

The Effects of Caffeine Intake on Cardiovascular Parameters in Sleep Deprived Medical Residents

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Physicians and medical residents are particularly affected by sleep deprivation are, especially in East European countries. The aim of our study is to analyze the effect of caffeine intake on cardiovascular functions in sleep deprived residents (clinicians in-training) after continuous 24h on-call duty. 26 medical residents aged between 22-33 years old, 12 men and 14 women, who began their activity at 2 pm were included. Each subject consumed coffee or caffeinated drinks such as Coca cola during this period, after 2 am, expressed in caffeine units. We have evaluated their cardiovascular function using impedance cardiography (ICG-M501) and blood pressure measurement using the manometric method, before (at 7 pm) and after caffeine consumption (at 7 am), during one night of on-call duty. Surprisingly, after caffeine consumption, all subjects have had a decrease of the heart rate after one night of sleep deprivation (from mean: 83 b/min before to 69.73 b/min after, $p = 0.000$), also the mean arterial blood pressure is lower after the overnight call (from mean: 95.3 mmHg before to 88.9 mmHg after). Moreover, cardiac output, stroke volume and cardiac index decreases along with an increase of peripheral vascular resistance. Caffeine intake exerts a paradoxical effect on sleep deprived subjects; acute sleep loss, due to continuously, intense on-call work, modifies several cardiovascular parameters, such as heart rate, blood pressures, stroke volume and cardiac output.

Keywords: caffeine, impedance cardiography, on-call duty, sleep deprivation

Sleep is an important process for the human body, providing the restoration of metabolic and neurocognitive functions. Sleep loss have been associated with alterations in emotional status and the decrease in the quality of life in young adults; in the same time, studies showed evidence of increased caffeine consumption in young adults and even adolescents, to counterbalance the sleep loss [1]. Physicians, especially medical residents are exposed to long term sleep deprivation during overnight calls (fig. 1).

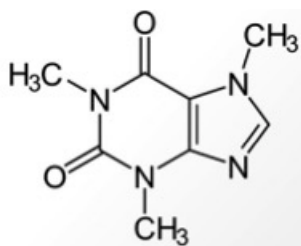


Fig. 1 Caffeine structure
formula C₈H₁₀N₄O₂

Studies have shown that lack of sleep affects the individual performances. After 24h on-call duty, residents have experienced attention and cognitive performance deficit, deterioration in their capacity of correct judgment. Sleep deprivation combined with extreme stressful cases causes psychological changes, such as anxiety and irritability [2-3].

After a one-night duty call, the number of errors increased and the practical abilities of doctors decreased in a manner comparable to alcohol ingestion (equivalent to a level of 0.5 g alcohol/ liter of blood) [4]. In this context, there are only few studies focused on cardiovascular changes in residents after on-call duty. The main objective of present study is to characterize the evolution of cardiovascular parameters after sleep deprivation among medical

residents who finalized a complete, active, 24 h on call duty in hospital.

Experimental part

Our study is a prospective research with 26 subjects (volunteers) aged between 22 and 33 (Mean-24.92; Std. deviation 2.544): 26 residents, 12 male and 14 female, from Bucharest hospitals, in clinical specialties, most of them in-training in emergency medicine. All participants read and signed an Informed consent form regarding personal protection data and confidentiality of the study. All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee (Committee of scientific research of University of Medicine and Pharmacy Carol Davila) and have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

We evaluated the cardiovascular parameters using impedance cardiography (ICG-M501 from Physiology Department of University of Medicine and Pharmacy Carol Davila, Bucharest, Romania) recordings and blood pressure measurements using the manometric method. Impedance cardiography is a non-invasive method of cardiovascular parameters assessment which determines parameters such as: cardiac output, cardiac index, stroke volume, peripheral vascular resistance, ventricular pre-ejection time. The measurements were made before and after caffeine consumption (at 7 pm and at 7 am next day), in on-call duty over the night. The quantity of caffeine consumed was estimated in caffeine units. We described the caffeine unit as the quantity of caffeine (60 mg) contained in 100 mL liquid [5].

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Measuring the most consumed types of caffeinated beverages in our country based on their caffeine content and data literature we found : Coca-cola contains 8.85 mg caffeine/100 mL or 0.15 units; Starbucks brewed coffee (236 mLK) contains 160 mg caffeine (1.12 units); ordinary coffee contains 67.6 mg caffeine/100 mL of (1.12 units). According to the USDA*, 1 rounded teaspoon of instant coffee (1.8 g in weight) contains 57 mg of caffeine (0.95 units), close to that contained in 100 mL comercial coffees.

Data analysis was performed using IBM SPSS statistics (SPSS software, version 20.0, Inc., Chicago, IL, USA). Continuous variables were reported as mean (\pm SD) or median (range) and categorical variables are presented as n (%). Statistical significance was set to $p < 0.05$.

