Valsartan in the Treatment of Hypertension

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Introduction: Hypertension represents an important public health problem. Effective treatment of hypertension is imperative for primary care. Goal: The goal of this study was to examine the efficacy of Valsartan in the treatment of hypertension with emphasis on the overall efficacy in reduction of systolic and diastolic blood pressure in a sample of 738 patients.

Material and methods: The study lasted for 12 months (from January 1, 2012 until December 31, 2012 year) and conducted in 18 public health institutions in B&H. Parallel follow up of Valsartan antihypertensive effect through repeated measurements every three months was conducted.

Results and discussion: Our results indicate that both systolic and diastolic blood pressure decreased significantly after 12 weeks of Valsartan treatment. Analysis of adverse effects did not showed statistical significance of side effects for total sample. Statistical analysis by Yates chi-square did not show the presence of statistically significant differences in adverse effects by gender.

Conclusion: We conclude that Val or Val plus are effective and safe antihypertensive drugs for the treatment of mild to moderate hypertension.

Key words: hypertension, valsartan.

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1. INTRODUCTION
Hypertension is the most important chronic health problem. It is estimated that hypertension affects approximately one billion people and that this number will increase by 60% until the year 2025. Hypertension is the first risk factor for cerebrovascular accidents and cardiovascular disorders. The degree of hypertension based on blood pressure as continuous variable that changes from minute to minute, depending on the patient’s mental and physical condition and environmental factors. Hypertension represents a challenge for family physicians because the need of early detection and treatment, but also to achieve blood pressure control. According to the World Health Organization and the International Society of Hypertension, it is defined as elevated blood pressure when the level of systolic blood pressure is 140 mmHg (18.7 kPa) or more and/or the level of diastolic blood pressure is 90 mmHg (12.0 kPa) or more, in repeated measurements. It can occur as isolated systolic or diastolic hypertension but most often both pressures are elevated. Due to the changes that occur in large arteries by aging, systolic blood pressure after the fifty year is increasing with each year of life by about 2 mmHg and diastolic blood pressure by 0.5 to 1 mmHg. Men have higher levels of blood pressure than women until age 60. Later, this difference disappears so in the older age women have higher values of blood pressure and higher prevalence of hypertension. Lowering blood pressure for 9/5 mmHg reduces the risk of stroke by 30% and the risk of ischemic diseases by 20% (1, 2).

The majority of patients with hypertension have essential or primary hypertension, which have unknown cause and in which the initially high blood pressure is the only manifestations of disease. In other patients hypertension is caused by disease of some other organ and therefore is called secondary hypertension. The degree of clinical severity of hypertension is estimated on the basis of systolic blood pressure and current changes in other organ systems (1,3).

According to the causes, hypertension can be:
• Essential;
• Renal hypertension;
• Endocrine hypertension;
• Cardiovascular hypertension;
• Neurogenic hypertension;
• Hypertension in pregnancy or hypertension gravitas;
• Hypertension induced by drugs or iatrogenic hypertension.

Effect of hypertension manifests in the development of left ventricular hypertrophy due to the increased pressure load and acceleration of atherosclerosis in the coronary arteries, as well as in the arteries of the brain, heart, kidneys and lower limbs (3, 4).

Most hypertensive patients have no symptoms and such persons are detected only by physical examination. Symptoms that indicate hypertension
to a doctor can be divided into three
groups and relate to:
• Increase of blood pressure only;
• Hypertensive angiopathy;
• Primary disease in the case of sec-
ondary hypertension.

Clear family history of hypertension
with information about the occasional
increase of blood pressure in the past
goes in favor of the diagnosis of essen-
tial hypertension. Secondary hyperten-
sion mostly occurs before 35 or after 55
years of age. Data on the use of corti-
costeroids or estrogen is obviously very
significant. History of recurrent urin-
ary tract infections indicates chronic
pyelonephritis, although this situation
develops and asymptomatic, noctur-
nia and polydipsia indicate renal or en-
docrine disease and lumbar trauma or
episodes of acute pain in the groin can
be a guideline to kidney damage. Spec-
ifying weight gain is compatible with
Cushing’s syndrome and weight loss indi-
cates pheochromocytoma (2, 4, 5, 6).

