Monitoring the efficiency of a fixed combination of lisinopril and hydrochlorothiazide in the treatment of essential hypertension in duration of 12 weeks

Abstract

Objectives: The aim of the study was to test the efficiency, compliance of patients and tolerance to the lisinopril and hydrochlorothiazide treatment.

Methods: We conducted an observational, nonintervention multicentric study in 19 centers in Bosnia and Herzegovina. The study included 147 patients of both sexes diagnosed with essential hypertension who were already ordinated by antihypertensive therapy. The patients were monitored for 12 weeks, i.e. one initial and four control examinations.

Results: The fixed combination of lisinopril and hydrochlorothiazide lowered the values of systolic and diastolic blood pressure for an average of 31/15 mmHg in patients aged 30 to 59 and for an average of 30/10 mmHg in patients over 60 years. The aimed blood pressure values were achieved in 82.31% of patients. The patients’ compliance was evaluated as very good for 87.07% of patients, good for 10.88% of patients and unsatisfactory for 2.04% of patients.

Conclusion: Fixed combination of lisinopril and hydrochlorothiazide is efficient and well tolerable with very good compliance of patients.

Keywords: Lisinopril, hydrochlorothiazide, fixed combination, efficiency, compliance

© 2018 Folia Medica Facultatis Medicinae Universitatis Saravienstis. All rights reserved.

Introduction

Cardiovascular diseases represent the leading cause of death in Bosnia and Herzegovina. According to the report of the Institute of Public Health, cardiovascular diseases comprised 51.90% of all death causes. Among the leading five death causes are also stroke, acute myocardial arrest and hypertension. Cardiovascular diseases ranked this high in the total mortality may be connected with a high prevalence of risk factors and a high percentage of chronic diseases in medical conditions of the populace. (1)

Hypertension, in addition to being one of the leading death causes (among the top 5) is also a very important factor of incurrence of other cardiovascular diseases. Hypertension is defined as the presence of increased blood pressure at the level in which the patient is exposed to an increased risk from damage in vital or organs in several vascular areas, including the retina, the brain, the heart, kidneys as well as major blood vessels. Precisely, hypertension is defined by the values of the blood pressure of over 140/90 mmHg. (2)

According to the report of the Federal Ministry of Health, based on the study on health of the adult population, it was discovered that 42.10% of adults have blood pressure levels over 140/90 mmHg or are already on antihypertensive treatment, which makes hypertension the most common chronic disease. (3)

The aim of treating hypertension is to achieve the aimed blood pressure result of <140/90 mmHg for all hypertonic patients, and the aimed blood pressure values of <130/80 mmHg for hypertonic patients with diabetes mellitus. (4)

Several medical studies have proven that strict control over the blood pressure ensures a maximal reduction of clinical cardiovascular results. The Framingham Heart Study has proven that the decrease in the dia-
systolic blood pressure by 2 mmHg results in decrease of the risk of stroke and of the transitory ischemia attack (TIA) by 14.00%, and on the decrease of the risk of developing a coronary arterial disease by 6.00%. (5) The meta-analysis of the nine great prospective observational studies demonstrated that the decrease of the diastolic blood pressure of 5 mmHg, 7.5 mmHg of 10 mmHg leads to the decrease of the risk of a stroke by 34.00%, 46.00% or 56.00%, and a decrease of the risk of developing a coronary arterial disease by 21.00%, 29.00% or 36.00%. (6)

The data indicates that an aggressive control over blood pressure ensures additional benefits. In some patients it may be achieved by using just one medicine, but in over 50.00% of patients it demands more than one medication to achieve a satisfactory control over the blood pressure. (4)

With a prescribed combination of antihypertensive medication, the aimed values of the blood pressure are achieved in almost 90.00% of treated patients. (7)

The fixed combination of lisinopril and hydrochlorothiazide has several benefits: a greater reduction of blood pressure attributed to the collective effect of active components, a greater percentage of the patients achieves aimed values of the blood pressure, a better organ-protective effect, a reduced frequency of unwanted effects, a lower price of treatment and better cooperation with the patients. (4, 8)

The primary aim of our study was to test the efficiency of the fixed combination of lisinopril and hydrochlorothiazide in treatment of essential hypertension and the secondary aim of the study was to test the tolerance towards the medication and compliance of patients throughout the study.

