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Original Article

Effects of sleep extension combined with HIIT exercise on cortisol, IGF-1, and lactate levels in adolescents with sleep disorders: A randomized controlled trial

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Abstract

Background and aims: Sleep disorders are associated with hormonal and metabolic disturbances in children and adults. This study aimed to investigate the effect of high-intensity interval training (HIIT), a sleep extension program, and the combination of both on blood cortisol (C), insulin-like growth hormone (IGF-1), IGF-1/C ratio, lactate concentration, and aerobic capacity (AC) in adolescent girls with disorders.

Methods: This randomized controlled trial involved 80 girls with sleep disorders (aged 14.81 ± 1.46 years) recruited from the Child and Adolescent Psychology Clinic of Langerod in 2022. They were randomly divided into four groups using Random Allocation Software: HIIT, a sleep extension program, a combination of HIIT + sleep extension, and a control group (n = 20 per group). They participated in pre-test and post-test sessions for laboratory measurements and AC tests. The HIIT and combined groups followed the RAST protocol for four weeks, with three sessions per week. In addition, each participant in sleep extension and combined groups adhered to the sleep schedule for four weeks.

Results: A paired *t* test revealed significant reductions in cortisol levels for the sleep extension and combined groups ($P = 0.006$). Moreover, IGF-1, IGF-1/C ratio, lactate, and AC significantly improved in all three intervention groups ($P < 0.001$). The analysis of covariance (ANCOVA) test showed significant differences between groups for cortisol ($F = 64.361$, $P = 0.001$), IGF-1 ($F = 21.706$, $P = 0.0001$), IGF-1/C ($F = 33.76$, $P = 0.001$), lactate ($F = 34.845$, $P = 0.001$), and AC ($F = 26.106$, $P = 0.001$).

Conclusion: The findings provide evidence that combining HIIT with sleep extension can be an effective and safe intervention for improving the outcomes of sleep disorders in adolescent girls.

Keywords: Aerobic capacity, Cortisol, High-intensity interval training, Insulin-like growth factor I, Sleep disorders, Sleep extension

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Introduction

Sleep is a vital physiological process with important recovery functions. Adequate sleep plays a restorative and protective role, enhancing physical strength, reducing stress and anxiety, improving adaptability, and supporting life activities (1). Conversely, poor sleep can be an early indicator of psychiatric illnesses and puts a person at risk by decreasing the quality of life and physical, mental, social, and emotional health (2).

Recently, sleep disorders have markedly increased. In most cases, this rise is associated with hormonal and metabolic disturbances such as high cortisol levels in adults and children (3). Cortisol, a corticosteroid hormone, is a stress hormone because it is released in response to mental stress and anxiety. About 75% of cortisol is secreted in humans between 4 and 10 a.m. Elevated cortisol concentrations resulting from sleep disorders are associated with decreased anabolic hormone concentrations such as testosterone, growth hormone, and insulin-like growth hormone (IGF-1). IGF-1 is a polypeptide hormone with endocrine, paracrine, and autocrine effects primarily secreted by the liver (4). These factors are linked to obesity and increased visceral fat (4,5). In addition, cortisol causes a significant increase in blood lactate levels in a rested condition, which is probably of neurological origin (6). Lactate is an important cerebral metabolite, playing a critical role at high concentrations both within cells and in the extracellular space between cells (7).

Several studies were designed to manage the consequences of sleep deprivation recommend sleep extension and increased physical activity. Regarding sleep extension, most studies investigated its impact on cognitive, biological, and neurophysiological functions in children, adolescents, and adults (8-12). However, few studies have evaluated sleep extension as a strategy to mitigate the harmful hormonal effects of sleep deprivation. Results from a controlled trial intervention study revealed that implementing a sleep extension program among professional athletes can improve sleep quality and affect stress hormone expression such as cortisol (12). On the other hand, some research examined the benefits of regular physical exercise on sleep disorders as an effective non-pharmacological strategy (13). Some researchers have found that physical exercise significantly reduces cortisol levels (2,14), improves lactate and growth hormone concentrations (2,15), and increases sleep quality (14,16).

