

Blood Pressure Levels and Pattern of Melatonin Secretion in a Population of Resident Physicians on Duty

Niveles de presión arterial y el patrón de secreción de la melatonina en una población de médicos internos residentes de guardia

To the Editor,

For a doctor, being on call typically involves stress and fatigue associated with moments of anxiety and sleeplessness. Resident physicians (MIR) are on call more than 4 times per month and during those periods may have to work for 24 h at a stretch. Several studies have associated being on call with increased cardiovascular risk,¹ and alteration in blood pressure (BP) is one of the causal mechanisms.^{2,3} Physiological oscillations of a function over 24 h are known as the circadian rhythm (CR). Blood pressure decreases during night-time resting.¹

Melatonin is the main hormone involved in CR. Its secretion is regulated by the effect of light on the suprachiasmatic nucleus, with darkness stimulating production and light inhibiting it. Studies have shown a relationship between an abnormal pattern of melatonin secretion and alterations in BP.⁴ The aim of this study was to determine BP values in a population of on-call-resident doctors and to investigate their relationship with the pattern of melatonin in urinary secretion.

This was a cohort study carried out in a tertiary hospital with a total of 18 resident doctors. Two BP Holter (Microlife®, WatchBP model) studies were carried out on participants. One was performed on a normal working day to provide baseline measurements and another was performed while residents were on call. Four isolated urine samples were collected: a) morning (8:00) and night (0:00) of the normal working day, and b) morning (8:00) and night (0:00) of the on-call day. Urine samples were analyzed to determine urinary concentrations of 6-hydroxymelatonin sulphate (6-SO₄MEL), the urinary metabolite of melatonin. Urinary concentrations of 6-SO₄MEL follow the circadian pattern of accumulated melatonin, which correlates with serum melatonin.⁵ A urine specimen first thing in the morning provides a proportional fraction of nocturnal melatonin production. The CR was defined as normal when 6-SO₄MEL concentration was greater in the morning than at night, as production of the hormone increases during the hours of darkness.⁵ The SPSS

17.0 statistical package (Chicago, Illinois) was used for all statistical analysis. Data with a normal distribution are presented as means ± standard deviations and nonnormally distributed data as medians. Continuous variables were compared using Student's t test or Mann-Whitney U. In all tests, *P* was considered significant at <.05.

Residents' mean age was 28±2.1 years. On a normal working day, systolic and diastolic BP decreased significantly between day and night-time readings (119±10.9 and 77±5.4 vs 108±7.6 mmHg and 67±6.1, *P*=.003). Furthermore, 6-SO₄MEL values showed that CR was maintained during normal working hours, with concentrations being higher in the morning (8.00) than at night (0.00) (48.6 [28.1 to 74.1] vs 12.4 [7.7 to 38.9] ng/ml, *P*<.023) (Figure). When samples taken when residents were on call for 24 h were analyzed, there were no statistically significant differences between day and night-time values for systolic and diastolic BP (121±9.9 and 81±6.3 vs 116±11.3 and 73±7.3 mmHg, *P*=.08). Analysis of 6-SO₄MEL values showed that CR was lost during the on-call work day, with values of 61.2 [43.7 to 89] at 8:00 am compared to 21.2 [14.4 to 75.2] ng/ml at 0:00 pm (*P*=.08) (Figure).

This study's novelty lies in its design and the population studied. These were young participants in whom lack of sleep led to a burden of stress and fatigue. The results observed are relevant for 2 reasons. First, we noted that BP, by decreasing at night, followed a circadian pattern on the normal working day, but that this pattern disappeared when participants were on call. Second, the pattern of melatonin secretion indicated a loss of CR during the day on call. Diet would not be relevant to the results as the main factor regulating secretion of melatonin is light.⁵

Melatonin is involved in regulating biological CRs, including sleep. In our study, the melatonin CR is lost because hyperpolarization of retinal photoreceptor cells occurs in doctors who are awakened for an emergency while on call. This in turn would inhibit the release of noradrenaline and therefore the synthesis and secretion of melatonin.⁵ The loss of this CR is likely to be at least partly responsible for the abnormal patterns of BP observed. These in turn could lead to increased cardiovascular risk during periods when doctors are on call.

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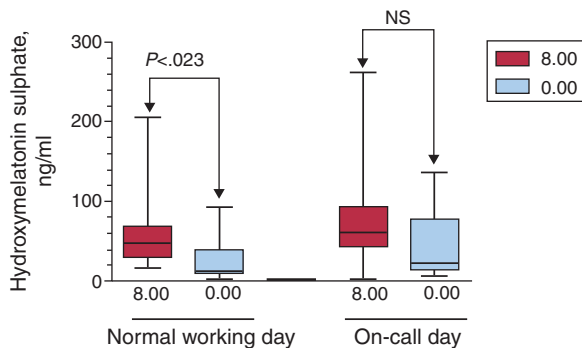


Figure. Box plot of urine concentrations of 6-hydroxymelatonin sulphate in a population of resident physicians during a normal working day and when on call. Urine samples were collected separately at 2 different times (during daylight hours, at 8:00, and during the hours of darkness, at 0:00). NS, not significant.

