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# HEART RATE AND ARTERIAL PRESSURE VARIABILITY INDICES IN PATIENTS WITH ARTERIAL HYPERTENSION IN GROUPS OF TREATMENT WITH BETA ADRENERGIC ANTAGONIST, INHIBITOR OF ANGIOTENSINCONVERTING ENZYME AND THEIR COMBINATIONS AND CLASSES OF ECG QRS COMPLEX DURATION

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Studied indicators of heart rate and arterial pressure variability (HRV, AP) in patients with arterial hypertension (AH) in treatment groups of beta -blocker (BB), inhibitors of angiotensinconverting enzyme (IACE) and their combination classes and duration of the QRS complex ECG ≤ 100 and > 100 ms. 138 patients with AH of the 1-2 degrees (60 men and 78 women) at the age of 57 ± 17 years old were examined. Registration and measurement of QRS complex duration and indices of HRV ECG were done on computer electrocardiograph conducted «Cardiolab+». In groups of thera-py classes of ECG QRS complex duration <100 ms and ≥100 ms were derived. Patients were treated with lisinopril in the average daily dose of 20 mg, bisoprolol − 5 mg. Patients were assessed before, after 2 weeks, 1, 6 and 12 months after of therapy. HRV was evaluated TP, VLF, LF, HF, SAP, DAP in groups of IACE, BB and IACE + BB and classes QRS ECG. The data were processed with the help of Microsoft Excel program. In patients with AH in IACE group the best response of HRV indices ontherapy was indicated in the class of ECG QRS complex duration ≤ 100 ms and in group IACE+ BB− > 100 ms. In patients with AH of ECG QRS complex duration ≤ 100 ms in antihypertensive therapy IACE lizinopril is preferable with ECG QRS complex duration > 100 ms − combination of IACE lizinopril and BB bisoprolol.

**KEY WORDS:** ECG QRS complex duration, arterial hypertension, heart rate variability, inhibitors of angiotensinconverting enzyme, beta adrenergic antagonist

ПОКАЗНИКИ ВАРІАБЕЛЬНОСТІ СЕРЦЕВОГО РИТМУ І АРТЕРІАЛЬНОГО ТИСКУ У ПАЦІЄНТІВ З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ В ГРУПАХ ТЕРАПІЇ БЕТА-АДРЕНОБЛОКАТОРОМ, ІНГІБІТОРОМ АНГІОТЕНЗИНПЕРТВОРЮЮЧОГО ФЕРМЕНТУ І ЇХ КОМБІНАЦІЄЮ ТА КЛАСАХ ТРИВАЛОСТІ КОМПЛЕКСУ QRS EKГ

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Вивчено показники варіабельності серцевого ритму (ВСР) і артеріального тиску (АТ) у пацієнтів з АГ в групах терапії бета-адреноблокатором (ББ), інгібітором ангіотензинперетворюючого ферменту (ІАПФ) і їх комбінацією та класах тривалості комплексу QRS  $EK\Gamma \leq 100$  і > 100 мс. Обстежено 138 пацієнтів з АГ ( 60 чоловіків і 78 жінок) 1-2 ступеня і ІІ стадії АГ у віці (  $50 \pm 17$  ) років. Реєстрація комплексу QRS проводилася на комп'ютерному електрокардіографі « Cardiolab + ». Виділено класи тривалості комплексу QRS  $EK\Gamma \leq \tau a > 100$  мс. Пацієнти отримували лізиноприл у середній добовій дозі 20 мг, бісопролол – 5 мг . Пацієнтів обстежували до, через 2 тижні, 1 , 6 і 12 місяців від початку терапії. Оцінювали ТР ВСР, VLF, LF, HF, CAT, ДАТ у групах ІАПФ, ББ і ІАПФ + ББ та класах QRS  $EK\Gamma$ . Для оцінки результатів використовували методи параметричної статистики. У пацієнтів з АГ в групі ІАПФ краща відповідь показників ВСР на терапію спостерігалася в класі тривалості комплексу QRS  $EK\Gamma \leq 100$  мс, а в групі ІАПФ + ББ - > 100 мс. У пацієнтів з АГ в класі тривалості комплексу QRS  $EK\Gamma \leq 100$  мс серед антигіпертензивної терапії треба віддавати ІАПФ лізиноприлу, а в класі тривалості комплексу QRS  $EK\Gamma \leq 100$  мс - комбінації ІАПФ лізиноприлу і ББ бісопрололу.