**Materials and methods**

An observational, nonintervention multicentric study was conducted in 19 centers in Bosnia and Herzegovina (Sarajevo, Zavidovići, Zenica, Visoko, Travnik, Jajce, Bužim, Velika Kladuša, Bihać, Cazin, Bosanska Krupa, Gračanica, Banovići, Orasje, Tuzla, Živinice, Livno, Posušje, Banja Luka). The study lasted from January to December 2015 and every patient was monitored in the time period of 12 weeks.

The study included 147 patients of both sexes diagnosed with essential hypertension who were already ordinated by antihypertensive therapy. The patients were monitored in the course of 12 weeks, one initial and four control examinations.

The first, initial examination included anamnesis of the disease, personal and family anamnesis of the patient, the clinical status, blood pressure, pulse measuring and an optional ECG mapping.

The criteria for including were a proven essential hypertension requiring a combined treatment with the ACE inhibitor and a diuretic in persons over 18. The criteria for non-inclusion were oversensitivity to active components of the medication, an angioneural edema in the anamnesis and additional clinical conditions that can affect the pharmacokinetics of lisinopril and hydrochlorothiazide. The criteria for excluding the patients from the study were aggravation of the basic disease, developing serious adverse effects requiring an interruption of the therapy and the development of the disease influencing the course of research.

The patients were previously under the treatment of lisinopril and failed to achieve a satisfactory control over the blood pressure or were already on the therapy with lisinopril and diuretic as a single-component medication. These patients were administered with a fixed combination of lisinopril and hydrochlorothiazide.

In this study we used drug Lopril H manufactured by Bosnalijek JSC, Bosnia and Herzegovina, in the form of tablets in two concentrations: 10 mg lisinopril and 12.5 mg hydrochlorothiazide and 20 mg lisinopril and 12.5 mg hydrochlorothiazide. After the initial examination, the patients were monitored throughout the four control examinations involving the blood pressure and pulse measuring and an optional ECG mapping. Based on the blood pressure values obtained, the dosage of the medication was adjusted.

The initial dosage of the medication was 10 mg of lisinopril combined with 12.5 mg hydrochlorothiazide, and the dosage was administered once a day. Due to the diuretic component, the recommendation was to administer the medication in the morning. If the control examination indicated a non-satisfactory control of the blood pressure values (<140/90 mmHg), the dosage was increased to 20 mg of lisinopril in a fixed combination with 12.5 mg of hydrochlorothiazide.

The blood pressure was measured twice with a mercury blood pressure gauge, after patient resting for 5-10 minutes. The average value of the two tests was taken for the blood pressure value.

During the last examination the values of the blood pressure and pulse were measured, and the doctors/examiners evaluated the efficiency of the treatment, the safety, the compliance of the patients and reported the potential adverse effects of the therapy.

The pulse was measured in the radial artery by counting the heartbeats during 15 seconds and the resulting number was multiplied by 4, resulting in the number of heartbeats in one minute.

The ECG was mapped with a standard 12-lead ECG machine and deviations from normal values were recorded.
The working hypothesis was that by administering a fixed combination of lisinopril hydrochlorothiazide there would occur a decrease in the blood pressure by 10-15 mmHg of the systolic blood pressure and by 5-10 mmHg of the diastolic blood pressure, i.e. we expect that the aimed blood pressure values (<140/90 mmHg) will be achieved by 55.00% of patients.

Testing was performed with a two-side test, with an alpha-value placed at the level of significance of 95.00% (α=0.05) and a statistic test power of 80.00% (β=0.20).

We are planning to implement the Chi square test for analyzing the differences in proportions after evaluating the influence of the therapy on controlling the blood pressure after 12 weeks of treatment (modifying the dosage of the medication) and monitoring.

**Results**

The study included 147 patients diagnosed with essential hypertension that required a combined treatment with lisinopril and hydrochlorothiazide. Of the total number, 71 (48.30%) were male patients, and 76 (51.70%) were female patients. The gender representation in the test sample was equal.

