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# THE CRONOPHARMACOLOGY AND CHRONOBIOLOGY OF THE ARTERIAL HYPERTENSION

Perederii Corina<sup>1</sup>, Hulbar Aurelia<sup>1</sup>, Orasan Alic Viorel<sup>1</sup>, Orasan Alic Irina<sup>1</sup>, Rusu Andrea<sup>1</sup>, Orodan Maria<sup>1</sup>, Conea Simona<sup>1</sup>, Toma Claudia Crina<sup>1</sup>, Osser Gyongyi<sup>1\*</sup>, Pasca Bianca<sup>2</sup>, Popescu Mircea Ioachim<sup>2</sup>

1"Vasile Goldis" Western University of Arad, Faculty Pharmacy 91-93, L. Rebreanu Street, Arad, Romania 2 University of Oradea, Faculty of Medicine and Pharmacy , 10, 1<sup>st</sup> December Square, Oradea, Romania"

e-mail: gyongyiosser@ymail.com

#### Abstract

The invention of a device called, at that time, a pulsilogium, by Sanctorius-Sanctorius (1561-

1636) a physiology professor at the University of Padua, was considered a ground-breaking event in the history of technological development. The device, similar to a pendulum, was used to record the heart rate in different days, and even in different moments of one day. Therefore, Sanctorius-Sanctorius is considered to be the first chronogiologist.

The development of automatic data processing tools for blood pressure and pulse, collected throughout 24 hours, has allowed in recent years a greater and more detailed understanding of concepts such as the circadian rhythm of cardiovascular parameters within the broader scientific field, suggestively called chronobiology.

Key words: blood pressure and pulse, cardiovascular parameters, circadian rhythm

### **INTRODUTION**

The chronodesm is a term which defines the time – dependency reference boundary, obtained by the computer analysis of a circadian rhythm's data, evaluated within a reference population (eg: TA automatically monitored) – provides predictable information about a biological rhythm.(Steflea et.al1986,Smolensky et al 2009, Balan et al 2002, Lemmer et, al 1984).

The elements of a biorhythm can be quantified and subjected to a graph analysis, after an initial processing via the cosine technique (Fourier, 2009).

The purpose of chronotherapy is to optimize the therapeutic effect and control or reduce side effects, without altering the drug's functions in the body (Hermida et.al 2007, Hermida et.al 2010, Mancia 2007).

Epidemiological association between hypertension and cardiovascular events suggest that significant reductions in values presiónale confers enhanced benefits, but they, for reasons difficult to explain, is associated with a consistent reduction in cerebrovascular events and less of the coronary artery (Staessen et al 2000, Reinberg et al 2003, Reinberg et.al 1984).

This failure was interpreted partly as a consequence of metabolic side effects associated with therapeutic classes (emphasis dyslipidemia and atherosclerosis or occurrence of electrolyte imbalance) (Toiton et al 1994, Hansen et al 2011, Nakana et al 2004).

Treatment of high blood pressure as a major objective aimed at reducing cardiovascular morbidity and mortality (Nakane et al 2004).

Since it is already proven linear relationship between cardiovascular risk and BP values aim friend of antihypertensive therapy is to restore values presiónale pressure levels considered optimal or normal (Asrup et al 2007, Bonhanick et al 2008).

Although hypertension is one individualized treatment preference is advisable choice, regardless of therapeutic areas, single dose per day. The number of daily administrations and the number of tablets are larger, the more likely the patient the treatment to adhere properly.(levey et.al 2009,Grudy et.al 2009)

Should not be considered in an extremely simplified because all drugs recommended once daily is equivalent.

In terms of magnitude and duration antihypertensive effects, invariably, there are differences in their ability to consistently prove an antihypertensive effect over 24 hours (or even beyond this range) (Hansen et al 2011, Nakana et al 2004).

# MATERIALS AND METHODS

The study included 108 subjects suspected of suffering from coronary heart diseases and who were scheduled for ultrasounds and heart echography and echocardiography, in the Interventional Cardiology department of Oradea County Hospital, were examined.

Consent was obtained from each patient, in writing, prior to their inclusion in the group. The patients had their weight and height measured.

They also had their body mass index (BMI) determined, as well as their blood pressure and heart rate.

# **RESULTS AND DISCUSSIONS**

First of all lab samples were taken, to determine the values of the total cholesterol, triglycerides (TG), high density lipoproteins (HDL), low density lipoproteins (LDL), uric acid (UA), glycosylated haemoglobin (hemoglobinA1c).

All patients taking part in the study, under treatment with betablockers at least 3-4 months prior to the trial, had their IMT, carotid – femoral PWV and ABI measured.

Statistical analysis was performed with 8.0 Statistics program and tests were used to compare student test data and chi-square test. The value was considered statistically significant value of p<0,05.

The patients' treatment	Used dosage (mg)	Treatment hour/day /4 months	Observations
Ramipril	2,5mg	7,30 a.m vs 7,30p.m	****
Perinodopril	4mg	8a.m vs 8 p.m	
Nebivolol	5mg	9 am vs 9 pm	
Enalapril	10 mg	Only at 8 am	

*Table 1* The anti-hypertensive effect of the drugs, depending on the time of administration (after 22-24)

*Table 2* The parameters of the batch of patients included in the study, according to sex

Parameters under observation	Male	Female	р
Aix	-0,97±24,47	-10,25±24,52	0,11
PWV	11,90±1,78	14,11±1,58	0,29
DTDVS	60,99±4,77	61,55±6,44	0,37

DTSVS	42,61±4,54	44,33±6,12	0,34
No. of hospitalizations	1,43±1,10	1,40±1,33	0,80
SBP	124,01±15,41	120,70±16,97	0,36
DBP	70,12±6,95	68,91±7,98	0,35
Disease duration	5,66±1,45	6,37±1,98	0,22
AHT	30(42,86%)	13(46,43%)	0,15
Creatinine clearance	57,88±15,67	56,51±23,23	0,65

Analyzing patients in two age groups, according to subgroups were not statistically significant differences between age contatat patients with angina pectoris, myocardial infarction and stroke, as shown in table

*Table 3* The average age of patients with angina pectoris, myocardial infarction and stroke in the 2 groups

	Age				
Subgroup	Groupel NP		Groupe P		
	Media	standard	Media	deviația	
			standard		
AP	67,43	11,87	68,22	11,87	
IM	67,40	11,79	67,66	11,72	
AVC	67,66	11,78	67,67	11,93	
Total	67,50	11,74	67,84	11,77	

#### CONCLUSIONS

The administration of Ramipril at 7:30 PM improved the nocturnal drop in BP levels, therefore we can notice a significant change, which is consistent with the literature in the domain.The Perindopril dose administered at 8 PM significantly decreased the SBP and DBP over 24 hours.

The administration of Nebivolol in the morning versus in the evening resulted in changes in the mean SBP/DBP values over 48 hours; they changes were insignificant over a 24 hour period.

The Enalapril administration at 8 AM significantly reduced BP values during the day, but not during the night; the administration at 8 PM had a stronger effect during the night and in the morning, but not in the afternoon, when only an insignificant change was noticed.

The possibility of measuring and recording blood pressure (BP) values during a 24-48 hour period was done via a special device left on the

patient, who went about his usual routine (Holter recording), which records important data regarding the variations of blood pressure (BP) during different activities or moments of the day/night. It can also assess the efficiency of the antihypertensive treatment.

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