*КЛЮЧОВІ СЛОВА*: тривалість комплексу QRS ЕКГ, артеріальна гіпертензія, варіабельність серцевого ритму, інгібітори ангіотензинперетворюючого ферменту, бета адренергічні антагоністи

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ПОКАЗАТЕЛИ ВАРИАБЕЛЬНОСТИ СЕРДЕЧНОГО РИТМА И АРТЕРИАЛЬНОГО ДАВЛЕНИЯ У ПАЦИЕНТОВ С АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ В ГРУППАХ ТЕРАПИИ БЕТА-АДРЕНОБЛОКАТОРОМ, ИНГИБИТОРОМ АНГИОТЕНЗИНПРЕВРАЩАЮШЕГО ФЕРМЕНТА И ИХ КОМБИНАЦИЕЙ И КЛАССАХ ПРОДОЛЖИТЕЛЬНОСТИ КОМПЛЕКСА ORS ЭКГ

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Изучены показатели вариабельности сердечного ритма (ВСР) и артериального давления (АД) у пациентов с АГ в группах терапии бета-адреноблокатором (ББ), ингибитором ангиотензинпревращающего фермента (ИАПФ) и их комбинацией и классах продолжительности комплекса QRS 3KГ  $\leq 100$  и > 100 мс. Обследовано 138 пациентов с АГ (60 мужчин и 78 женщин) 1-2 степени и II стадии АГ в возрасте ( $50 \pm 17$ ) лет. Регистрация комплекса QRS проводилась на компьютерном электрокардиографе «Cardiolab+». Выделены класся продолжительности комплекса QRS 3KГ:  $\leq 100$  мс и > 100 мс. Пациенты получали лизиноприл в средней суточной дозе 20 мг, бисопролол -5 мг. Пациентов обследовали до, спустя 2 недели, 1, 6 и 12 месяцев от начала терапии. Оценивали 1P BCP, VLF, LF, HF, САД, ДАД в группах ИАПФ, ББ и ИАПФ+ББ и классах QRS 1KГ. Для оценки результатов использовались методы параметрической статистики. У пациентов с АГ в группе ИАПФ лучший ответ показателей BCP на терапию наблюдался в классе продолжительности комплекса QRS 1KГ 100 мс и в группе ИАПФ+ 100 мс. У пациентов с АГ с продолжительностью комплекса QRS 1KГ 100 мс в антигипертензивной терапии преимуществами обладает ИАПФ лизиноприл и с продолжительностью комплекса QRS 1KГ 100 мс в комбинация ИАПФ лизиноприла и 1ББ бисопролола.

**КЛЮЧЕВЫЕ СЛОВА:** продолжительность комплекса QRS ЭКГ, артериальная гипертензия, вариабельность сердечного ритма, ингибиторы ангиотензинпревращающего фермента, бета адренергические антагонисты

Arterial hypertension (AH) prevalence according to the data of Ukrainian Medical Statistics Centre grew more than twice since 1998 to 2011 [1], which needs further improvement of prophylaxis and treatment measures.

In prescription rated in 2010 first place in AH monotherapy belonged to inhibitors of angiotensinconverting enzyme (IACE), second – to beta adrenergic antagonist (BB) and third – to these preparations combined therapy after IACE with diuretic and BB with diuretic, demonstrating significant positive dynamics comparing with 2000.

Pharmacological effects of IACE and BB are realized due to pharmacological control of renin-anhiotensine (RAS) and adrenergic systems activity connected with ECG QRS complex duration changes [2-4].

According to the data of Freminghem study ECG QRS complex elongation in patients with AH takes place in proportion to mass, walls thickness and finally-diastolic size of left ventricle (LV) increase [5-7]. ECG QRS complex duration > 120 msec is the indication to cardioresynchronizing therapy defined considering low pharmaceutical intrusion effectiveness connected with it [8, 9].

No research of heart rate variability (HRV) and arterial pressure (AP) indices were carried out in patients with AH in groups of BB, IACE and their combination therapy and classes of ECG QRS complex duration.

The research was done within the framework of scientific-research work «Elaboration and research of automatic control system of heart rate variability», state registration number 0109U000622.

## **OBJECTIVE AND METHODS**

138 patients with AH of the 1-2 degrees (60 men and 78 women) at the age of  $57 \pm 17$  years old were examined on the basis of city polyclinics N = 6 of Moscow and city polyclinics N = 24 of Kiev regions. Averaged duration of AH at the moment of examination was  $7 \pm 5$  years. Mild AH was found in 44 patients, medium AH – in 94 patients.