In the course of research, the participants were sepa-

---

**Table 1. Patient characteristics**

<table>
<thead>
<tr>
<th></th>
<th>M</th>
<th>F</th>
<th>M</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>71</td>
<td>76</td>
<td>48.3%</td>
<td>51.7%</td>
</tr>
<tr>
<td>Age groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-59</td>
<td>56</td>
<td>51</td>
<td>38.1%</td>
<td>34.0%</td>
</tr>
<tr>
<td>60+</td>
<td>91</td>
<td>95</td>
<td>61.9%</td>
<td>66.0%</td>
</tr>
<tr>
<td>Duration of hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>5 years</td>
<td>5 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>6 months</td>
<td>6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>25 years</td>
<td>25 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>83</td>
<td>64</td>
<td>56.5%</td>
<td>43.5%</td>
</tr>
<tr>
<td>No</td>
<td>64</td>
<td>64</td>
<td>43.5%</td>
<td>56.5%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>27</td>
<td>120</td>
<td>18.4%</td>
<td>81.6%</td>
</tr>
<tr>
<td>No</td>
<td>64</td>
<td>93</td>
<td>43.5%</td>
<td>56.5%</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16</td>
<td>12</td>
<td>10.9%</td>
<td>9.3%</td>
</tr>
<tr>
<td>No</td>
<td>55</td>
<td>54</td>
<td>37.4%</td>
<td>34.7%</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>55</td>
<td>55</td>
<td>37.4%</td>
<td>37.4%</td>
</tr>
<tr>
<td>No</td>
<td>92</td>
<td>91</td>
<td>62.6%</td>
<td>62.6%</td>
</tr>
<tr>
<td>Previous ACE inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>treatment</td>
<td>Yes</td>
<td>113</td>
<td>76.9%</td>
<td>23.1%</td>
</tr>
<tr>
<td>No</td>
<td>34</td>
<td>34</td>
<td>23.1%</td>
<td>76.9%</td>
</tr>
<tr>
<td>Previous thiazide</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diuretic treatment</td>
<td>Yes</td>
<td>41</td>
<td>27.9%</td>
<td>72.1%</td>
</tr>
<tr>
<td>No</td>
<td>106</td>
<td>106</td>
<td>72.1%</td>
<td>27.9%</td>
</tr>
<tr>
<td>BMI (Body Mass Index)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.5-24.</td>
<td>38</td>
<td>38</td>
<td>25.9%</td>
<td>25.9%</td>
</tr>
<tr>
<td>BMI 25-29.9</td>
<td>88</td>
<td>88</td>
<td>59.9%</td>
<td>59.9%</td>
</tr>
<tr>
<td>&gt;30</td>
<td>21</td>
<td>21</td>
<td>14.3%</td>
<td>14.3%</td>
</tr>
</tbody>
</table>

**Figure 1: Systolic blood pressure values prior to treatment and during the treatment with a fixed combination of Lisinopril-hydrochlorothiazide in both test groups**
rated into two groups. The first group consisted of patients aged 30 to 59, i.e. 56 (38.10%) patients. The second group consisted of patients aged 60 and over, i.e. 91 (61.90%) patients.

In our study, of the total number of patients, 113 of them (76.90%) were previously administered with an ACE inhibitor treatment, while 34 (23.10%) patients had not taken the ACE inhibitor treatment previously. The previous therapy with thiazide diuretic was taken by a smaller number of patients, approximately 41 (27.90%) patients, and a higher percent of patients, approximately 106 (72.10%) patients had never taken thiazide diuretic during their treatment. An average duration of hypertension with patients in our country was 5 years, i.e. minimally 6 months, and maximally 25 years.

A detailed overview of the characteristics of the test group of patients was stated in Table 1.

Figure 1 demonstrates the average values of the systolic blood pressure in both groups prior to administering the treatment and with treatment. In the group of younger participants, the pressure, prior to administering the treatment amounted to 160 mmHg on average, i.e. in the interval of 157-177 mmHg, and with the usage of a fixed combination of Lisinopril-hydrochlorothiazide the systolic blood pressure decreased to the average 130 mmHg i.e. to the interval 127-137 mmHg. With older participants the systolic blood pressure prior to using the fixed combination of Lisinopril-hydrochlorothiazide amounted to 160 mmHg on average, i.e. in the interval 150-177 mmHg while after administering the fixed combination of Lisinopril-hydrochlorothiazide the systolic blood pressure decreased to 130 mmHg on average, i.e. in the interval 130-140 mmHg.