In recent decades, high-intensity interval training (HIIT) has emerged as a novel exercise widely studied by researchers. HIIT consists of repetitive sessions with short periods of intense training that involve multiple muscle groups and aim to approach maximum VO2 max (14). To the best of our knowledge, no study has yet investigated the combined effects of sleep regulation and physical exercise on stress and growth-related hormones in individuals with sleep disorders. Therefore, this study aimed to compare the effects of four weeks of HIIT, sleep extension, and the combination of HIIT + sleep extension on blood levels of IGF-1, cortisol, lactate, the IGF-1/cortisol ratio, and aerobic capacity (AC) in adolescent girls with sleep disorders.

Materials and Methods

Study design and setting

This trial was a randomized, controlled, parallel-design study aimed at assessing the efficacy of sleep regulation via an HIIT program, compared to sleep regulation or HIIT alone, over four weeks in adolescents with sleep disorders. Participants were referred to the Child and Adolescent Psychology Clinic of Langerod in 2022. The flow diagram of the study design is presented in Figure 1.

Sample size calculation

The sample size was calculated to for the analysis of covariance (ANCOVA) using G*Power version 3.1.9.4.15. Conservative estimates were made for power (0.80) and an effect size of 0.40. An alpha level of 0.05 was selected. The required sample size was determined to be 73 participants. To account for potential participant dropout, a total of 80 participants were recruited.

Inclusion and exclusion criteria

Patients were adolescent girls aged 13 to 17 years, diagnosed with sleep disorders (Pittsburg Sleep Quality Index score of 9 or higher), having a regular menstrual cycle, and reporting a lack of regular exercise in the past six months. They had no history of mental illness or hormonal disorders and had a body mass index (BMI) greater than 40 kg/m^2 (3). Exclusion criteria included missing two or three consecutive training sessions. Finally, eighty girls were voluntarily selected and randomly divided into HIIT (n = 20), sleep extension (n = 20), the combination of HIIT + sleep extension (n = 20), and control (n = 20) groups. The randomization sequence was computer-generated using random blocks, with the order unknown to both the researcher and the participants. Participants and the researcher were blind to group allocation. A statistician prepared the list, which was only accessible to personnel responsible for randomization.

Intervention and control groups

Participants in the first and third groups participated in the HIIT program for four weeks, with three 60-minute