Diagnosis of AH was stated according to the recommendations of the Working group on AH of Ukrainian cardiologists association (2009, 2013) [10].

Concomitant chronic ischemic heart disease (CIHD) was found in 42, sugar diabetes of the 2-nd type – in 6, ulcer of the stomach – in 12, osteoarthrosis – in 14 patients. Heart failure

(HF) of the I-st stage was in 45, of the IIA stage - in 60. FC HF (according to NYHA criteria) in 25 patients was I, in 20 - II, in 60 - III.

Patients with stable stenocardia of tension, acute coronary syndrome, HF of IIB-IV FC, AH of the I-st and III-rd stages, 3 -rd degree, ECG QRS complex duration > 120 ms, secondary arterial hypertension were not included into the study.

Limitations by ECG complex > 120 ms duration are connected with a possibility of medical beyond cardiosynchronizing therapy.

Systolic and diastolic arterial pressure (SAP and DAP) in orthostasis and clinostasis were measured by Korotkov method using tonometer Microlife BP AG1-20 on shoulder, where they were higher. Patients did not use the food products, influencing the measured parameters (strong tea, alcohol, medical preparations, etc.) the day before examination.

Registration and measurement of QRS complex duration and indices of HRV ECG were done on computer electrocardiograph «Cardiolab+» during orthostasis clinostasis. Complex QRS duration on ECG was measured in leads II, V<sub>I</sub>, V<sub>5</sub>, V<sub>6</sub> (three consecutive complexes) with the choice of maximal values for leads registered complexes. Registration of HRV was done in orthostasis and clinostasis in 7 min intervals. General volume of spectrum (TP) was defined, volume of very low (VLF), low (LF) and high (HF) frequencies with calculation of LF/HF frequencies proportion as measures simpatho-vagal balance on internal temporal 5 min interval.

In allocated classes of ECG QRS complex duration patients were divided into therapy groups, consequently, of IACE, BB and IACE+BB therapy. Therapy was done in accordance with the recommendations of the working group on AHof Ukrainian cardiologists association (2009, 2013) [10]. Lizinopril was used in ICAE group with average daily doze 20 mg (minimal daily doze comprised 10 mg, maximal - 40 mg), BB bisoprolol in average daily doze 7,5 mg (minimal daily doze comprised 5 mg, maximal - 10 mg), IACE+ BB - lizinopril and bisoprolol in average daily dozes 20 mg and 5 mg, consequently (minimal daily doze comprised 10 mg and 2,5 mg, consequently, maximal - 40 mg and 10 mg, consequently). Depending on detected syndromes stains,

antithrombotic preparations (acetylsalicylic acid) were prescribes if necessary.

In groups of therapy classes of ECG QRS complex duration < 100 ms and  $\ge 100$  ms were derived [5, 11]. Patients with QRS complex < 60 ms were absent.

Patients in which target AH was not achieved by lizonopril, bisoprolol therapy or their combination, with concomitant reactions on ICAE and/or BB in history of disease or developed during the therapy coursed were excluded from the research and converted to hypotensive preparations of other groups or their combinations.

Patients were examined up to one month, 6 and 12 months in allocated groups of therapy and classes of ECG QRS complex.

The data were processed with the help of Microsoft Excel program. Parametrical criteria were used for statistical estimation of the results (average meaning – M, standard deviation – sd). The significance of differences between the groups and classes of the patients was defined for parametrical criteria with the help of Student t-criterion, for non-parametrical – Mann-Whitney criterion. The data were accepted significant at p < 0,05 and p < 0,01 levels of significance.

# RESULTS AND DISCUSSION

Indices of HRV and AP in control groups and AH group in clinostasis and orthostasis of the class of ECG QRS complex duration before and during lizinopril and bisoprolol therapy and their combination were presented in tables 1-3, consequently.

High HRV TP was observed before the therapy in control groups and AH group in the class of ECG QRS complex duration  $\leq 100$  ms (p < 0,05). In transition from clinostasis to orthostasis decrease of TP in both groups tool place which was more prominent in control group and the class of QRS duration  $\leq 100$  ms — 10 % and 13 %, consequently, against 8 % in the class > 100 ms. In both classes of ECG QRS complex duration low TP prevailed (70 % in class  $\leq 100$  ms and 75 % in class > 100 ms). The transition to orthostasis was not accompanied by the change of percentage correlation of TP levels in both classes of ECG QRS duration.

