Introduction

Mobile phone or smartphone is one of the advances in science and technology in this past decade. About 1.4 billion smartphones are sold worldwide annually and the number of smartphone users worldwide today surpasses three billion [1]. Besides being used for communication tools, smartphones are also used for watching videos, listening to music, playing games, and many people use it in daily life. Although the smartphone brings conveniences to people’s daily lives, it is also associated with patterns of addictive usage involving adverse outcomes [2], [3].

Excessive smartphones used will cause various health problems. The increased excitement and stimulation resulting from this exposure may be associated with difficulties falling asleep or poor sleep quality [4]. Sleep plays an essential role in cognitive mood function. Sleep loss, sleep restriction, and sleep disorders might harm mood and cognitive functions [5].

Free radical flux theory of sleep by Reimund states that free radicals accumulate during wakefulness and are removed during sleep. With sleep, there are a decreased cerebral metabolic rate and a lower free radical generation rate [6].

Free radicals are removed during sleep by a decreased rate of free radicals and increased efficiency of the endogenous antioxidant mechanism. Thus, sleep essentially has an antioxidative role. Free radicals play a several beneficial roles for the organism. For example, they are needed to synthesize some cellular structures, defense systems to fight pathogens, cellular signaling pathways, intracellular signaling cascades, and signaling molecule. Summarizing, free radicals, when maintained at low or moderate levels, are of crucial importance to human health [7].

Excess free radicals and oxidants give rise to a phenomenon known as oxidative stress. Mitochondria contribute to reactive oxygen species (ROS) production, a side product of electron transport
during oxidative phosphorylation. It can negatively affect several cellular structures, such as membranes, lipids, proteins, lipoproteins, and deoxyribonucleic acid; if this condition persists, it will cause diseases such as cancer and heart disease and other degenerative diseases. Lipids are susceptible targets of oxidation because of their molecular structure abundant with reactive double bonds [8], [9]. Excess free radicals can damage cell membranes and lipoproteins by a process called lipid peroxidation. This reaction leads to malondialdehyde (MDA) formation and conjugated diene compounds. This molecule is cytotoxic and mutagenic. In other words, oxidative stress results from an imbalance between formation and neutralization of ROS/RNS [10], [11].

Sleep deprivation increases free radicals, which can be shown by estimating plasma MDA. We performed a study designed to test the hypothesis that there is an association between addictive smartphones usage, lack of sleep, and serum MDA levels.

Methods

This study was quasi-experimental with a pre- and post-test group that involved 24 students of the Faculty of Medicine Universitas Baiturrahmah that qualified as a subject. Sleep quality was assessed with Pittsburgh Sleep Quality Index (PSQI) [2], and the smartphone addiction was assessed based on Smartphone Addiction Scale (SAS) score which has validated for adolescent. SAS scale cutoff for addiction was >31 for male and >33 for female [12]. The subjects were divided into four groups (n = 6) based on their PSQI and SAS score. The first group was the subjects with good sleep quality and non-smartphone addicts. The second group was the subjects with good sleep quality but smartphone addicts, the third group was the subjects with lousy sleep quality and non-smartphone addicts. Furthermore, the fourth group was the subjects with lousy sleep quality and smartphone addicts.

The subject was instructed to sleep at least 8 h/day and use a smartphone just as necessary for 7 days before the study was conducted. On the 8th day, the subject lived like their regular habits. Blood plasma was collected from the subject before and after day 8th at 7 AM for MDA measurement. Plasma MDA was determined using a thiobarbituric acid reactive substance. Health Ethical Research Committee has approved this study, Faculty of Medicine, Universitas Baiturrahmah (Approval Number: 031/ETIK-FKUNBRAH/03/03/2019).

Statistical analysis

Paired t-tests were used to evaluate the levels of serum MDA before and after measurement.

Results

The PSQI score of the subject

The PSQI score of the subject is shown in Table 1. A global PSQI score more prominent than 5 indicated that the subject had poor sleep quality. Lesser than five global PSQI scores indicated good sleep quality. Regarding the component of PSQI score, the good sleep quality group had sleep latency lesser than 15 min, sleep duration more than 7 h and habitual sleep efficiency greater than 85%. In another group with poor sleep quality, the subjects had fairly bad sleep quality with 31–60 min sleep latency, 6–7 h sleep duration, and 75–85% habitual sleep efficiency.

Table 1: The subject’s PSQI global score and by components

| Variable                  | Good sleep quality group (n=12) | Poor sleep quality group (n=12) | p-value     |
|---------------------------|---------------------------------|---------------------------------|-------------|
| PSQI global score         | 4.92 ± 0.29                     | 11.58 ± 1.78                   | < 0.001     |
| PSQI sleep quality        | 0.92 ± 0.67                     | 2.17 ± 0.72                    | < 0.001     |
| PSQI sleep onset latency  | 0.92 ± 0.67                     | 2.06 ± 0.67                    | < 0.001     |
| PSQI sleep duration       | 0.42 ± 0.51                     | 1.25 ± 0.97                    | 0.015       |
| PSQI sleep efficiency     | 0.25 ± 0.45                     | 1.67 ± 0.78                    | < 0.001     |
| PSQI sleep disturbance    | 0.92 ± 0.29                     | 1.42 ± 0.51                    | 0.008       |
| PSQI hypnotic drug        | -                               | -                               |            |
| PSQI daytime dysfunction  | 1.33 ± 0.98                     | 2.58 ± 0.51                    | < 0.001     |

Data are displayed as mean, standard deviation.