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Echocardiographic and Electrical Reverse Remodeling in Cardiac Resynchronization Therapy

Remodelado inverso ecocardiográfico y eléctrico en terapia de resincronización cardíaca

To the Editor,

Cardiac resynchronization therapy (CRT) has been shown to be an effective, economically viable tool¹ in patients with severe acute heart failure and intraventricular conduction disorders.

Recent publications suggest the presence of electrical remodeling in patients with smaller ventricular volumes after CRT.² We undertook a pilot study to determine the potential relationship between ventricular and electrical remodeling.

The study included 20 patients with idiopathic dilated cardiomyopathy and an indication for CRT, in whom the QRS duration and ventricular volumes were measured before implantation and after 6 months. The study excluded patients with atrial fibrillation or previous pacing by a pacemaker, as well as when the patients' own rhythm precluded measurement of the native or intrinsic QRS width. The study complied with all principles of the Declaration of Helsinki.

Left ventricular reverse remodeling was defined as a decrease $\geq 10\%$ in end-systolic volume at 6 months, and electrical remodeling as a decrease in intrinsic (unpaced) QRS width.

Of the 20 patients included (age, 61 [10] years; 40% women), 15 (75%) had echocardiographic evidence of reverse remodeling. These patients showed a significant decrease in intrinsic or

unpaced QRS on follow-up (169 [15] vs 154 [12] ms; $P=.032$) compared to the others (180 [23] vs 180 [16] ms; $P=.977$), in addition to a significant decrease in left ventricular end-diastolic volume ($P<.01$) and an improvement in ejection fraction ($P=.02$). Both groups showed similar clinical and echocardiographic profiles at baseline and similar device programming characteristics, but the patients who presented a decrease in QRS on follow-up were characterized by a shorter paced QRS achieved with CRT implantation (121 [15] vs 146 [24] ms; $P=.021$) (Table).

The main finding of this pilot study is a significant reduction in the intrinsic or unpaced QRS width in patients who present a decrease in ventricular volumes on follow-up, which is consistent with the findings of recent publications that report an improvement in intraventricular conduction among patients who present reverse remodeling.² This finding differed from the results reported by Stockburger et al.,³ who found no such relationship, but the series was much smaller and included patients with ventricular dysfunction of various etiologies, unlike this study which specifically analyzed patients with idiopathic dilated cardiomyopathy, a characteristic that could explain the different results obtained. The presence of mitral regurgitation has also been associated with the appearance of intraventricular conduction disorders.⁴ In our study we observed a decrease which was not statistically significant (probably due to sample size) but could partly be due to an improvement in electrical conduction after CRT. Another noteworthy finding is the possible relationship between the presence of ventricular and electrical reverse remodeling with the duration of the QRS complex achieved with implantation. It has been extensively reported in the literature that patients with wider

Table

Comparative Analysis of Clinical, Electrical, and Echocardiographic Variables According to Presence or Absence of Left Ventricular Reverse Remodeling at the 6-Month Follow-up

	LV reverse remodeling (n=15)		Absence of reverse remodeling (n=5)	
	Baseline	Follow-up	Baseline	Follow-up
Age, years	61 (11)	—	62 (8)	—
Women, %	47	—	20	—
Ejection fraction, %	21 (7)	39 (8) ^a	25 (4)	24 (13) ^b
LVEDD, mL	190 (83)	130 (57) ^d	264 (62)	284 (73) ^b
LVESD, mL	146 (65)	81 (35) ^a	191 (57)	215 (82) ^b
ERO, cm ²	0.15 (0.13)	0.06 (0.02)	0.27 (0.16)	0.13 (0.20)
Intrinsic QRS, ms	163 (15)	153 (31) ^d	180 (23)	182 (15) ^b
Paced QRS	121 (15)	122 (17)	146 (15) ^c	140 (14)
AV, ms	145 (22)	—	125 (7)	—
VV, ms	-20 (15)	—	-12 (02)	—

AV, programmed atrioventricular delay; ERO, effective regurgitant orifice area; LV, left ventricle; LVEDD, left ventricular end-diastolic volume; LVESD, left ventricular end-systolic volume; VV, programmed interventricular delay.

Data are expressed as mean (standard deviation).

^a $P<.05$ compared to intragroup follow-up.

^b $P<.05$ compared to intergroup follow-up.

^c $P<.05$ compared to intergroup baseline.