The difference in the value of the systolic blood pressure before and during the treatment is statistically significant (p=0.0001), so it can be concluded that the fixed combination of Lisinopril-hydrochlorothiazide is efficient in lowering the increased systolic blood pressure.

Figure 2 demonstrates the average values of the diastolic blood pressure in both groups prior to administering the treatment and with treatment. In the group of younger participants, the pressure, prior to administering the treatment amounted to 160 mmHg on average, i.e. in the interval of 157-177 mmHg, and with the usage of a fixed combination of Lisinopril-hydrochlorothiazide the diastolic blood pressure decreased to the average 80 mmHg i.e. to the interval 80-85 mmHg.

Figure 2: Diastolic blood pressure values prior to treatment and during the treatment with a fixed combination of Lisinopril-hydrochlorothiazide in both test groups
With older participants the systolic blood pressure prior to using the fixed combination of Lisinopril-hydrochlorothiazide amounted to 95 mmHg on average, i.e. in the interval 90-100 mmHg while after administering the fixed combination of Lisinopril-hydrochlorothiazide the diastolic blood pressure decreased to 80 mmHg on average, i.e. in the interval 80-85 mmHg.

The difference in the value of the diastolic blood pressure before and during the treatment is statistically significant (p=0.0001), so it can be concluded that the fixed combination of Lisinopril-hydrochlorothiazide is efficient in lowering the increased diastolic blood pressure.

Figure 3 demonstrates the average values of the differences in the systolic blood pressure between the first and the end measuring, i.e. the average therapy effect (drop) in the systolic pressure in both groups. With younger participants the systolic pressure decreased to the average 31 mmHg i.e. to the interval 23-42 mmHg.

With older participants the systolic blood pressure decreased to 30 mmHg on average, i.e. in the interval 20-42 mmHg.

The differences in the drop of blood pressure are not statistically significant (p=0.312), i.e. there is no statistically significant difference between the efficiency of the fixed combination of Lisinopril-hydrochlorothiazide with older and younger patients.

Figure 4 demonstrates the average values of the differences in the diastolic blood pressure between the first and the end measuring, i.e. the average therapy effect (drop) in the diastolic pressure in both groups. With younger participants the systolic pressure decreased to the average 15 mmHg i.e. to the interval 10-20 mmHg.

With older participants the diastolic blood pressure decreased to 10 mmHg on average, i.e. in the interval 15-20 mmHg.

The differences in the drop of blood pressure are not statistically significant (p=0.081), i.e. there is no statistically significant difference between the efficiency of the fixed combination of Lisinopril-hydrochlorothiazide with older and younger patients.

In conclusion we can state that the fixed combination of Lisinopril-hydrochlorothiazide efficiently lowers the systolic and diastolic blood pressure in older and younger patients equally, i.e. there is no statistically significant difference in efficiency between the group of younger and older patients. The fixed combination of Lisinopril-hydrochlorothiazide is equally efficient in both tested groups of patients.

Figure 5 presents collectively the efficiency of the treatment, patients’ compliance during the treatment and evaluation of tolerance. The efficiency and compliance of the patients were evaluated by the researchers (doctors) and the tolerance were evaluated by the patients (subjective evaluation).

With 82.31% of patients the treatment was evaluated by very good, which, according to criteria meant that 82.31% of patients achieved the aimed blood pressure values, i.e. the pressure values of under 140/90 mmHg.
With 17.69% of patients the therapy was evaluated as good, which means that with 17.69% of patients the blood pressure was decreased by ≥10 mmHg but no aimed blood pressure values were reached.

With 87.07% of patients the researchers evaluated the patients’ compliance as very good, in 10.88% of patients as good, and with 2.04% of patients as dissatisfactory.

The tolerance towards the therapy was evaluated by the patients. 93.88% of patients evaluated the tolerance as very good, 6.12% of patients as good, and no patients evaluated the tolerance as dissatisfactory.

**Discussion**

In the conducted study, the administration of the fixed combination of lisinopril and hydrochlorothiazide in patients with hypertension was proven to be an efficient treatment in both test groups of the patients.

The stated combination in the group of patients aged 30 to 59 resulted in a decrease of the systolic pressure value for an average of 31 mmHg and the diastolic blood pressure for an average of 15 mmHg.