VLF and LF before the therapy in AH group in both classes of ECG QRS duration were lower in comparison with control group. High indices of VLF and LF were observed in

the class of ECG QRS duration > 100 ms. In transition from clinostasis to orthostasis decrease of VLF was detected in both classes of ECG QRS complex duration (6 and 4 % in classes of QRS duration  $\le$  and >100 ms, consequently) and its increase in control group (5 %), LF lowering in control groups (3 %) and AH group of both classes of ECG QRS complex duration (in class of ECG QRS  $\le$  100 ms - 5 %, and  $\ge$  100 ms - 6 %).

In AH group HF was decreased in comparison with control group before the beginning of the therapy. Higher HF in AH group was observed in the class of ECG QRS complex duration  $\leq 100$  ms. The transition into orthostasis was accompanied by HF decrease more prominent in control group (54 %) in comparison with the classes of ECG QRS

complex duration QRS  $\Im K\Gamma \le$  and > 100 ms (16 % and 12 %, consequently).

The relation of LF/HF to the therapy in control group was within the limits of normal range in both classes of QRS complex duration but elevated with increase in orthostasis transition - 4 % and 6 % in classes  $\leq$  and > 100 ms, consequently.

Higher levels of both SAP and DAP were in the AH group (p < 0,05) in comparison with control group, 27 % for SAP and 35 % for DAP in 12 % and 18 % in the classes of ECG QRS complex duration, consequently. Positive growth of SAP and DAP in control groups and AH group was initially detected under transition from clinostasis to orthostasis more prominent in AH group for SAP but not more than 20 % from initial indices.

Table 1

Indices of BCP and AP in control groups and AH group before therapy in classes of ECG QRS in clinostasis and orthostasis (M±sd, ms)

| Groups  |                  | Position    |                  | HRV                    |                         |                     |                     |                  | SAP, mm         | DAP,              |
|---------|------------------|-------------|------------------|------------------------|-------------------------|---------------------|---------------------|------------------|-----------------|-------------------|
|         |                  |             |                  | AD,<br>ms <sup>2</sup> | VLF,<br>ms <sup>2</sup> | LF, ms <sup>2</sup> | HF, ms <sup>2</sup> | LF/HF, limitless | Hg              | mm Hg             |
| Control |                  | clinostasis |                  | 2477□<br>1807*         | 994□<br>562             | 927□<br>613         | 529□<br>412**       | 1,75□<br>1,62    | 122 ±<br>12**   | 75 ±<br>9**       |
|         |                  | orthostasis |                  | 2229*<br>□1323         | 1044□<br>742            | 899□<br>747         | 243 □<br>207        | 3,73□<br>2,74    | 130 (7%) ± 9**  | 79 (5%) ±<br>8**  |
| AH      | ECG QRS complex, | ≤<br>100    | Clino-<br>stasis | 1100 ±<br>890*         | 491 ±<br>197            | 445 ± 167           | 172 ± 15*           | 2,6 ± 1,3        | 146 ±<br>15*    | 84 ± 12*          |
|         |                  |             | Ortho-<br>stasis | 957 ± 439              | 462 ± 146               | 423 ± 316           | 144 ±<br>10*        | 2,7 ± 1,9        | 157 (7 %) ± 10* | 92 (7%) ± 19*     |
|         |                  |             | Clino-<br>stasis | 871 ±<br>611*          | 741 ± 305               | 532 ± 270           | 169 ±<br>15**       | 3,1 ± 2,3        | 165 ± 15**      | 88 ± 12**         |
|         |                  | 0           | Ortho-<br>stasis | 801 ± 383*             | 711 ± 357               | 500 ± 220           | 149 ±<br>18**       | 2,8 ± 1,6        | 174(5 %) ± 18** | 96 (9%) ±<br>16** |

Comment:

Lowering of AD in IACE group was observed in 2 weeks of therapy in both groups of the classes of ECG QRS complex duration (11 % and 17 % in the classes ≤ 100 ms and > 100 ms, consequently) and its growth in other groups of therapy and classes of duration (p < 0,05). Further in 1, 6 and 12 months growth of AD was revealed in all groups in both classes of complex duration. In 12 months AD prevailed the initial meanings in 25 %, 21 %

and 18 % in IACE, BB and IACE +BB groups, consequently, in class  $\leq$  100 ms and in 17 %, 27 % and 31 % in IACE, BB and IACE +BB groups, consequently, in class > 100 ms, approaching to moderate meanings in both classes of complex duration. In the class of ECG QRS complex duration  $\leq$  100 ms high and moderate AD increased in 5 %, low one decreased in 10 %, critically low AD were absent. In the class of ECG QRS duration >