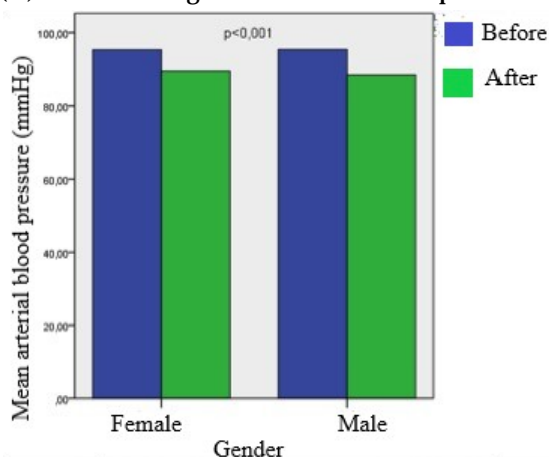


Fig.2 Gender distribution of mean arterial blood pressure before and after caffeine consumption in sleep deprived residents

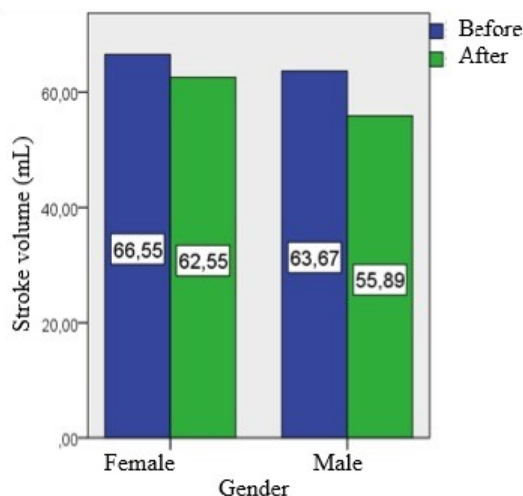


Fig. 3 Variation of stroke volume before and after caffeine consumption in sleep deprived residents

Table 1
VARIATION OF VENTRICULAR RATE WITH DEPARTMENTS

Department		Ventricular rate before (b/min)	Ventricular rate after (b/min)
EMERGENCY	Mean	81.2	69.73
	N	15	15
	Std. Deviation	11.66	8.43
INTERNAL MEDICINE	Mean	79.75	68
	N	4	4
	Std. Deviation	8.84	8.52
CARDIOLOGY	Mean	92.5	64.5
	N	2	2
	Std. Deviation	10.60	13.43
Other	Mean	74.2	73.2
	N	5	5
	Std. Deviation	42.83	7.46
Total	Mean	80.5	69.73
	N	26	26
	Std. Deviation	20	8.35

Results and discussions

Analysing the cardiovascular parameters provided by impedance cardiography we can conclude that most of them decreased, while peripheral vascular resistance increased.

All sleep deprived subjects in our study presented a significantly decrease of the Mean arterial blood pressure (MBP), calculated as $(2 \times \text{DBP} + \text{SBP}) \div 3$ after the overnight call (before on-call duty 95.3 versus after on-call duty 88.9 mmHg); correlating MBP and gender reveals that women have a lesser decrease than men (fig.2).

All sleep deprived subjects in our study presented a significantly decreased of ventricular rate after caffeine consumption; Mean: 83 b/min before to 69.73 b/min after ($p = 0.000$) (table 1); these changes are correlated to the type of department where on call duty was done: as the intensity of work increased, heart rate decreases (from mean 81.2 b/min before to 69.73 b/min after in Emergency Department. The most significant changes were in Cardiology Department followed by Emergency Department, $p < 0.05$ - (table 1).

Figure 3 shows a decrease of stroke volume in both genders after sleep deprivation from 66.55 to 62.55 mL in the female group and 63.67 to 55.89 mL in the male group. Extending the cardiac output formula (Cardiac output = Stroke volume * heart rate) to these modifications we obtained that cardiac output also decreases after sleep deprivation from an average of 5.754 to 4.908 ($p < 0.05$), represented in figure 4.

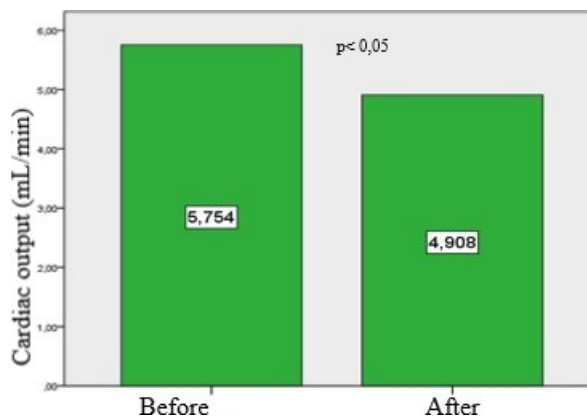


Fig. 4 Variations of cardiac output

Data literature regarding the effects of sleep deprivation on cardiovascular parameters, showed several findings; the research of Dettoni et al. revealed that after sleep deprivation a vasodilator endothelial response may occur [6-7]. This effect can explain the increase of peripheral vascular resistance and also, can be a cause for cardiac output decrease. Sauvet et al. showed a modification of acetylcholine release due to sleep deprivation and pointed out that endothelial dysfunction is independent on blood pressure or sympathetic nervous system effect [8].