The clinical evaluation of patients
with hypertension should:
• Confirm the presence of hyper-
tension;
• Determine the presence and ex-
tent of hypertension effects on the
other organs;
• Identify cardiovascular risk fac-
tors and other existing diseases that
affect prognosis and treat-
ment;
• Exclude or confirm the causes of
secondary hypertension (2, 5, 6).

Therapeutic approach to the indi-
vidual patient with hypertension de-
pends on associated risk factors that
favor the development of cardiovascu-
lar disease, the existence of cardiovas-
cular disease and target organ damage.

Essential hypertension cannot be
cured, but proper treatment can signif-
ically influence its course. Changing
the lifestyle is an important component
in the treatment of essential hyper-
tension. Correction of body weight, regu-
lar physical activity, diet with limited
intake of salt (<6g per day), saturated fat
and alcohol and smoking cessation can
significantly reduce blood pressure and
increase the effectiveness of antihyper-
tensive therapy.

Treatment with antihypertensive
medications is indicated if by lifestyle
changes the blood pressure cannot be
maintained in the desired range.
• Diuretics (thiazides);
• Beta-blockers;
• ACE inhibitors;
• Angiotensin II receptor blockers;
• Calcium channel blockers.

All these medications can be used
as first-line medications for the treat-
ment of hypertension. Antihyperten-
sive effect of thiazides is reflected in the
reduction of plasma volume and beta-
blockers in reducing sympathetic activ-
ity and negative inotropic effect on the
myocardium.

ACE inhibitors and angiotensin II
receptor blockers are vasodilators be-
cause by indirect effect on certain areas
of the renin-angiotensin system reduces
peripheral vascular resistance. ACE in-
hibitors prevent conversion of angioten-
sin I to angiotensin II, and angiotensin
receptor blockers block the binding of
angiotensin II to angiotensin receptors.

Calcium channel blockers are pow-
erful vasodilators, because they directly
reduce tension of blood vessels smooth
muscles and thereby reduce peripheral
vascular resistance. Treatment of sec-
ondary hypertension is directed at the
case (7, 8, 9, 10).

Valsartan is competitive angioten-
sin II receptor antagonist, selective for
their AT1 subtype. Specific selective
blockade of AT1 receptors and consec-
tive antagonizing of all the effects not
only of angiotensin II, but also other com-
ponents of the renin-angiotensin-
alosterone system is essential effect
of valsartan from which derive all of
its pharmacodynamics and therapeu-
tic effects.

It is used as monotherapy or in com-
bination with HCTZ for all types of re-
novascular and essential hypertension.

Valsartan is not metabolized in a
way that it produces active metabolite,
it is effective for 24 hours and is taken
once a day.

For the majority of patients after the
use of single oral dose antihyperten-
sive activity occurs within two hours.
The greatest reduction in blood pres-
sure with any dose is achieved within
2–4 weeks and maintained during long-
term treatment. Co-administration
with hydrochlorothiazide produces a
considerable further reduction in blood
pressure.

In patients with congestive heart
failure it improves hemodynamics, in-
cluding pulmonary capillary wedge
pressure, pulmonary artery diastolic
pressure and systolic blood pressure,
systemic vascular resistance and car-
diac stroke volume. In clinical studies it
was shown that Valsartan can help re-
duce the risk of heart failure—patients
were treated with Valsartan showed signi-
ficant improvement in signs and symp-
toms of heart failure including dyspnea,
fatigue, edema, compared to placebo.

Valsartan is used to treat hyperten-
sion and congestive heart failure. Thera-
peutic doses ranging from 80 to 320 mg.

Pregnant women should not use
Valsartan, while special caution is
needed in patients who are receiving
high doses of diuretics as symptomatic
hypotension may occur. Also, caution is
needed in patients with liver and kidney
damage. Possible side effects are usually
dizziness and headache (7, 8, 9, 10, 11).

2. RESEARCH GOALS

To evaluate patients suffering from
hypertension who were treated with
Valsartan (Val or Val plus), in one of the
18 medical institutions in Bosnia
and Herzegovina, with the emphasis on
the effectiveness of antihypertensive ef-
fact of Valsartan from pharmaceutical
company Farmavita.

