

## Medication of isolated systolic hypertension stage 3 complicated by gout in senile patients

Vladimir A. Gorshkov-Cantacuzene <sup>1</sup>, Irina M. Peskova <sup>2,\*</sup>

<sup>1</sup>Hypertension Research Foundation, Russian Delegation of the Pontifical Georgian College, Moscow, Russia

<sup>2</sup>Moscow State University of Education, Moscow, Russia

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### Abstract

The present work reports a clinical case of medication of a senile woman having isolated systolic hypertension Stage 3 complicated by gout. The uniqueness of this case is due to the absence of possible medication in the current Guidelines and other medical literary sources. Consequently, the possibility of administration of high doses of ARB in combination with CCB, which resulted in significant SBP decrease (-41.5 mmHg) and very small DBP decrease (-0.5 mmHg), which is the most beneficial for this pathology.

Isolated systolic hypertension (ISH) is a kind of hypertension characterized, according to the current Guidelines [1-3], by systolic blood pressure (SBP) readings  $\geq 140$  mmHg with normal ( $< 90$  mmHg) diastolic blood pressure (DBP). Although, using such classification, it is difficult to tell the borderline between Hypertension Stage 1 and ISH Stage 1, as, for instance, blood pressure (BP) readings equal to 145/86 mmHg may be attributed to either of them. Therefore, the authors claim that ISH should be diagnosed if BP readings are 140-160/ $< 80$  mmHg and  $\geq 161$ / $< 90$  mmHg.

ISH is characteristic in elderly and senile people and is diagnosed approximately in 15-30% of them

[4]. Sometimes ISH also occurs in young and healthy males, and according to existing recommendations [3], such patients are advised to change their lifestyle, as the prospective data [5] indicate that the condition is not bound to lead to stable SBP/DBP elevation and, respectively, to the development of hypertension. It is proved that ISH found in elderly and senile patients is a predictor of cardiovascular disease, and is also associated with the 2-5 times increase of cardiovascular mortality rate, the 2,5 times increase of stroke rate and 51% increase of total mortality. Besides, every BP increase by 10 mmHg in such patients (if SAD is higher than 140 mmHg) leads to 30% increase of complication rate, that is several times higher than in younger patients [6-8].

The main pathogenetic mechanism of BP increase in elderly women is estrogen deficiency, primarily 17-B-estradiol concentration decrease and associated disappearance of protective influence of

\* Correspondence to: Vladimir A. GORSHKOV-CANTACUZENE, ThD, JCD, DSc(med), FRAMI, AACC (int)  
1395 S. Columbia Rd. No. 139, Grand Forks, ND 58201, USA.  
e-mail: hypfoundation@gmail.com

these hormones on the cardiovascular system [9,10]. Production of nitrogen oxide and prostaglandin I<sub>2</sub> (strong vasodilatation and antiplatelet factors) decreases, tissue renin-angiotensin system and sympathetic nervous system are activated, sodium chloride delay is observed, insulin resistance is formed, and therefore, hyperinsulinemia occurs.

Until recently, treatment of patients with ISH was believed to be inexpedient due to possible complications as the result of anti-hypertension medication: however, the SHEP, EWPHE, SYS-EUR, FEVER and MRFIT studies demonstrated [11-16] the efficacy of such therapy, in particular, stroke rate was reduced by 40%, cardiovascular complications proved 30% reduction, ischemic heart disease showed 15% reduction, and the decrease of common cardiovascular and coronary mortality rate was evident. Nevertheless, SBP decrease to slightly lower readings than 140 mmHg, in comparison with SBP 145 mmHg, results in considerable reduction of cardiovascular diseases. SBP was proved to be highly linked with the risk of development of coronary, cerebral and renal complications, than DBP, and, consequently, medication of patients with ISH may considerably improve the forecast.