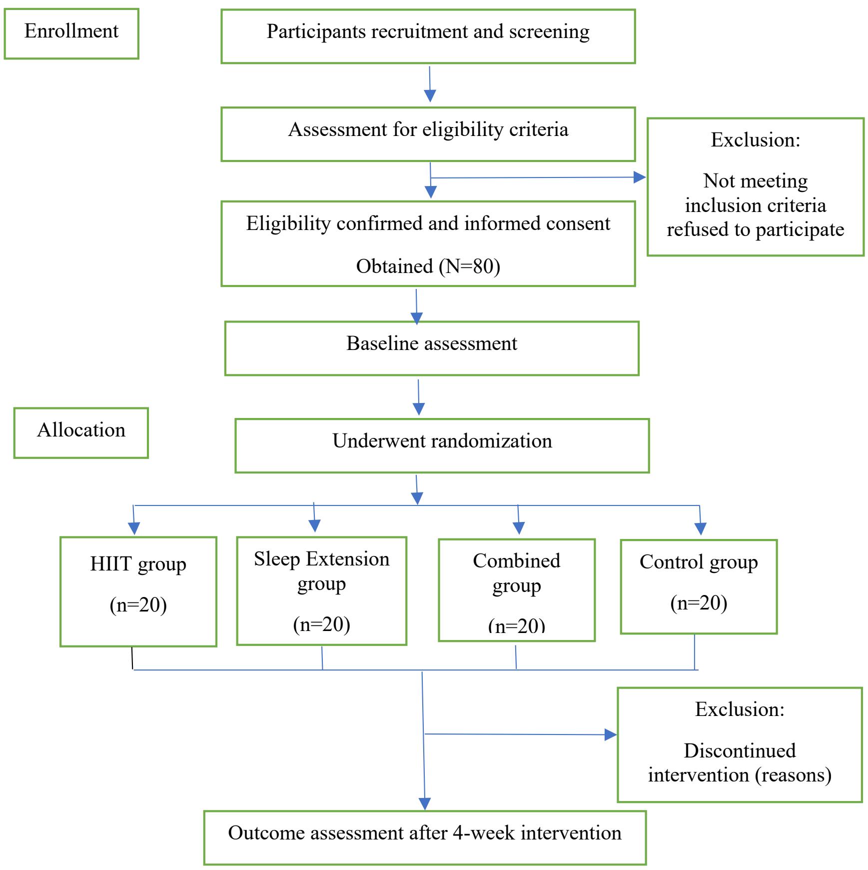

Figure 1. Consort flow diagram

sessions per week (totaling 12 sessions). The HIIT program followed three sets of the RAST protocol, with a 3-minute rest between each set in the first week. One additional set was added each week, eventually reaching six sets by the fourth week. Each set consisted of six 35-meter sprints, with 10 seconds of rest between each repetition. Each set was separated by a 4-minute rest period (14). Training sessions were performed between 9 and 11 am. Polar heart rate monitors (Finland) were used to control the training intensity. The HIIT program was administered at the university gym, and a fitness trainer supervised all the training sessions.

Participants in the second and third groups received a sleep extension program for four weeks. Each participant received a sleep plan, determining the bedtime, lights-out time, and wake-up time for each day. These times were recorded in a sleep diary to track progress. On non-holiday nights, bedtime and lights-out times were increased by 5 minutes every day (gradual sleep extension). The bedtime and lights-out time for the first night were set 10 minutes earlier than the participant's average time. By the end of the intervention, the times for going to bed and turning off the lights were 55 minutes earlier than at the start. The bedtime and lights-out times on holidays or weekends remained the same as the previous night, but participants were allowed to delay their wake-up time by up to one hour compared to their usual wake-up time.

Along with the individual sleep program, all participants received sleep hygiene guidelines such as limiting social media use (no gaming or watching TV for at least one hour before bedtime), avoiding beverages containing caffeine after 8 pm, and correcting napping habits (not sleeping during the day). If a person needs to take a daily nap, it should not exceed 30 minutes and should not be taken within 4 hours before bedtime. To optimize the environmental sleep conditions (e.g., temperature, light, darkness, and silence), participants were instructed to dim the lights one hour before bed and open the curtains immediately upon waking up in the morning (10). The control group was asked to maintain their regular daily routine and leisure activities and refrain from participating in any new physical activity or treatment programs throughout the study.

Procedure

First, an informative session was held to explain the research program to all participants. Informed consent was obtained from both the participants and their parents before enrollment, along with the collection of personal information and medical history. A physician then screened the participants for eligibility to participate in the HIIT program.

Two assessments were performed, one at the beginning and one at the end of the intervention (48 hours before and after the study protocol). Participants' anthropometric features, including weight, height, and BMI, were taken while wearing light clothing and no shoes. In addition, patients were instructed weekly during group educational sessions (lasting 15-20 minutes) to better understand the importance of a healthy diet and its impact on sleep quality.

Measures

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) is a self-report scale designed to assess sleep quality by querying multiple sleep-related variables over the past month. It uses both the Likert scale and open-ended response formats. The PSQI includes seven subscales: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, sleep medication, and daytime dysfunction. It contains 19 items, 18 of which are used to calculate the final scores. Subscale scores range from 0 to 3, and these scores are summed to obtain a global score ranging from 0 to 21. Higher scores suggest greater sleep disturbance, with a global score greater than 5 indicating a significant disturbance. Previous research has confirmed the validity and reliability of the PSQI, with Cronbach's alpha coefficient ranging from 0.78 to 0.82 (17).

Laboratory measurements

Five milliliters of blood samples was taken from an antecubital vein while participants were seated at the Razi Laboratory after a 12-hour fast, between 7 and 9 AM. According to the kit instructions, Plasma cortisol and IGF-1 levels were measured using a chemiluminescent assay (Liaison, England; IDS-iSYS; Immunodiagnostic Systems, respectively). Blood lactate concentration was determined by a finger blood sample using a lactometer (Lactate Scout, Senslab GmbH Leipzig, Germany).

