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Prevention of Prehypertension Complications in Conditions of Volatile Blood Pressure.

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ABSTRACT

The research was aimed at producing a methodology of prevention of complications of cardio-vascular diseases with elderly patients who have prehypertension. In a gerontological clinic 45 people of both sexes aged between 65 and 87 by the start of the research have been monitored for five years. All patients had their blood pressure measured constantly for 24 hours and compared with the dynamics of pressure during the day and night time. Patients were prescribed angiotensin-converting enzyme inhibitor (ACE inhibitor) – Ramipril in a daily dose of 10 mg as a monthly course with a consequent monthly break for five years. The results of the multiple measuring of arterial pressure revealed statistically significant profiles and predictability of arterial blood changes with the patients. It has allowed us to use the term «volatility» to describe the dynamics of arterial pressure changes in a way similar to currency rate changes on the exchange. This is why the «volatility» term is even part of the headline of our article. Basing on changes of arterial pressure with in 24 hours, patients were split into two groups. The first group included patients who had a high blood pressure mainly during the daytime. These patients had Ramipril prescribed in a 10 mg/day dose to be taken in the morning. The second group includes patients whose arterial pressure rose at night. Patients of this group had a prescription for Ramipril in a dose of 10 mg/day in the evening. During the five years of monitoring five out of 45 people died. The cause of death of three of them was brain disorders (brain attack with two people) and myocardial infarction with one person. Two people died of oncological diseases. The remaining 40 patients thanks to the prescription of Ramipril which takes into consideration the daily fluctuations of arterial blood pressure were alive and felt well despite their elderly age. Such an approach to prescribing Ramipril ensures efficient prevention of cardio-vascular complications and encephalitic disorders with elderly patients in a prehypertension condition.

Keywords: prevention; prehypertension; prevention of cerebral and cardio-vascular illnesses; angiotensin-converting enzyme inhibitors; Ramipril; 24-hour monitoring of blood pressure

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INTRODUCTION

Statistics show that life expectancy in developed countries is rising steadily. It entails a whole range of economic and social problems caused by the change in the age structure of the nation. Such changes call for state and public support. As a result, state expenses require new sources for social provision of the elderly. It can be either higher taxes and collections for social insurance, or a higher retirement age. Most countries have opted for the second way, by raising the retirement age. But the key condition here is preserving health and capability to work in the middle and old age that ensures active long years. This is why prevention of brain disorders development and complications in a prehypertension condition is one of the most urgent goals in the extension of active ageing.

The WHO believes that prevention of such complications must be based on stabilizing blood pressure at safe levels. This idea defines the long-term tactic of a doctor when choosing a correct therapy. Hypertension is common in care home residents and is commonly treated with antihypertensive drugs, which were prescribed more frequently in more recent studies but with no better BP control. These studies indicate a tendency toward increasing polypharmacy over time, with associated risk of adverse events, without demonstrable benefit in terms of BP control [1].

Sometimes the use of a constant doze of a hypotensive drug does not produce any expected therapeutic effect as early as by the end of the first year of use and requires a higher dosage. But it is important to note that such a tactic often triggers a higher frequency of unwanted side effects with patients with a high blood pressure due to heavy medicaments doses [2].

When analyzing various approaches to therapy one can note that attaining an optimal blood pressure level via prescribing medicines that lower blood pressure is not often possible because the failure to attain an optimal blood pressure is often fraught with the development, for example, of hypertensive heart attacks and strokes, while aggressive therapy and a quick lowering of blood pressure may lead to the development of hypotensive (pale) infarctions and strokes. This is the technical contradiction when implementing all known ways of prevention based on attaining the optimal level of blood pressure. This means that blood pressure should be lowered because of a high risk of hypertension complications but at the same time one should not lower blood pressure fast because it may lead to complications of hypotensive character. The traditional way of removing this contradiction is a combined therapy based on modern medicines [3].