Holmes et al. noticed a lower effect of the sympathetic nervous system on heart activity expressed as a decrease of pre-ejection time and an increase of parasympathetic tonus [9]. This research supports and may even be a explanation for our results.

Caffeine is a widely consumed stimulatory substance worldwide; its metabolite, paraxanthine is excreted in urine but also in saliva [10]. The ability of caffeine to inhibit adenosine receptors is highly important for its effects on behaviour and cognitive function. Caffeine indirectly affects the release of norepinephrine, dopamine, acetylcholine, serotonin, glutamate, gamma-aminobutyric acid (GABA), and perhaps neuropeptides [11]. However, caffeine is a weak inhibitor of phosphodiesterase enzymes, so behavioral effects occurrence probably is too low to be associated with meaningful phosphodiesterase inhibition [12-13].

The effects of caffeine on the heart are primarily stimulatory and are accompanied by increased coronary blood flow. These effects are not mediated through adenosine receptors but instead via phosphodiesterase inhibition [14].

Benowitz et al. demonstrated that both caffeine and paraxanthine significantly increased diastolic blood pressure, plasma concentrations of epinephrine, and free fatty acids [15].

An interesting proposed mechanism of action for caffeine involved the mobilization of intracellular calcium. Caffeine in high concentrations (1-10 mM) was found to interfere with the uptake and storage of calcium in the sarcoplasmic reticulum of striated muscle and to increase the translocation of Ca^{2+} through the plasma membrane [16-17].

Caffeine may also increase myofilament sensitivity to Ca^{2+} through its binding to ryanodine receptors in calcium channels of muscle and brain and may be modulated by stress, cortisol and derivatives parameters [18].

Despite these researches about caffeine actions, there are few studies about caffeine intake cardiovascular effect during sleep deprivation.

According to a study on mice, stress response after sleep deprivation is influenced by caffeine intake [19]. Our study also shows a direct link between caffeine units intake during sleep loss and cardiovascular response.

Another study on mice showed in opposition, that after sleep deprivation, lower doses of caffeine produces a decrease of stress response (a higher alteration of cardiovascular parameters) and of the locomotor system function while higher doses of caffeine induce a stimulation of the dopamine receptors D1 and D2 and the release of catecholamines (a better adaptation of heart during stress factors impact [20-21]). The results of our study show that subjects that consumed lower doses of caffeine (2.00-3.00 units) have the most significant changes of arterial blood pressure and heart rate, compared with those who consumed higher doses (5.00 units). So we can assume that a higher intake of caffeine increases cardiovascular response to stress, expressed in a lower decrease of heart rate and arterial blood pressure after sleep loss.

The research of Vaara et al. on 20 healthy sleep deprived volunteers show that after 24 h of sleep deprivation heart rate decreased, but no changes in arterial blood pressure occurred. [22]. However, in our study, the decrease of cardiovascular parameters, including arterial blood pressure and heart rate, after one night of sleep loss, in a department of medical services, may be explained by overstimulation of the sympathetic nervous system during the night, and a decrement of it in the morning. This observation is sustained by the research of Spiegel K et al., who concluded that after sleep loss, the blood level of the thyrotropin is lower than normal, and the sympathoadrenal balance is altered, fact that can contribute to a lower heart rate [23].

According to Kato et al., after one night of sleep deprivation the arterial blood pressure increases and muscle sympathetic nerve activity decreases [24]. Other studies realized by Almeida FR et al. suggest that acute paradoxical sleep loss (REM sleep) induces autonomic imbalance expressed by impaired baroreflex sensitivity, cardiovascular disfunctions, increased arrhythmia susceptibility and also changes related to oxidative stress or other cerebral pathologies [25-27]. The variation of arterial blood pressure in our study can be associated with the alteration of baroreflex sensitivity.

A correlation between stress response and sleep deprivation demonstrated that after sleep deprivation, stress response is altered because of changes in the release of stress hormones [28, 29]. More, a decrease in plasma cortisol in partially sleep deprived subjects (only until 3.00 a.m.), sustained a decrease of stress response [30].

The limitation of our study is represented by the small number of subjects, but interestingly, most of them presented a similar pattern of response. Another limitation was the fact that we couldn't exactly measure caffeine blood level, but only caffeine intake.

Conclusions

Impedance cardiography is a non-invasive method which provides a lot of cardiovascular parameters.

Our study reveals significant reduction of cardiovascular parameters (blood pressure, heart rate, stroke volume, cardiac output) in healthy young subjects after intense on-call duty in opposition to the expected increased values related to stress, effort and caffeine intake. These changes emphasize the impact of stress during on-call duty on cardiovascular function and its importance for a possible of early cardiovascular risk associated with sleep deprivation in young physicians. However, to clarify these results, future studies are necessary.

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