The main difficulty in selection of medication is low readings of DBP, as well as its possible unexpected and/or dramatic decrease during medication. Moreover, the research by SHEP proved that the decrease of DBP readings per every 5 mmHg facilitates the risk of stroke.

The treatment of elderly and senile patients with ISH must be commenced with lifestyle changes, paying attention to lowering salt uptake to 5 gpd (in case of heart failure – to 3 gpd), weight loss, rejection of bad habits (smoking, alcohol consumption). This may be difficult due to social and cultural environment of the patient, and also the patient reluctance to give up or change their habitual lifestyle.

Medication is administered as a rule to the patients having SBP >160 mmHg, as well as to those having SBP 140-160 mmHg together with such risk factors as diabetes mellitus, angina pectoris and left ventricular hypertrophy.

In elderly and senile patients, hypertension, in particular, ISH, is characterized by lower activity of blood plasma rennin, reduction of artery walls exten-

sibility and elevation of general peripheral blood vessel resistance. In theory, in such conditions diuretics and calcium channel blockers (CCB) seem to be the most beneficial. Therefore, to treat ISH in elderly and senile age, according to the current Guidelines, thiazide-type diuretics and dihydropyridine CCB [2,3] should be used. Moreover, some evidence [8,11,14] indicate that the mentioned drugs are the most beneficial, although it is also possible to use ACE inhibitors and  $\beta$ -blockers. There is also some evidence of using olmesartan [17]. In practice, thiazide-type diuretics are most often used in low doses (12.5-25 mg for  $\Gamma$ hydrochlorothiazide), which are believed to be promising in antihypertension therapy.

## Materials and Methods

Ms. L., is a 86-year-old Caucasian woman. She complains about high BP (up to 200/55 mmHg) and, consequently, bad state of health, vertigo, weakness and sometimes insomnia. She has been noticing BP over 140/90 mmHg since the age of 40, when she first measured her BP because of severe headache. ISH was diagnosed at the age of 80 but the patient does not receive constant therapy, as the scheme administered earlier proved to be inefficient. If SBP raises over 200 mmHg, she takes 10 mg of nifedipina. Gout was diagnosed at the age of 84, and this complicates the selection of antihypertension therapy: at present, the level of uric acid is normal, and the patient does not take any drugs. She works 3 days a week and it should be noted that it takes her to walk 500 m and 40 minutes by public transport (usually standing) to get to work.

By the beginning of the participation in the research program of the Hypertension Research Foundation, Russian Delegation of the Pontifical Georgian College, BP was 186/62 mmHg, that is, ISH Stage 3.

According to the ECG data, amplitude criteria of left atrial enlargement (without repolarization defects) are present, as a result of high BP; heart rate is 61 bpm. CBC (FBC), blood test and urine test were unremarkable. Osler's test is negative. The MMPI questionnaire did not reveal any deviations. So high BP readings in combination with relatively insignificant pathologies may show the evidence of good compensatory mechanisms and the organism endurance. This

effect may result from the patient’s being a professional musician playing a string musical instrument all her life in addition to teaching.

**Results**

The presence of gout limits and complicates the selection of therapy, as it excludes the administration of thiazide-type diuretics. The current Guidelines [2,3] do not imply such a situation. At the same time it should be kept in mind that even when diuretics may be administered to senile patients, the following must be taken into consideration: manifestations of cellular dehydration and redistribution of electrolytes between the cell and the environment with the tendency to hypokalemia, the properties of neuroendocrine regulation and water and electrolyte exchange in senile patients. As a rule, diuretics are administered in smaller doses, mostly in short courses with obligatory control (and correction) of the electrolyte profile and acid-base state of the organism. Excessive diuretic

therapy may lead to hypokalemia and cardiac output reduction as well as kidney bloodstream and filtration reduction and azotemia [18]. Some researchers note low efficiency of diuretic therapy in elderly and senile patients in comparison with middle age patients because of water drinking disorders.