Ramipril produces a good therapeutic effect. The drug is prescribed «nocte» in a dose of between 2.5 to 5.0 mg/day and if tolerance is good the dose can be increased to 10 mg/day. Supportive therapy with the help of Ramipril should last for 5 years [4]. Such treatment tactics allows the doctor to diminish the risk of cardio-vascular diseases complications by 30% in 74% of cases [5]. The problem is in the existence of a large enough groups of patients whose blood pressure fits the WHO norms in one-time morning measuring. Doctors do not often classify such conditions as prehypertension conditions. Such patients think they are conditionally healthy and naturally, avoid prevention. This is why brain disorders and complications of cardio-vascular diseases occur often among them. The ischemic heart disease and heart strokes account for 55% and 24% of deaths in men and 41% and 36% in women in the structure of death causes as a result of cardio-vascular diseases [6]. Besides, it is also a fact that strokes more often develop in the early morning hours (4-5 in the morning), and it is high blood pressure during night hours that leads to their occurrence. This confirms the necessity of measuring blood pressure not only in the morning, but also during the 24 hours.

The goal of our research is a safe method of prevention of brain disorders development and complications of cardio-vascular diseases in a prehypertension condition of elderly people.

MATERIALS AND METHODS

We have constantly monitored 45 people of both sexes aged between 65 and 87 for 5 years, who stayed in a gerontological in-patient facility. Patients were included in the clinic research on grounds of the absence of blood hypertension and the presence of at least one of the risk factors for the development of cardio-vascular disease complications, such as the ischemic heart disease, diabetes, smoking and others. Along with the usual daily blood pressure measuring all the patients were under an ambulatory blood pressure monitoring (ABPM). Ramirpil was prescribed as a prevention medicine in 10 mg/day.

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RESULTS

Patients had their arterial pressure measured at blood vessels in the bend of right and left elbows in the morning hours, at rest, when seated. Statistically important changes of arterial pressure which would testify to a high risk of brain disorders development or possible complications of cardio-vascular diseases were not registered.

The ambulatory arterial pressure monitoring conditionally split the patients into two groups. The first group (24 people) included patients who registered a high arterial pressure during morning or day hours (ref. Table №1 and 2), and the second group (21 people) included patients who registered a high arterial pressure during the night (ref. Table 3 and 4).

Table 1: Change of arterial pressure during daytime of patients with predominantly daytime rise of arterial pressure (ABPM results)

Statistic figures	Maximum		Average		Minimum	
	SAP	DAP	SAP	DAP	SAP	DAP
Number of values (n)	24	24	24	24	24	24
Average (X av)	135.08	90.38	115.92	74.25	95.54	62.17
Standard deviation (S)	3.3740	7.5228	4.3331	8.8821	6.5805	7.7103
Standard deviation from average (S av)	0.6887	1.5356	0.8845	1.8130	1.3432	1.5739
Confidence interval (CI)	1.4215	3.1692	1.8255	3.7419	2.7723	3.2483
Relative error (δ)	0.0105	0.0351	0.0157	0.0503	0.0290	0.0523
Mode (M)	136	94	119	67	96	63
Maximum (max)	140	98	122	88	103	78
Minimum (min)	127	69	106	58	78	52
Student's test (95%, n-1)	2.06390	2.06390	2.06390	2.06390	2.06390	2.06390

SAP – systolic arterial pressure; DAP – diastolic arterial pressure.
Source: Table 1 reflect results of statistical analysis of our own data.

Table 2: Change of arterial pressure during nighttime of patients with predominantly daytime arterial pressure (ABPM results)

Statistic figures	Maximum		Average		Minimum	
	SAP	DAP	SAP	DAP	SAP	DAP
Number of values (n)	24	24	24	24	24	24
Average (X av)	123.08	82.54	107.92	68.00	88.83	57.46
Standard deviation (S)	5.7401	11.4245	4.2006	10.6117	8.3075	4.9692
Standard deviation from average (S av)	1.1717	2.3320	0.8574	2.1661	1.6958	1.0144
Confidence interval (CI)	2.4183	4.8131	1.7697	4.4706	3.4999	2.0935
Relative error (δ)	0.0197	0.0583	0.0164	0.0657	0.0394	0.0364
Mode (M)	126	89	108	69	87	62
Maximum (max)	129	94	112	84	105	66
Minimum (min)	110	55	95	51	69	49
Student's test (95%, n-1)	2.06390	2.06390	2.06390	2.06390	2.06390	2.06390

SAP – systolic arterial pressure; DAP – diastolic arterial pressure.
Source: Table № 2 reflect results of statistical analysis of our own data.

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Table 3: Change of arterial pressure during daytime of patients with predominantly nighttime rise of arterial pressure (ABPM results)

Statistic figures	Maximum		Average		Minimum	
	SAP	DAP	SAP	DAP	SAP	DAP
Number of values (n)	21	21	21	21	21	21
Average (X av)	128.62	80.86	118.33	74.14	98.86	63.38
Standard deviation (S)	5.7920	7.3979	8.7312	5.6417	7.3911	4.3529
Standard deviation from average (S av)	1.2639	1.6143	1.9053	1.2311	1.6129	0.9499
Confidence interval (CI)	2.6285	3.3572	3.9623	2.5602	3.3541	1.9754
Relative error (δ)	0.0204	0.0415	0.0335	0.0345	0.0339	0.0312
Mode (M)	135	75	110	72	95	67
Maximum (max)	137	92	129	84	109	75
Minimum (min)	120	73	97	65	83	56
Student's test (95%, n-1)	2.07961	2.07961	2.07961	2.07961	2.07961	2.07961

SAP – systolic arterial pressure; DAP – diastolic arterial pressure.
Source: Table № 3 reflect results of statistical analysis of our own data.

Table 4: Change of arterial pressure during nighttime of patients with predominantly nighttime rise of arterial pressure (ABPM results)

Statistic figures	Maximum		Average		Minimum	
	SAP	DAP	SAP	DAP	SAP	DAP
Number of values (n)	21	21	21	21	21	21
Average (X av)	134.67	87.43	125.38	79.05	109.67	67.05
Standard deviation (S)	6.2796	7.5005	9.0026	5.8777	8.9852	5.3430
Standard deviation from average (S av)	1.3703	1.6367	1.9645	1.2826	1.9607	1.1659
Confidence interval (CI)	2.8497	3.4038	4.0855	2.6673	4.0775	2.4247
Relative error (δ)	0.0212	0.0389	0.0326	0.0337	0.0372	0.0361
Mode (M)	135	82	124	78	110	70
Maximum (max)	143	101	137	91	127	82
Minimum (min)	124	78	101	72	92	59
Student's test (95%, n-1)	2.07961	2.07961	2.07961	2.07961	2.07961	2.07961

SAP – systolic arterial pressure; DAP – diastolic arterial pressure.
Source: Table № 4 reflect results of statistical analysis of our own data.

Patients who made the first group had systolic artery blood pressure of 115.9±4.3 Torr on average during daytime, and diastolic pressure of 74.3±8.9 Torr. As we see, these are the values of artery pressure that do not require medically induced corrections. However, blood pressure peaked at 140/98 Torr in the morning and during the day, which means pressure overshot the values recommended by the WHO and required drug treatment because it represented the risk of a hypertonic catastrophe (Table 1. Change of arterial pressure during daytime of patients with predominantly daytime rise of arterial pressure (ABPM results)).

The arterial pressure with patients of this group amounted to 107.9±4.2/68.0±10.6 Torr at night on average with peaks of between 129/94 and 105/66 Torr, or within the WHO recommended values, which do not require any drug treatment. At that, the patients demonstrated a collapse of arterial pressure to 69/49 Torr, this is why prescription of a medicine that lowers pressure in the evening with these patients is fraught with a hypotonic catastrophe (Table 2. Change of arterial pressure during nighttime of patients with predominantly daytime arterial pressure (ABPM results)).

Patients that made the second group demonstrated systolic blood pressure at 118.3±8.7 Torr and diastolic of 74.1±5.6 Torr on average during the day, with maximal peaks of systolic pressure at 137/92 and minimal collapses of diastolic pressure to 83/56 Torr (Table 3. Change of arterial pressure during daytime of patients with predominantly nighttime rise of arterial pressure (ABPM results)). This means that prescription of

an antihypertensive medicine in the morning or during the day to patients with a predominantly nightly rise of the artery blood pressure may lead to a hypotonic attack. However, we saw quite a different picture during the night. This group of patients ran an average pressure of 125.4±9.0/79.0±5.4 at night, but night pressure peaks amounted to 143/101, which exceeds WHO recommended values significantly (Table 4. Change of arterial pressure during nighttime of patients with predominantly nighttime rise of arterial pressure (ABPM results)).

When analyzing the data from tables 1-4, you can see that patients with predominantly day rises of arterial blood pressure had daily and nightly fluctuations between systolic and diastolic pressure of 9.7 ÷ 7.6%, and diastolic in a range of 9.5 ÷ 8.2% (Table 5. The difference in changes of artery pressure during daytime compared to night of patients with predominantly daytime increase of artery pressure). We take financial terminology as example and call such fluctuations of blood pressure a «spread».

Patients with predominantly nightly rise of blood pressure demonstrate an absolutely different picture: the night/day spread of systolic pressure amounted to 4.7 ÷ 10.9%, and diastolic to 8.1 ÷ 5.8% (Table 6. The difference in changes of artery pressure during nighttime compared with daytime of patients with predominantly nighttime arterial pressure rise).

Considering all this we choose the following method: if the spread is predominantly daily, medications are prescribed during the day. If the night spread dominates, medications are prescribed for the night time.

Table 5: The difference in changes of artery pressure during daytime compared to night of patients with predominantly daytime increase of artery pressure

	Daytime compared with nighttime (maximum)		Daytime compared with nighttime (average)		Daytime compared with nighttime (minimum)	
	SAP	DAP	SAP	DAP	SAP	DAP
By F criterion	0.0136764	0.050617	0.882909	0.399852	0.271022	0.040151
Percent (%)	9.7	9.5	7.4	9.2	7.6	8.2

SAP – systolic arterial pressure; DAP – diastolic arterial pressure.

Table №5 shows that arterial pressure rises to statistically important values compared with nighttime hours, from 7.4 to 9.7% on average.

Table 6: The difference in changes of artery pressure during nighttime compared with daytime of patients with predominantly nighttime arterial pressure rise

	Nighttime compared with daytime (maximum)		Nighttime compared with daytime (average)		Nighttime compared with daytime (minimum)	
	SAP	DAP	SAP	DAP	SAP	DAP
By F criterion	0.721263	0.951493	0.892437	0.856368	0.389862	0.367018
Percent (%)	4.7	8.1	6.0	6.6	10.9	5.8

SAP – systolic arterial pressure; DAP – diastolic arterial pressure.

Table 6 shows that arterial pressure rises at night compared with day hours in statistically important values, between 4.7 to 10.9% on average.

Tables №5 and №6 show that patients of these two groups registered statistically important differences of arterial pressure during daytime and nighttime.

By comparing table's № 5 and № 6, we receive a range of statistically important changes of arterial pressure at different times of the day of between 4.7% and 10.9. Prevention can take time at any time convenient for the patient if fluctuations of arterial pressure are smaller. If fluctuations of arterial pressure are wider, we should not talk about prevention, but about medical aid. In this case medicinal drugs are introduced on medical orders until the arterial pressure tentatively stabilizes and it is only then when prevention measures should be taken.

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High changeability of arterial pressure typical of elderly patients has allowed us to apply the term «volatility», used to describe exchange trading in economy when currency rates are hard to predict, in medicine and use it in the headline of the article.

Example

Patient Ch-va Yu.V. born in 1932 has a diagnosis of a chronic atrophic gastritis, chronic pancreatitis, cachexia of grade 1, circulatory encephalopathy of stage 2, dorsopathy, and polyangioneuropathy. She had her arterial pressure measured at admission by an electronic blood pressure monitor in the usual way. It amounted to 110/80 mm Hg. The electrocardiogram dated 08.05.2007 showed no pathological findings. Clinical blood analysis: hemoglobin 103 g/L; ESR 8 mm/h; leucocytes 3,2 $x10^9$/l; banded neutrophils 2 $x10^9$/l; segmented neutrophils 48 $x10^9$/l; lymphocytes 47 $x10^9$/л; monocytes1 $x10^9$/l.

Biochemical blood assay: ALT 59 u/l; AST 65 u/l; total protein 75 g/l; creatinine 100 mcmol/l; urea 5.8 mmol/l; uric acid 218 mcmol/l; bilirubin 6.8 mcmol/l; direct (conjugated) bilirubin 2.6 mcmol/l; cholesterol 5.3 mmol/l; low density lipoproteins 4.14 mmol/l; alkaline phosphatase 102 u/l; natrium 144 mmol/l; potassium 4.5 mmol/l; chlorides 106 mmol/l; glucose 5,2 mmol/l; iron 16.6 mcmol/l.

All data available to the doctor show no susceptibility to a sudden elevation of the arterial pressure and consequently to a high risk of brain disorders development or complications of cardio-vascular diseases. The patient was exposed to a daily monitoring of arterial pressure (Figure 1), and a daily monitoring of heart rate (Figure 2).

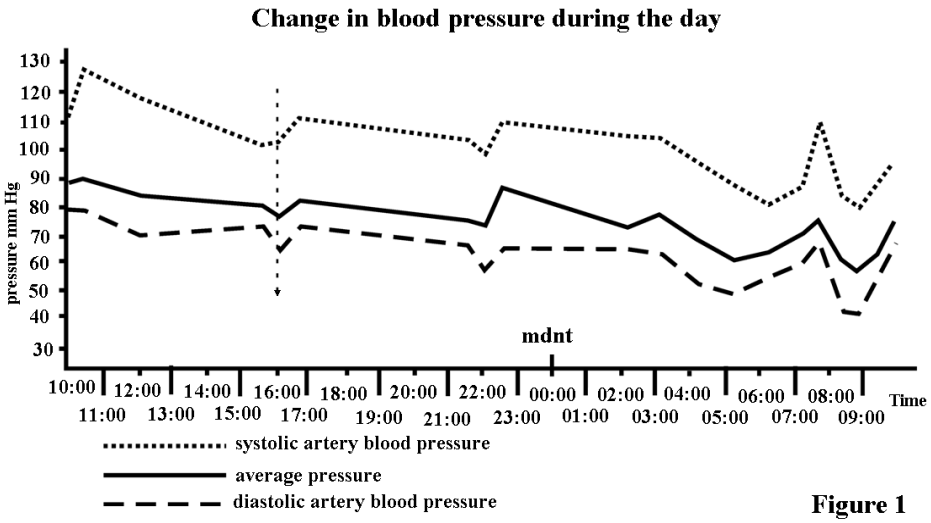

Figure 1

From 8:00 a.m.to 12:00 the patient showed a higher systolic artery blood pressure as compared with the evening and night periods at values that exceeded values recommended by the WHO. It should be noted that a fall in blood pressure accompanied by a quicker pulse was registered with the patient at this moment.