Identify mean systolic blood pres-
sure in the study group of patients by
measuring blood pressure during the
study time period: every three months
(measured once a month).

Identify the differences between the
patients examined in our study in rela-
tion to gender, age, age groups.

Provide a cross section evaluation
of the Valsartan side effects.

3. MATERIAL AND METHODS

Data used in our study were ob-
tained from the studies and analyzes
conducted in 18 health facilities in
the territory of B&H. This study in-
cluded 738 patients who underwent
three consecutive medical examina-
tions after they had been on Valsartan
therapy. Patients treated in our study
completed three examinations in three
months: one review a month. Inclusion
criterion was hypertension treated with Valsartan.

Valsartan which we used in the study is a manufactured by FarmaVita.

Each doctor treated a group of patients from 20 to 50 patients by treating doctor. All doctors keep track of hypertension in a specially designed table on the basis of which they drafted the report. After collecting the data are transformed into the same group study that we presented in tables and figures.

Needed data for monitoring the effectiveness of Valsartan (Val and Val plus) are collected on the basis of medical examinations and notes:

- Anamnesis and previous status.
- Measuring the blood pressure during first, second and third examination.
- Keeping record on side effects during the three months.
- Laboratory tests.
- Diagnostic tests.

Study results are presented in tables and figures by number of cases, percentage and mean with standard deviation and range. Analysis of the statistical significance of the differences is conducted by Pearson and Yates chi-square test and one-way analysis of variance (ANOVA). The results of all these tests were considered statistically significant with p <0.05 or 95% confidence level (ANOVA). The results of all these tests were conducted by Yates chi-square showed the presence of statistically significant differences in adverse events by gender (χ²=8.737; p=0.001).

4. RESULTS

Results are presented tables 1-4 and figures 1-2. Review of the gender structure of the sample indicated that women were slightly more represented with 396 or 53.7% of the respondents in relation to men with 342 or 46.3%.

Analysis of age distribution shows that the majority of respondents were in the older age groups (over 50 years) and that statistically significant difference by chi-square test is recorded in relation to gender (p> 0.05). Larger number of patients has been subjected to the treatment of hypertension for the first time (421 or 57.0%) compared to those who had previously treated hypertension (317 or 43.0%). Analysis of the average blood pressure during the initial examination, the first and second follow-up shows a linear decrease and statistically significant difference between the groups according to the results of analysis of variance (ANOVA) for both systolic and diastolic blood pressure. Majority of patients have been subjected to the treatment of hypertension for the first time (421 or 57.0%) compared to those who had previously treated hypertension (317 or 43.0%).

... conclusion...

5. DISCUSSION

In our research, we had 738 patients. Review of the gender structure of the sample indicated that women were slightly more represented with 396 or 53.7% of the respondents in relation to men with 342 or 46.3%. Analysis of age distribution shows that the majority of respondents were in the older age groups (over 50 years) without statistically significant difference by chi-square test in relation to gender (p>0.05).

Analysis of adverse events by gender shows that the higher total number is recorded among women as well as hypertension, dizziness, fatigue, nausea and diarrheee, while dizziness, headache and abdominal pain were more often reported by men. Given the small number of side effects statistical analysis using Yates chi-square showed the presence of statistically significant differences in adverse events by gender (χ²=8.737; p=0.001).

Table 1. Gender structure

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>342</td>
<td>46.3</td>
</tr>
<tr>
<td>Female</td>
<td>396</td>
<td>53.7</td>
</tr>
<tr>
<td>Total</td>
<td>738</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 2. Review of the sample by gender and age χ²=2.018; p=0.7325

<table>
<thead>
<tr>
<th></th>
<th>20-40 yrs.</th>
<th>40-50 yrs.</th>
<th>50-60 yrs.</th>
<th>60-70 yrs.</th>
<th>70+ yrs.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>40.0</td>
<td>48.6</td>
<td>47.7</td>
<td>44.1</td>
<td>47.2</td>
<td>46.3</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>60.0</td>
<td>50.4</td>
<td>52.3</td>
<td>55.9</td>
<td>52.8</td>
<td>53.7</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>8.1</td>
<td>15.9</td>
<td>26.2</td>
<td>25.5</td>
<td>24.3</td>
<td>23.4</td>
</tr>
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</table>