In the group of patients over 60, a fixed combination of Lisinopril-hydrochlorothiazide resulted in a decrease in value of the systolic blood pressure for an average of 30 mmHg and diastolic blood pressure for an average of 10 mmHg. There was no statistically significant difference between the efficiency of the stated combination in the group of younger patients in reference to the group of older patients, so we can conclude that it is equally efficient in both test groups.

Patients’ consent is one of the important factors that influence the efficiency of the treatment. Consent is often associated to the notions of compliance and adherence. Compliance is the ability of the patient to follow the instructions of a health worker. Adherence is a measure to which the behavior of the patient matches the recommendations of the person prescribing the medication. Adherence is in the actual sense of the word the partnership between the patient and the prescriber in the perspective of proper administration of the medication or medications. Adherence is particularly important in treatment of chronic diseases in which a medication is taken in long-term and most often for life. The results of the previous research indicate to a 50% adherence in patients with chronic diseases, meaning that the recommendation by the doctor in the terms of taking the medications is followed by only 50% of patients suffering from a chronic disease. (9)

One of the reasons for low adherence may be the factors originating from the medication itself, such as a complicated dosage regime, unpleasant flavor of the medication, adverse effects of the medication, etc.

With patients who take more medications, a better compliance can be achieved by implementing fixed combination of medications, i.e. taking two or three active components in one tablet. Fixed combinations of antihypertensive medications are increasingly used in treating patients with hypertension with whom the aimed values of blood pressure are not achieved by administering a single-component medication in a maximal dosage.

A fixed combination of antihypertensive medications simplifies the treatment and improves compliance of the patients. Fixed combinations enable a more simple dosage and the patients accept them better. The oscillation process to an optimal effect is simplified, which contributes to a better following of the instructions on taking the medication (adherence) and a greater efficiency of the treatment. (10)

In combining the medication, it is recommended to use medications with different active mechanisms. The most often medication combinations are: angiotensin inhibitor of a converting enzyme (ACE inhibitors) and diuretics, the angiotensin I antagonists (AATII) and diuretics, combination of ACE inhibitor and calcium channel blockers, AATII and calcium channel blockers. The fixed combination of ACE inhibitors of lisinopril and diuretics of hydrochlorothiazide intended for treatment of hypertension in patients whose hypertension has been previously stabilized by applying individual components of the medication, in the same ratio.

The medication is also intended to the patients with an initially elevated blood pressure values, i.e. initial blood pressure values either equal to or exceeding 20 mmHg above aimed values for the systolic blood pressure, i.e. equal or higher than 10 mmHg above aimed values for the diastolic blood pressure. (4)

Lisinopril is the third generation of the ACE inhibitors (after captopril and enalapril) introduced in the treatment in the early nineties of the former century. (11)

Lisinopril inhibits the activity of angiotensin converting enzyme and the incurrence of the great vasoconstrictor angiotensin II. Acting on renin-angiotensin-aldosterone system, lisinopril decreases the exudation of aldosterone and thereby the retention of water and salt. The degradation of bradykinin additionally contributes to the vasodilatory action. Lisinopril expresses the following activities: it reduces the preload /afterload, the sympathetic stimulation and need for oxygen, the mass of the left ventricle, it positively affects the function of the endothelium, stabilizes the atherosclerotic plaque and acts antiatherogenically.

Hydrochlorothiazide is a diuretic, and expresses its antihypertensive acting by reducing the reabsorption of
electrolytes in a distal tubules of the kidney which increases diuresis, reduces the blood volume in the blood vessels and contributes to a decrease of the blood pressure.

In the prospective open multicentric clinical study that researched the efficiency of the fixed combination of Lisinopril-hydrochlorothiazide in reference to the regression of the hypertrophy of the left chamber in patients with essential hypertension, the administration of the stated combination resulted in the decrease of the value of the systolic blood pressure for an average of 33.22 mmHg and of the diastolic blood pressure for an average of 19.17 mmHg. The stated therapy resulted in a decrease of the systolic blood pressure value for an average of 20.56%, i.e. in the range from 15.36% to 26.57%, and a decrease in the blood pressure value for an average of 19.43% i.e. in the range from 15.66% to 22.28%. (12)

The efficiency of the fixed combination of lisinopril and hydrochlorothiazide was similar in the study we conducted.