During the first phase (Fig. 1), monotherapy was administered: 160 mg valsartan (ARB) in the morning, two days later the dose was increased to 320 mg valsartan in the morning and in four more days - to 160 mg valsartan in the morning and 320 mg valsartan in the afternoon.

During the second phase (Fig. 1) the transition to combined therapy was made: 160 mg valsartan in the morning, 320 mg valsartan in the afternoon and 10 mg nifedipina (CCB) in the evening (before bedtime); in five days the dose was increased to 160 mg valsartan + 10 mg nifedipina in the morning, 320 mg valsartan in the afternoon and 10 mg nifedipina in the evening (before bedtime).

Thus, during the first phase, total daily take of 480 mg valsartan resulted in gradual reduction of BP

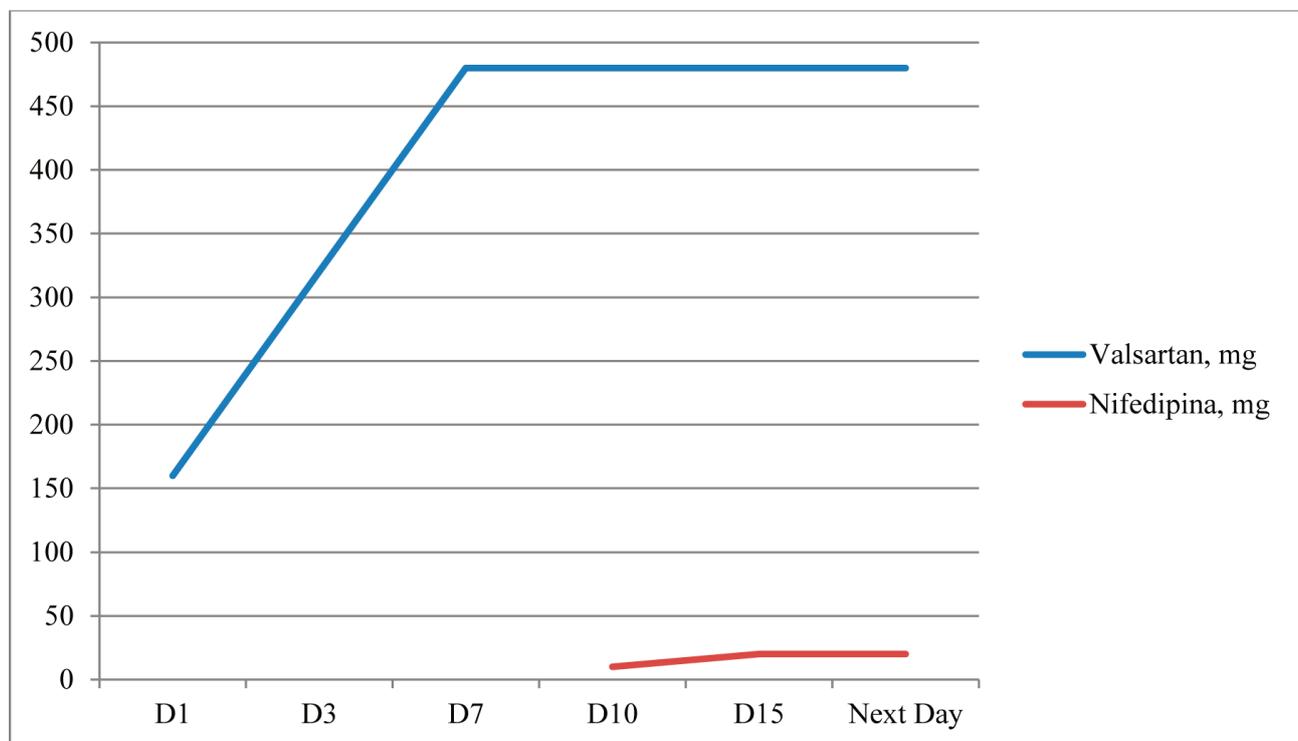


Fig.1. The diagram representing valsartan and nifedipina doses. D1 corresponds to the beginning of the therapy, D1-D7 represent Phase I, D10-Next Day corresponds to Phase I, Next Day represents the present medication.

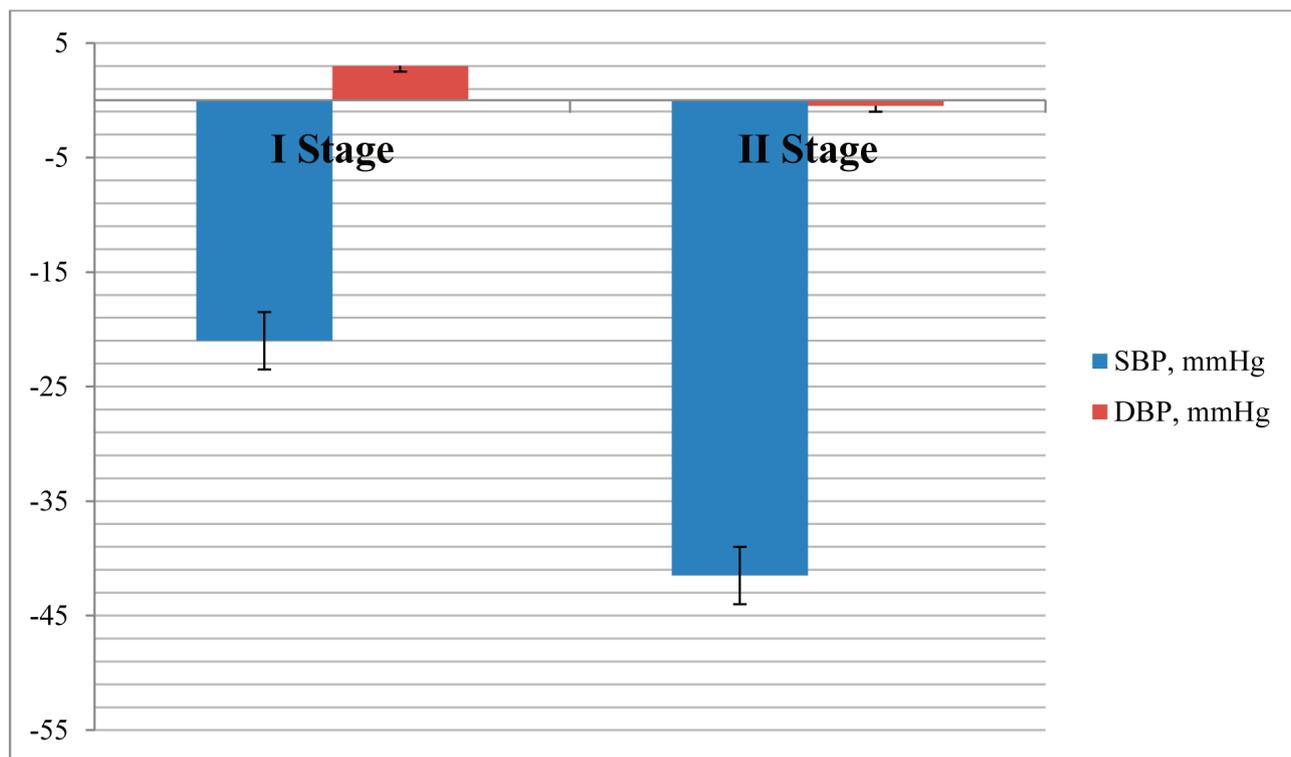


Fig.2. The diagram of BP changes for phases I and II.