Table 3. Previous hypertension treatment

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>First treatment</td>
<td>421</td>
<td>57.0</td>
</tr>
<tr>
<td>Previously treated hypertension</td>
<td>317</td>
<td>43.0</td>
</tr>
<tr>
<td>Total</td>
<td>738</td>
<td>100.0</td>
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</tbody>
</table>

Table 4. Review of average BP by treatment duration

<table>
<thead>
<tr>
<th></th>
<th>Systolic</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
<th>Diastolic</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>First examination</td>
<td>152.36</td>
<td>20.25</td>
<td>118-182</td>
<td>98.24</td>
<td>17.573</td>
<td>86-112</td>
<td></td>
<td></td>
</tr>
<tr>
<td>First follow-up</td>
<td>143.24</td>
<td>14.38</td>
<td>116-170</td>
<td>91.57</td>
<td>12.348</td>
<td>82-105</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Second follow-up</td>
<td>132.26</td>
<td>9.52</td>
<td>110-154</td>
<td>84.26</td>
<td>6.421</td>
<td>69-98</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

F=5.364 p=0.001 F=6.382 p=0.001
ria (13, 14). In a series of large-scale clinical trials is established the value of Valsartan in reducing cardiovascular complications and mortality in high-risk patients. Study of Val-HeFT and VALIANT demonstrated that the cardiovascular benefit of valsartan is comparable to or better than angiotensin-converting enzyme (ACE) inhibitors and other antihypertensive agents and with better tolerability. We did not compare these results with our study because our goal was not the prevention of cardiovascular complications. In the future, we will follow the patients from our study, while special emphasis will be given to the cardiovascular complications of patients treated with Valsartan and compared with patients who are not treated or treated by other antihypertensive medications. Most frequent side effect of ACE group, which Valsartan does not cause, a dry cough that occurs in 5% to 35% of patients and does not depend on the dose of the medication. The incidence of cough depends on the applied representative groups, and so for example, Amir et al. 2005 found that is the most common when taking Enalapril (17.3%), followed by Fosinopril (14.7%), Perindopril and Quinapril (14.3%), Lisinopril (12.5%) and Ramipril (8.3%). Within the side effects we did not have any patient with these symptoms which represents a significant advantage of Valsartan in relation to this group of drugs when it comes to the foregoing side effects (15, 16, 17). Initial blood pressure was measured at the first visit and averaged 152 mmHg for systolic blood pressure and 98 mmHg for diastolic blood pressure. After one month of treatment with Valsartan (Val or Val plus) systolic blood pressure was reduced to an average of 143 mmHg and diastolic pressure to 91 mmHg. The reduction was also observed with the third visit, when the average systolic blood pressure was 132 mmHg and diastolic pressure 84 mmHg. Total reduction of blood pressure has averaged 20 mmHg for systolic and 14 mmHg for diastolic, which is consistent with previously published results. During the treatment a total of 56 adverse events occurred in 56 patients out of 738 and were similar to those on which reported Bisvas et al. (18). Most often was hypotension (2.8%), followed by dizziness (1.6%), fatigue in 1.1% and other adverse effects in less than 1% of patients. Above side effects are statistically not significant. Farmavita Valsartan and its fixed dose combination with hydrochlorothiazide (Val and Val Plus) are so valuable therapy for the area of internal medicine. A study of this agent has confirmed the effectiveness of the treatment of hypertension.

6. CONCLUSIONS

The study was conducted on 738 patients at 18 medical institutions during 2012. Criteria for inclusion in the Valsartan treatment was newly discovered hypertension, hypertension which could not be continued due to adverse effects. Our results indicate that both systolic and diastolic blood pressure decreased significantly after 12 weeks of treatment with Valsartan. Analysis of adverse events did not show statistically significant side effects for the total sample. Statistical analysis using Yates chi-square showed the presence of statistically significant differences in adverse events by gender. Val or Val plus is an effective and safe antihypertensive drug for the treatment of mild to moderate hypertension.

REFERENCES