In the stated study the fixed combination of lisinopril and hydrochlorothiazide resulted in a significant decrease in the mass of the left chamber in patients with essential hypertension and left chamber hypertrophy. The mass of the left chamber decreased on average for 4.18%, i.e. 3.93% in men and 4.37% in women. (10)

In our study there were no tests in reference to the effect of the fixed combination of lisinopril and hydrochlorothiazide on the mass of the left chamber.

The second study compared the efficiency of the fixed combination of lisinopril and hydrochlorothiazide and the fixed combination of candesartan and hydrochlorothiazide. The fixed combination of lisinopril and hydrochlorothiazide resulted in a decrease of the systolic blood pressure for an average of 18.4 mmHg and of the diastolic pressure for an average of 10.3 mmHg. A fixed combination of candesartan and hydrochlorothiazide resulted in the decrease of the systolic blood pressure for an average of 16.2 mmHg and of the diastolic pressure for 9.8 mmHg. There was no statistically significant difference in the reduction of the blood pressure between the two stated fixed combinations and it can be concluded that the fixed combination of lisinopril and hydrochlorothiazide is as equally efficient as the fixed combination of candesartan and hydrochlorothiazide. (7)

In a study that compared the efficiency of the fixed combination of amlodipine and valsartan and the fixed combination of lisinopril and hydrochlorothiazide there was no statistically significant difference in lowering the systolic and diastolic blood pressure between the two stated fixed combination. In reference to the percentage of the patients who reached the aimed blood pressure values there was also no statistically significant difference between the two tested fixed combinations. (13)

We can conclude that the fixed combination of lisinopril and hydrochlorothiazide is as equally efficient as the fixed combination of amlodipine and valsartan.

In order to achieve the treatment goals, the fixed combinations of two or more medications are increasingly being used in medical practice. Therapy guidelines for the treatment of hypertension, fixed combinations of anti hypertensive are recommended as the initial treatment in patients in the second or third degree of hypertension. The administration of fixed combinations of medications with different action mechanisms ensures a synergistic antihypertensive action and it decreases the risk of incurring adverse effects of every component. The fixed combination of lisinopril and hydrochlorothiazide ensures a significant reduction of blood pressure and is equally efficient as the fixed combination of calcium channel blockers and diuretics, the fixed combination of antagonist of angiotensin II and a diuretic and a fixed combination of beta blockers and diuretics. (14)

In the conducted study, the fixed combination of lisinopril and hydrochlorothiazide is efficient and safe, and easy to use which is proven by the high rate of compliance in patients. The acquired results resemble previously conducted studies.

In 82.31% of patients the aimed blood pressure values were achieved (≤140/90 mmHg) which is a significantly higher percentage than expected (expected in 55% of patients). In 17.69% of patients the blood pressure was decreased by ≥10 mmHg, but no aimed values were achieved.

The doctors evaluated the patients’ compliance as very good in 87.07% of patients, as good in 10.88% of patients and as dissatisfactory in 2.04% of patients. 93.88% of patients evaluated the treatment as very tolerable and 6.12% of patients as tolerable.

The main limitation of the study was the lack of division of patients according to the used dose in terms to determine which dose of analyzed fixed combination leads to blood pressure reduction. The limitation is the lack of insight of the influence of patients’ characteristics (hypertension, diabetes mellitus angina pectoris, smoking, BMI) in this study on blood pressure reduction.

**Conclusion**

Based on the results of the conducted observational, multicentric research of the efficiency of the fixed combination of lisinopril and hydrochlorothiazide in
treating the essential hypertension in duration of 12 weeks we conclude that the stated fixed combination is efficient, safe and very well tolerable.

The fixed combination of lisinopril and hydrochlorothiazide in the group of patients of a certain age resulted in a decrease of the systolic and diastolic blood pressure value for an average of 31/15 mmHg, and in the group of patients over 60 for an average of 30/10 mmHg. The fixed combination of lisinopril and hydrochlorothiazide was very well tolerable and the patients’ compliance was evaluated as very good.

ACKNOWLEDGEMENTS

The study was funded by Bosnalijek JSC. The sponsor support was restricted to the development of protocol, data collection, data analysis and medical writing.

CONFLICT OF INTEREST

Authors declare conflict of interest. Some of authors are employees of Bosnalijek JSC.

REFERENCES:


