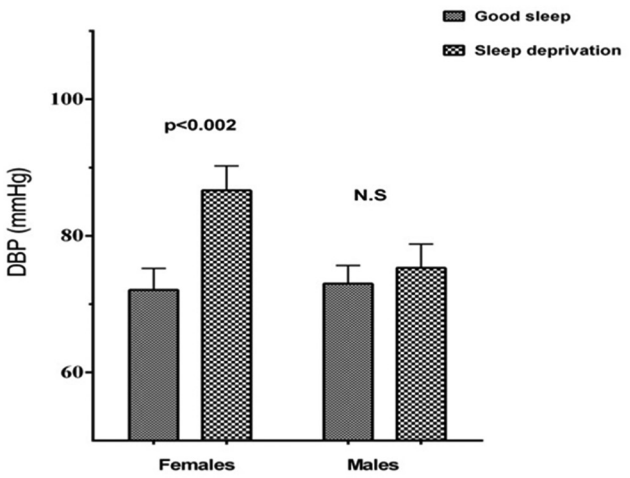

Fig. 2. Effect of one-night sleep deprivation on diastolic blood pressure in female and male volunteers.

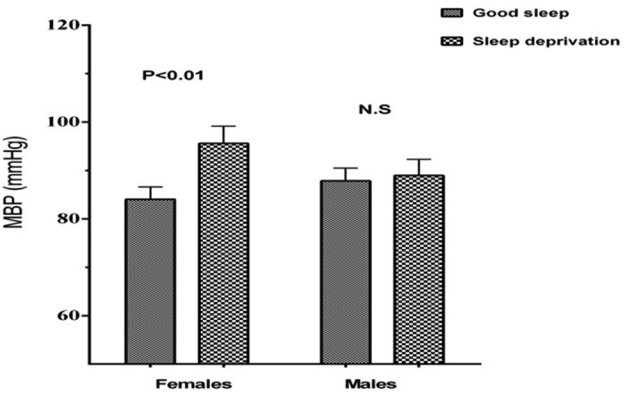

Fig. 3. Effects of one-night sleep deprivation on mean blood pressure in female and male volunteers.

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synthesis, attenuates the association of melatonin with night-time BP and dipping in humans is unclear [13]. On the other hand, plasma cortisol levels were slightly enhanced during SD [24] Cortisol may increase the capacity of the immature kidney to play a role in fluid and electrolyte homeostasis by increasing GFR and delivering more sodium and water

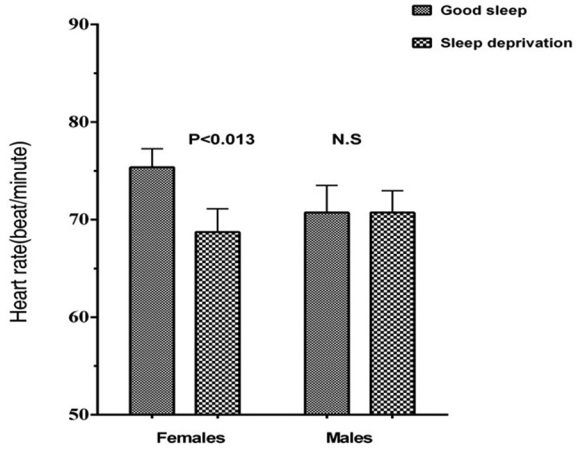

Fig. 4. Effect of one-night sleep deprivation on heart rate in female and male volunteers.

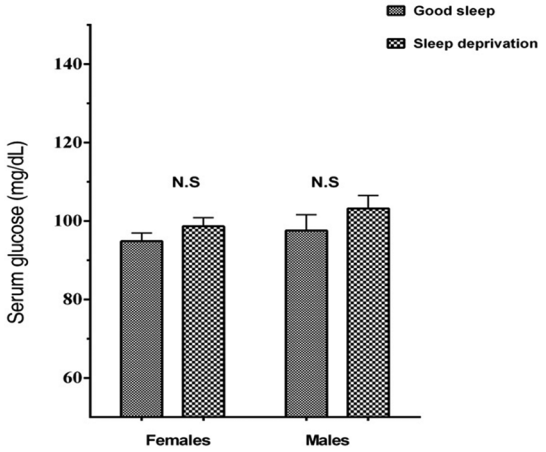

Fig. 7. Effect of one-night sleep deprivation on serum glucose levels in female and male volunteers.

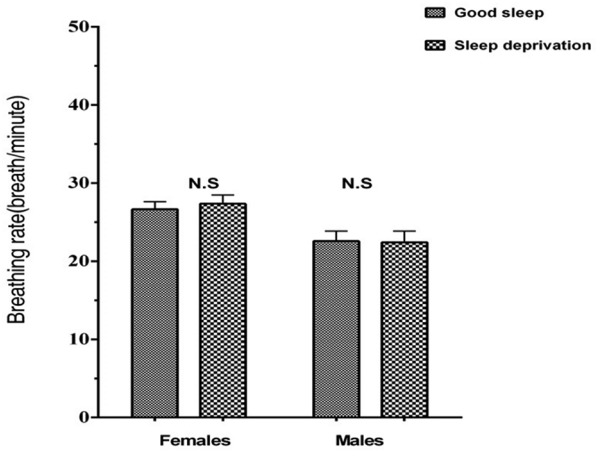

Fig. 5. Effect of one-night sleep deprivation on breathing rate in female and male volunteers.

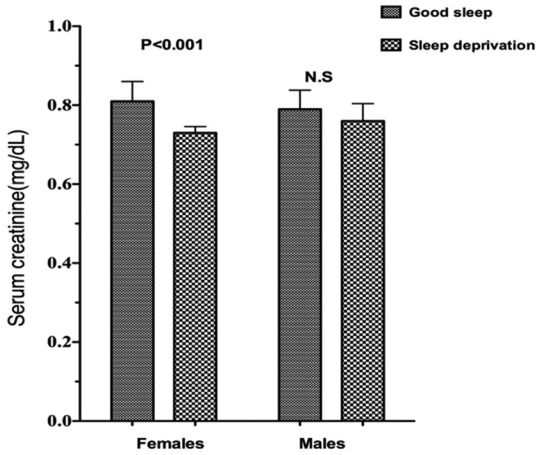

Fig. 8. Effects of one-night sleep deprivation on serum creatinine levels in female and male volunteers.

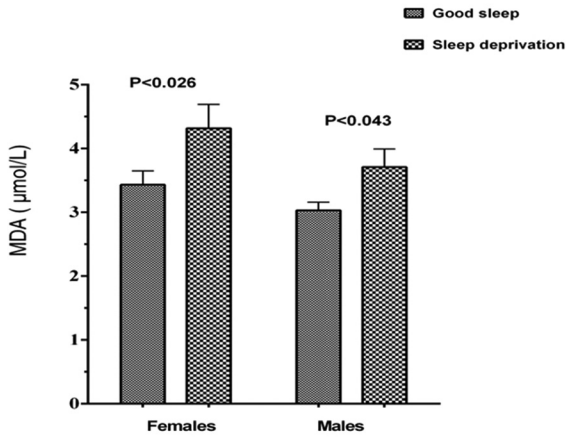

Fig. 6. Effect of on night sleep deprivation on serum malondialdehyde levels in female and male volunteers.

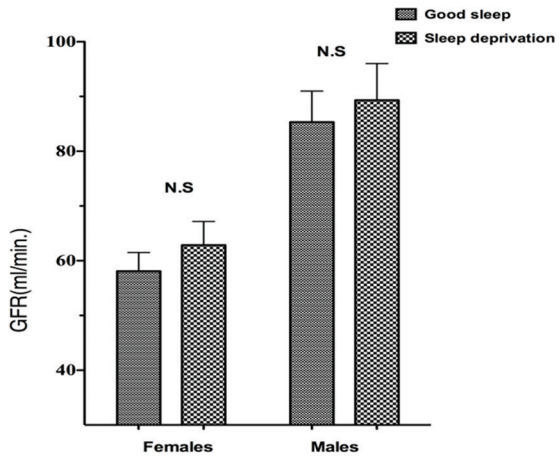

Fig. 9. Effects of one-night sleep deprivation on glomerular filtration rate values in female and male volunteers.