20 m Shuttle run test

The Shuttle run test was utilized to measure aerobic power. This test involves running between two lines spaced 20 meters apart. Participants were asked to perform repeated 20-meter shuttles in response to an audible signal. The initial speed for the incremental test was set at 8 km/h, with an increase of 0.5 km/h every 2 minutes. After hearing the first beep, participants should move toward the end of the 20-meter route at a slow speed to reach it by the time they hear the second beep. If participants reached the end of the 20-meter before hearing the second beep, they must wait for the next one and then return. During this test, participants were required to adjust their speed as the number of round trips increased, and the time between two beeps decreased. They gradually raised their running speed until they felt tired or were unable to follow the rhythm. The final score for each participant was registered in their name (18). Additionally, the maximum AC (V_{o2max}) of each participant was estimated using the following formula (19):

$$VO_{2max} = (61.1 - 2.20) - (0.462 * age) - (0.268 * BMI) + (0.192 * rounds\ repeat)$$

Statistical Analysis

All values are expressed as mean (standard deviation). Data were analyzed for normality and homogeneity of variance using the Kolmogorov–Smirnov and Levene tests, respectively. A paired *t-test* was used to compare baseline and post-intervention values within each group. The analysis of the covariance (ANCOVA) test was used to compare the changes across the four groups after four weeks. When a significant F value was achieved, the Bonferroni post hoc test was conducted to find the differences between groups. All statistical analyses were performed using SPSS® 26.0 (IBM Corporation, Armonk NY, USA) for Windows® with a significance level set at $P<0.05$.

Results

All 80 participants completed the trial, with a mean age of 14.81 (SD = 1.46) years. Table 1 presents the demographic data and sleep quality scores, measured using the PSQI. No statistically significant difference was observed in any demographic and research variables at the beginning of the intervention. Descriptive statistics indicated that all participants in this study had high sleep disturbance scores at baseline (mean = 11.73, range = 9-14).

Cortisol and IGF-1 serum levels

Paired t-tests revealed that serum cortisol levels significantly decreased in both sleep extension and combined groups ($P<0.001$). In addition, the results of a paired t-test showed a significant reduction in cortisol (AC) in HIIT and combined groups ($P<0.001$) and in the sleep extension group ($P<0.002$), as illustrated in Table 2. Furthermore, the results of the ANCOVA test showed significant differences between groups for both cortisol (F = 64.361, $P=0.001$) and IGF-1 (F = 21.706, $P=0.001$) levels, as depicted in Table 2. Bonferroni's post hoc test results indicated that cortisol serum levels are significantly lower in the combined and sleep extension

Table 1. Descriptive statistics of age, height, weight, BMI, sleep disorder score at baseline in four research groups

Variable	HIIT (n = 20) Mean (SD)	Sleep extension (n = 20) Mean (SD)	Combined (n = 20) Mean (SD)	Control (n = 20) Mean (SD)	*P* value
Age (y)	14.80(1.6)	14.95(1.46)	14.75(1.40)	14.75(1.48)	0.141
Height (cm)	1.47(0.09)	1.47(0.09)	1.47(0.10)	1.46(0.09)	0.245
Weight (kg)	49.70(8.24)	49.30(9.57)	51.50(9.46)	48.65(9.48)	0.086
BMI	22.76(1.55)	22.36(1.92)	23.40(1.66)	22.51(1.70)	0.512
Sleep	12.70(3.04)	11.20(3.01)	11.75(3.16)	11.30(2.81)	0.183

Note. HIIT: High-intensity interval training; BMI: Body mass index; SD: Standard deviation.

Table 2. The comparison of changes in variables before and after four weeks of interventions

Variables	Groups	Mean (SD)		Within group (*P* value)	F	Between groups (*P* value)
		Pre-test	Post-test			
Cortisol	HIIT group	10.41(2.82)	10.69(2.45)	0/296	64.361	0.001
	Sleep extension	10.77(2.93)	8.62(2.65)	0.001		
	Combine	11.29(2.98)	5.59(1.10)	0.001		
	Control	11.27(2.87)	11.31(3.04)	0/791		
IGF-1	HIIT group	1.87(1.01)	4.45(2.13)	0.001	21.706	0.001
	Sleep extension	1.90(0.99)	3.55(1.23)	0.001		
	Combine	1.85(0.97)	5.35(2.08)	0.001		
	Control	2.46(1.41)	2.21(1.23)	0.270		
IGF-1/C Ratio	HIIT group	0.18(0.11)	0.44(0.27)	0.001	33.760	0.001
	Sleep extension	0.19(0.11)	0.45(0.21)	0.001		
	Combine	0.17(0.10)	0.93(0.44)	0.001		
	Control	0.22(0.12)	0.20(0.11)	0.286		
Lactate	HIIT group	3.87(1.25)	2.35(0.87)	0.001	34.845	0.001
	Sleep extension	4.45(1.19)	3.85(0.87)	0.001		
	Combine	4.30(1.30)	2.05(0.75)	0.001		
	Control	3.80(1.43)	3.65(1.22)	0.330		
AC	HIIT group	46.64(0.69)	48.38(1.22)	0.001	26.106	0.001
	Sleep extension	46.63(0.69)	47.05(0.82)	0.002		
	Combine	46.40(0.77)	52.45(2.06)	0.001		
	Control	45.78(1.17)	45.48(1.20)	0.090		

Note. HIIT: High-intensity interval training; IGF: Insulin-like growth factor; IGF-1/ C: IGF-1/ Cortisol; AC: Aerobic capacity.

groups compared to the HIIT and control groups ($P=0.001$). Nevertheless, cortisol levels did not differ significantly in the HIIT and control groups ($P=1.000$). IGF-1 serum levels showed a significant increase in the combined, sleep extension, and HIIT groups compared to the control group ($P=0.001$).

Insulin-like Growth Factor 1/ Cortisol Ratio, Lactate, and Aerobic Capacity

The dependent t-test showed that the differences in IGF-1, IGF-1/C ratio, and lactate were significant ($P<0.001$) following all three intervention protocols (HIIT, sleep extension, and combined). Moreover, the results of the ANCOVA test demonstrated significant differences between groups in IGF-1/C ratio ($F=33.76$, $P=0.001$), lactate ($F=34.845$, $P=0.001$), and AC ($F=26.106$, $P=0.0001$), as depicted in Table 2. Bonferroni's post hoc test results indicated that IGF-1/C and Lactate levels significantly improved in the combined HIIT and sleep extension groups compared to the control group ($P=0.001$). Nevertheless, no significant difference was observed between the HIIT and sleep extension groups in cortisol levels ($P=1.000$). Lactate levels in the combined and HIIT groups significantly decreased compared to the sleep extension and control groups ($P=0.001$).

Discussion

This is the first trial to compare the efficacy of HIIT, sleep extension, and their combination in improving hormone levels in patients with sleep disorders. The results shed light on a new method for ameliorating hormone regulation, suggesting that the combination of both interventions was more effective than either intervention alone, making it a good option for individuals with sleep disorders.

The results obtained from the present study indicated that all three interventions (i.e., HIIT training, sleep extension, and the combined approach) improved serum levels of IGF-1 and the ratio of IGF-1 to cortisol. In addition, sleep extension and the combined HIIT training and sleep regulation approach significantly reduced serum cortisol levels in adolescent girls with sleep disorders. However, HIIT alone caused no significant change in cortisol levels. This finding is consistent with the result from Swinbourne and colleagues' study (12) which reported a slight decrease in cortisol levels following a six-week sleep extension program in 25 professional rugby players.

However, our results are different from those reported by Irandoust et al (14), Barari et al (20), Chennaoui et al (5), and Sasaki et al (21). Irandoust et al found that performing HIIT exercises reduces cortisol levels in obese females with sleep disorders. Moreover, Barari et al and Sasaki et al did not observe significant changes in serum cortisol levels in inactive subjects following four weeks of endurance, resistance, and HIIT training. Furthermore, Chennaoui et al showed that a sleep regulation program does not significantly affect growth hormone levels. These discrepancies may be due to differences in participant characteristics, varying activity levels, and training duration.

Previous studies have demonstrated that sleep deprivation disrupts endocrine secretions, including an increase in cortisol levels at night and a decrease in anabolic hormones such as IGF-1 (4). The physiological mechanisms by which sleep deprivation contributes to pathophysiological metabolic disorders are not yet fully understood. One possible mediator is the hypothalamus-pituitary-adrenal (HPA) axis, which plays a critical role in regulating the stress response. The HPA axis is involved in the physiological effects associated with both homeostatic sleep (from regular sleep time), disordered sleep (from limited or irregular sleep time and duration), and wakefulness patterns of a message system (22).