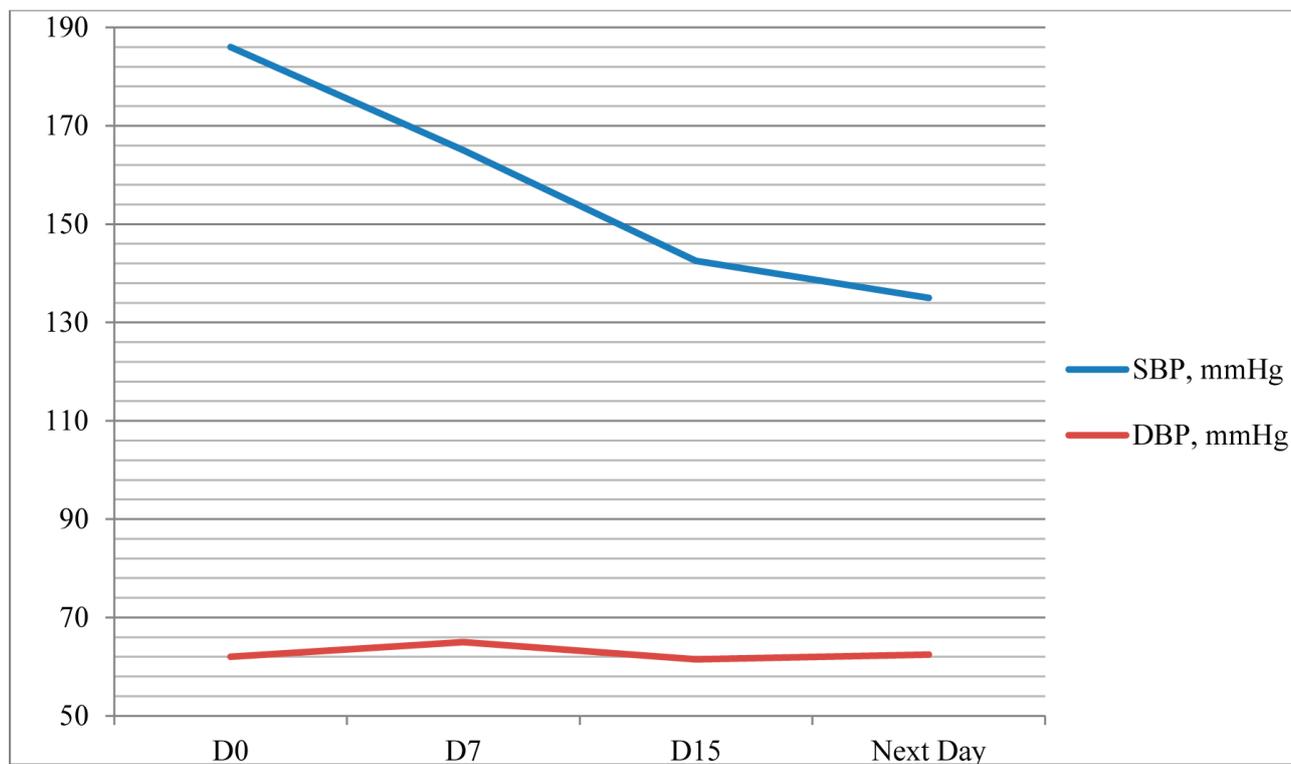


Fig.3. The diagram of BP changes.

to 163-167/60-65 mmHg. The patient noticed improvement of well-being and absence of vertigo and insomnia. During the second phase, as the result of total daily take of 480 mg valsartan and 20 mg nifedipina stable range of BP equal to 140-145/60-63 mmHg was maintained together with better health and mood, sound sleep and absence of dizziness (Fig. 2).

Although in this case the total dose of valsartan was 480 mg (that is higher than the maximum allowable value), some researchers [19] note the possibility of such medication, besides, when using high doses, the frequency of restoring normoalbuminuria is twice higher than when low doses are used (24% and 12%, respectively). It is pointed out that high doses are well tolerated. Dose-dependent undesirable side-effects, including hyperkalemia, were not registered.

In 2 months BP readings range was 130-140/60-65 mmHg (Fig. 3) with occasional SBP elevations to 160 mmHg (most often as a response to stress or weather changes). The patient remarks considerable improvement of well-being, absence of vertigo and weakness, sound sleep.

## Conclusion

The clinical case under consideration evidently demonstrates the possibility of administering high doses of valsartan in clinical practice, as well as high efficiency of combined ARB+CCB therapy in the treatment of ISH Stage 3 complicated by gout. Thus, the selected strategy lead to SBP decrease by 41.5 ( $\pm 5$ ) mmHg and DBP decrease by 0.5 ( $\pm 0,05$ ) mmHg, and SBP changes proved to be twice efficient in comparison with average results according to the current Guidelines [2,3]. Moreover, relatively small decrease of DBP should be emphasized.

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prophylaxis and control of hypertension in particular, cannot be overestimated.

## References

- 1999 World Health Organization / International Society of Hypertension Guidelines for the Management of Hypertension. Guidelines Subcommittee. *J Hypertens*; 17:151-183 (1999).
- Cardiology: National Guidelines / edited by E.V. Shlyakht. - 2th publ. - M.: GEOTAR-Media, 2015. - 800 c.
- 2013 Guidelines for the Management of Arterial Hypertension, *J Hypertens*. 2013; 31(7):1281-1357
- Gobas I.M. Estimation of prevalence of arterial hypertension among the population of Ukraine // *News of medicine and pharmacy. Arterial Hypertension*; 229:22-24 (2007).
- O'Rourke MF, Adji A. Guidelines on guidelines: focus on isolated systolic hypertension in youth. *J Hypertens*; 31:649-654 (2013).
- Kearney P.M., Whelton M., Reynolds K. et al. Global burden of hypertension: analysis of worldwide data. *Lancet*; 365:217-223 (2005).
- Mancia G., De Backer G., Dominiczak A. et al. 2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens*; 25:1105-1187 (2007).
- Lever A.F., Brennan P.J. Medical research council trial of treatment of hypertension in older adults. *Clin Exp Hypertens*; 15:941-949 (1993).
- Saveleva G.M., Breusenko V.G., Kruchenkova M.E., Grazianskyi N.A., Averkov A.V. Replacement hormone therapy for ischemic heart disease. *Practical gynecology*; 1:12-20 (1990).
- Samaan S.A., Crawford M.H. Estrogen and cardiovascular function after menopause. *JACC*; 26 (1465):1403-1410 (1995).
- Celis H., Yodfat Y., Thijs L. Systolic hypertension - Europe. *Fam. Pract.* 1996; 13:138-143.
- Dahlof B. Swedish trial in old patients with hypertension (STOP-Hypertension). *Clin Exp Hypertens*. 1993; 15:925-939.
- Lindholm L.H., Hansson L. Swedish trial in old patients with hypertension 2 (STOP-Hypertension 2). *Blood Press*. 1996; 5:300-304.
- Wang J.G., Liu G., Wang X. Systolic hypertension in the elderly: Chinese trial. *J Hum Hypertens*. 1996; 10:735-742.
- The Multiple Risk Factor Intervention Trial (MRFIT). *JAMA*. 1982; 248:1465-1477.
- Zhang Y, Zhang X, Liu L, Zanchetti A. Is a systolic blood pressure target <140mmHg indicated in all hypertensives?

- Subgroup analyses of findings from the randomized FEVER trial. *Eur Heart J*, 2011; 32:1500–1508.
17. Drapkina O.M. Isolated systolic hypertension is the destiny of elderly hypertension. *Difficult patient*; 12(10):10-13 (2007)
  18. Gurevich M.A. Heart failure in elderly patients // *RMJ*; 12:874 (2014)
  19. Kobalova Zh.D., Kotovskaya Yu.V. Combination of a blocker of the renin-angiotensin system / dihydropyridine calcium antagonist and nephroprotection in patients with diabetes mellitus. *Consilium medicum*; 12:44-48 (2010)