The charts (ref. Fig.1) showing changes in systolic and diastolic pressure help us calculate pulse pressure, which equals the difference between the value of systolic and diastolic pressure. In Figure 1, apart from systolic and diastolic pressure the line shows changes in average pressure, which is an average value (not an arithmetic value) between systolic and diastolic pressure, which in the absence of pulse fluctuations of blood could produce the same hemodynamic effect as when blood flows naturally, with fluctuations. Average pressure represents energy of a continuous blood flow. Since the duration of the diastolic blood output is higher than the systolic one, average pressure is closer to the value of diastolic pressure and is calculated as a sum of diastolic pressure plus 1/3 of pulse pressure. (ref. Fig.1)

The protocol shows, that a 6.1% elevation of systolic blood pressure during the day and a 9.1% elevation of diastolic arterial pressure during day time compared to arterial pressure during night hours took place. At that, arterial pressure suddenly peaked in the morning at 10:30. The data of daily monitoring of heart

rate (ref. Fig. 2) demonstrates that a higher heart rate at 3:30 p.m. was not accompanied by a higher blood pressure.

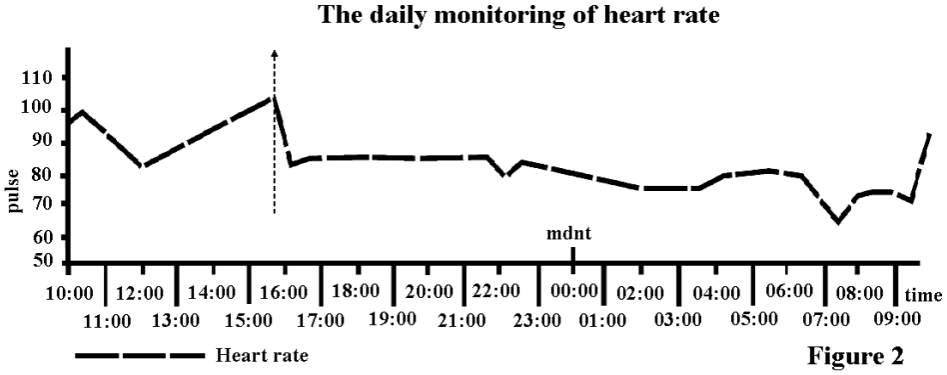

Figure 2

A quicker heart rate is not connected with the value of artery blood pressure. Thus, the acceleration of pulse to over 100 beats per minute at 3:45 p.m. was accompanied by a deceleration of both systolic and diastolic pressure and naturally, average pressure.

The patient was prescribed the Ramipril drug to be taken in the morning (at 9 in the morning) as a long-term therapy in a 10 mg/day dose. The patient has been watched for five years. Despite the elderly age, there were no preconditions for the development of brain disorders or complications of cardio-vascular diseases during the monitoring at hospital.

The hypertension disease did not develop and no brain disorders or complications of the cardio-vascular system were discovered.

CONCLUSIONS

Summing up, we can say that all patients that we have monitored received such therapy for a month within five years with month-long breaks. In the five years of our monitoring 5 people out of 45 died. Brain disorders became the reason for the death of three of them (a brain attack with two people) and complications of a cardiovascular disease (myocardial infarction – one person). Two people died of cancer. The other 40 patients are alive and well despite their elderly age thanks to such prevention that takes into consideration daily changes of arterial pressure. So, the percentage of elderly people whom we monitored who died from natural causes amounted to 6.67%, while the percentage of deaths of natural causes in a group of the same age, but who took Ramipril at 10 мg/day only in the morning amounted to 30%.

We received similar clinical results with the use of Ramipril in prevention of complications in prehypertension conditions when using specific angiotensin-2 receptor antagonist - the Diovan® medication, which selectively blocks receptors of AT_1 subtype in a dose of 160 mg/day. The consequence of the AT1-receptor blockade is a higher plasma concentration of angiotensin-2.

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