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to the distal nephron where the reabsorption of sodium and water can be modified independently and in accordance with need [25]. Cortisol will stimulate sodium and water reabsorption and increase BP [26]. Results revealed that DBP significantly elevated in female with one-night SD, such elevation mostly due to vasoconstriction. Furthermore, thyroid hormone activity sharply increases when an individual is in a state of SD. During SD, the hypothalamic-pituitary-thyroid axis initially increases as a consequence of increased release of thyroid stimulating hormone from the pituitary. Subsequently, as SD continues, the sympathetic nervous system is recruited through its anatomical connection with the thyroid gland whereas thyroid stimulating hormone levels markedly increase during SD.

It has been suggested that these increases are secondary to SD [27]. Increase in heart rate in female volunteers with one-night SD, and also slight breathing rate elevation might be due to increases in arterial BP as a bar reflex followed by increases in PO_2 and reduces blood pH, the current results show in Fig. 6 indicated that one-night SD caused a significant increase in serum MDA level compared with good sleep control group. Several previous studies reported that light exposure the elevate free radicals and Ca^{+2}, followed by NO and tumor necrosis factor-alpha, which can be facilitated to cell demise [28]. The causes behind this elevation mostly due to reduction in melatonin levels because melatonin's antioxidant activity is the result of three different but complementary actions: (1) A direct action due to its ability to act as a free radical scavenger; (2) an indirect action that is a consequence of melatonin's ability to reduce free radical generation (radical avoidance); and (3) its ability to upregulate antioxidant enzymes [29]. Light-at-night exposure can disrupt the human circadian rhythm through clock gene expressions. The circadian rhythm influences antioxidant enzymes' activity and cellular mRNA levels of these enzymes. The employees working based on a shift system adjust to the changes occurring both on the cell level and on the level of the whole organism [14]. The antioxidant nature of melatonin involves both direct scavenging of ROS exerted by high-mill molar concentrations of melatonin or stimulation of the activity and expression of antioxidant enzymes, response observed at low nanomolar concentrations [30]. Furthermore, there was evidence that SD with light exposure enhances some hormones, catabolism which hydrolyzes glucose to energy formation and during adenosine triphosphate formation from electron transport chain, some of the electrons leak the mitochondria and hence ROS produces.

Interestingly, MAP in female volunteers rather than males is highly significantly elevated. This difference may be returned to high-fat mass content in females which might easily peroxidation by free radicals during SD. However, the exact explanations need further *in vivo* and *in vitro* studies. The slightly increases in blood confirmed that ROS produce during light exposure. SD impairs neurocognitive functions assuming that this effect is mediated by reduced cerebral glucose supply due to prolonged wakefulness inducing a progressive depletion of cerebral glycogen stores hypothesized that short-term sleep loss amplifies the deteriorating effects of acute hypoglycemia on neurocognitive functions [16]. Subsequent nights with partial sleep restriction result in impaired glucose tolerance, but the effects on insulin sensitivity have not been characterized, sleep restriction resulted in increased endogenous glucose production during the hyperinsulinemic clamp study compared to the unrestricted night, partial SD during only a single night induces insulin resistance in multiple metabolic pathways in healthy subjects [17]. Here, there is increasing evidence that sleep loss adversely affects glucose metabolism and increases the risk of developing T2DM, a number of experimental studies have investigated the effects of severe sleep curtailment on glucose metabolism [18]. Urine flow and GFR slightly increased in both female and male volunteers with one night SD. Serum creatinine tended to reduce in SD. The reason behind these results are most precisely known, however, the possible hypothesis for explaining this effect is that SD with light exposure caused BP elevation as shown in Fig. 3. Such increase in blood induces pressure diuresis. On the other hand, reduces in melatonin levels may follow by ameliorating some hormones such as endothelin-1, atrial natriuretic peptide, and antidiuretic hormone which consequently affect GFR and urine flow [31].

V. Conclusions

The results suggested that one-night SD increases BP and lipid peroxidation. Interestingly, the elevated BP mostly may be returned to high free radical production. According to the obtained results, the elevated BP may be due to vasoconstrictions, which highly increases DBP rather than SBP; consequently, urine flow and GFR were changed in night sleep derivative persons.

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