It has been previously reported that a threshold exercise intensity is required to induce changes in growth hormone levels with long-term exercise. This may be due to the increase in acidity caused by muscle activity, which stimulates metabolic receptors and sends sensory feedback to the central nervous system and hypothalamus, ultimately causing an increase in growth hormone secretion. On the other hand, this phenomenon may be related to the onset of hypoglycemia, the stimulating effect of the motor cortex, and the sympathetic system's activity on growth hormone-releasing hormone in the hypothalamus (23).

Additionally, aerobic activity significantly increases serum IGF-1 levels. This increase is accompanied by an increase in the proteolytic activity of IGFBP-3. Proteolysis is believed to be caused by the activation of calcium-dependent protease and may contribute to anabolic effects on muscle tissue. HIIT training causes an acute elevation in circulating IGF-1 levels (24).

Another finding of this study was that all three interventions reduced serum lactate levels. This result is consistent with the findings of Arshadi et al (2) and Bayati et al (25) who showed that the blood lactate concentration of active men decreased significantly following a sleep regulation program and four weeks of intense intermittent training.

Recently, a significant increase in the buffering capacity of skeletal muscles was observed only after three weeks of HIT training. This may be due to an increased ability to buffer hydrogen ions (26) and a rise in the activity and content of lactate transporters such as monocarboxylate transporters 1 and 4 (27).

Regarding AC, we observed that all three interventions improve AC in adolescent girls with sleep disorders. This finding is consistent with Roche and colleagues' (28) results which examined the long-term effects of physical exercises combined with a balanced diet. They observed that a combination of supervised aerobic exercises and a balanced diet led to an increase in maximum aerobic power and $VO_{2\,max}$.

Previous studies have reported that HIIT training improves the heart's ability to pump blood more effectively than moderate-intensity training (29). HIIT exercise provides physiological benefits in aerobic energy, lactate accumulation, and creatine phosphate synthesis. The mechanism behind this type of exercise is that intense exercise increases the concentration of energetic substrates and the activity of enzymes related to anaerobic metabolism. By increasing the frequency of intense repetitions and alternating them with recovery periods, the need for muscle cells and metabolic pathways changes. As a result, the contribution of energy recovery from the anaerobic system to the aerobics system changes, leading to the involvement of both aerobic and anaerobic energy production systems in ATP reconstruction. Therefore, HIIT exercises probably improve both aerobic and anaerobic systems (25).

Moreover, the speed of aerobic phosphorylation increases after training, regardless of the type of training (HIIT or continuous). This adaptation may be achieved by increasing the number and activity of muscle oxidative enzymes (30), which can be considered one of the potential mechanisms for increasing the maximum oxygen consumption (31,32). Increased oxygen delivery (e.g., through increased stroke volume) and increased oxygen utilization by active muscles (e.g., through greater capillary and mitochondrial density) can be considered the primary mechanisms for improving AC (33).

Limitations of the Study

The current study has several limitations. First, a follow-up evaluation is needed to assess the stability of these positive effects over time. Second, since this study included adolescent girls with sleep disorders, future studies should include participants from other age groups.

Conclusion

In conclusion, the present findings, for the first time, revealed that four weeks of combined HIIT training and sleep extension significantly affect cortisol, IGF-1, lactate levels, and AC in adolescent girls with sleep disorders. Therefore, this interventional strategy would be an effective and non-pharmacological alternative for improving the blood concentration of stress and metabolic hormones and enhancing cardiorespiratory endurance.

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Authors' Contribution

Conceptualization: Alireza Elmieh.
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Project administration: Maryam Rezaei.
Resources: Fahimeh AdibSaber.
Software: Soleyman Ansari.
Supervision: Alireza Elmieh.
Validation: Soleyman Ansari.
Visualization: Alireza Elmieh.
Writing–original draft: Fahimeh AdibSaber.
Writing–review & editing: Alireza Elmieh, Fahimeh AdibSaber.

Competing Interests

The authors declare no conflict of interests.

Ethical Approval

This study was approved by the local ethics committee (IR.IAU.Rasht.REC.1400.027) and registered with the Iranian Registry of Clinical Trials (IRCT20180503039517N11).

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