Relationship of sleep quality and serum MDA levels

The serum MDA level from the good sleep quality group (I and II) and the poor sleep quality group (III and IV) is shown in Table 2. There was no difference in serum MDA levels among the subject before the treatment. Post-test MDA levels in the poor sleep quality group were significantly greater than pre-test condition (p < 0.05).

Table 2: MDA levels between good sleep quality group and poor sleep quality group

| Group                  | n      | MDA levels (mmol/L) | p-value     |
|------------------------|--------|--------------------|-------------|
|                        |        | Pre-test           | Post-test   |
| Good sleep quality     | 12     | 3.80               | 3.38        | 0.425     |
| Poor sleep quality     | 12     | 3.55               | 5.91        | 0.003     |

Relationship of sleep quality and smartphone addiction to serum MDA level

The levels of serum MDA before and after the treatment are shown in Table 3. There was no significant difference in serum MDA levels among the
subjects before the treatment (p > 0.05). Smartphone addiction did not cause an increase in MDA levels both in the good sleep quality group (I and II) and poor sleep quality group (III and IV) (p > 0.05). Statistical analysis showed that sleep quality was the main contributor to the elevation of MDA levels (p < 0.05). Both smartphone addiction groups tend to have lower MDA levels than those of the non-smartphone addiction group in the same sleep quality.

Discussion

Smartphone usage before bedtime became the most frequent activity at night among young adults daily. Most university students use smartphones for leisure before sleep, including social networking sites, website surfing, instant messaging, and games. Using a smartphone at least 30 min before bedtime with the light turned off is positively associated with poor sleep quality [2]. This behavior leads to sleep disturbance and poor sleep quality [13]. Our study found that subjects in poor sleep quality groups had fairly bad sleep quality with a sleep latency of 30–60 min, sleep duration of 6–7 h, and habitual sleep efficiency 75–85% — poor sleep quality related to a negative effect on the next day. Inadequate sleep due to smartphone use before sleep contributed to many consequences for the next day, such as fatigue on waking, an impression of not having slept enough, irritability, and headaches that disrupt daily activity [14], [15].

A smartphone is a device with short blue-light emitting related to sleep disturbance due to the brightness. Decreased sleepiness at night is related to later bedtimes and more sleep difficulties in adults [5], [16]. The light-emitting diodes (LED) of a smartphone are an essential source of artificial light at night which influence the circadian regulation of the sleep-wake cycle [3], [17]. This effect can suppress melatonin secretion [18], [19], alter mood, and cognitive function and contributes to fatigue [20]. Blue-light emission from smartphones is associated with declining levels and later onset of melatonin secretion [21].

As a significant component of circadian rhythm, sleep is related to many physiological processes. Sleep had defense function mechanisms against oxidative stress, the condition when unbalanced antioxidant activity and pro-oxidant happened [19], [22]. ROS and reactive nitrogen species (RNS) are known as a pro-oxidant in the body. ROS are products of normal metabolism, mainly in the mitochondria. ROS such as superoxide radicals (O$_2^-$), peroxides (H$_2$O$_2$), and hydroxyl radicals (OH$^-$) can have a beneficial effect on the cell by playing a critical role in many cellular processes. Superoxide and H$_2$O$_2$ serve as cellular signaling controlling a variety of biological processes. However, tight regulation is needed to control ROS as their detrimental effect. Oxidative stress leads to structural damage due to oxidative modification of nucleic acids, protein, and lipids [23]. Accumulation of ROS during the wake-cycle will be neutralized in the sleep cycle [6]. Body neutralized ROS during sleep-cycle [24], [25].

MDA is a biological marker of oxidative stress, which also has a circadian rhythm of formation with the higher levels at noon than 2 p.m. [26]. Our study found that subjects with poor sleep quality had greater MDA levels than good sleep quality groups. Smartphone addiction and sleep late behavior related to this poor sleep quality and high MDA serum on the next day (p < 0.05). The level of MDA increases during the awakening period and decreases during sleep by endogenous antioxidant with the lowest level of MDA in the morning [27]. Poor sleep quality with smartphone addiction had slight low MDA levels than poor sleep quality group with sleep late behavior. This finding indicated that the main contributor for the elevation of MDA levels was sleeping late, even if it was a result of smartphone addiction that led to sleep late among the subject or another reason for sleeping late.

Sleep late behavior decreased sleeping time and prevented the onset of melatonin. Melatonin, an endogenous hormone, is produced by the pineal gland produce in response to darkness. This tryptophan derivate was essential to regulate the internal body clock’s, sleep cycle, and wakefulness. However, it is sensitive to light. Melatonin contributed as an antioxidant and free-radical-scavenging in humans [28]. It effectively scavenged hydroxyl radical [29]. Melatonin, also known as a hormone, induced both antioxidant enzyme activity and gene expression, including catalase and glutathione peroxidase. Hence, during sleep, the body had a greater chance to neutralize more free radicals due to the increasing melatonin in the evening. Serum melatonin reached a peak value (80–150 pg/mL) between night and 3 a.m., while its concentration during the day is low (10–20 pg/mL) [30]. Both standard melatonin patterns and the influence of light can vary considerably between individuals [31]. Hours of smartphone usage correlated to melatonin secretion. High-hours smartphone users had lower melatonin levels [32]. Consequently, melatonin’s neutralization of both ROS and RNS decreased and led to MDA levels the next day.

Conclusion

Smartphone usage before bedtime effected on sleep quality. Sleep late due to smartphone usage is
associated with the later onset of metalotin secretion, an antioxidant, and free-radical scavenging. Even though there was no relation between smartphone addiction and serum MDA levels, inadequate sleep lead to high levels of serum MDA in the morning. Inadequate sleep is associated with a high level of oxidative stress in the morning.

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