<sup>\*</sup> p < 0,05, \*\* p < 0,01 in current indices between subgroups on the research stages;

<sup>#</sup> p < 0.05, # p < 0.01 between the meanings in subgroups on the research stages

100 ms high AD increased in 8 %, moderate — in 5 %, low one decreased in 8 %, critically low AD were absent. Thus redistribution of the

part of the patients from the class of low and critically low AD into the class of high and moderate AD took place.

Table 2
Indices of BCP, AP and HFR in AH group in 2 weeks and 1 month of lizinopril,
bisoprolol and their combinations therapy in classes of ECG QRS complex (M±sd, ms)

| Therapy stages / indices |                       | Class of ECG QRS complex duration, ms |                |                |               |               |               |  |  |
|--------------------------|-----------------------|---------------------------------------|----------------|----------------|---------------|---------------|---------------|--|--|
|                          |                       |                                       | ≤ 100          |                | >100          |               |               |  |  |
|                          |                       | L                                     | В              | L+B            | L             | В             | L+B           |  |  |
|                          | TP, ms <sup>2</sup>   | 979 ± 590                             | $1120 \pm 790$ | 1145 ± 690     | 722 ± 511*    | 981 ± 611*    | 1100 ± 711*   |  |  |
|                          | VLF, ms <sup>2</sup>  | 582 ± 297                             | 521 ± 145      | 595 ± 207      | $741 \pm 305$ | 749 ± 215     | 751 ± 332     |  |  |
| S                        | LF, ms <sup>2</sup>   | 545 ± 217                             | 555 ± 189      | 494 ± 204      | 573 ± 159     | $562 \pm 185$ | 612 ± 197     |  |  |
| 2 weeks                  | HF, ms <sup>2</sup>   | 256 ± 25*                             | 289 ± 21*      | 297 ± 19*      | 279 ± 17**    | 293 ± 21**    | 295 ± 19**    |  |  |
|                          | LF/HF, dimentionless. | $2,1 \pm 1,3$                         | $1,9 \pm 1,3$  | $1,7 \pm 1,3$  | 2,1 ± 2,3     | $1,9 \pm 2,3$ | $2,1 \pm 2,3$ |  |  |
|                          | SAP, mm HG            | 129 ± 13*                             | 132 ± 17*      | 131 ± 16*      | 148 ± 15**    | 152 ± 15**    | 143 ± 15**    |  |  |
|                          | DAP, mm Hg            | 88 ± 12*                              | 88 ± 12*       | 86 ± 12*       | 87 ± 12       | 89 ± 12       | 80 ± 12       |  |  |
|                          | TP, ms <sup>2</sup>   | $1080 \pm 481$                        | 1144 ± 679     | $1259 \pm 591$ | 821 ± 511*    | 981 ± 611*    | 1100 ± 711*   |  |  |
| 1 month                  | VLF, ms <sup>2</sup>  | $611 \pm 297$                         | 521 ± 145      | $595 \pm 207$  | $772 \pm 299$ | $749 \pm 215$ | $785 \pm 305$ |  |  |
|                          | LF, ms <sup>2</sup>   | $558 \pm 217$                         | $562 \pm 189$  | 534 ± 114      | 586 ± 149     | 579 ± 185     | 637 ± 207     |  |  |
|                          | LF/HF, dimentionless. | $1,9 \pm 1,3$                         | 1,9 ± 1,3      | 1,9 ± 1,3      | $2,0 \pm 2,3$ | $2,1 \pm 2,3$ | $2,0 \pm 2,3$ |  |  |
|                          | SAP, mm Hg            | 138 ± 13*                             | 143 ± 17*      | 139 ± 16*      | 139 ± 15**    | 141 ± 15**    | 137 ± 15**    |  |  |
|                          | DAP, mm Hg            | 87 ± 12*                              | 88 ± 12*       | 86 ± 12*       | 86 ± 12       | 87 ± 12       | 81 ± 12       |  |  |

### Comment:

Growth of VLF and LF in all groups of therapy in both classes of QRS complex duration was observed in 2 weeks of the therapy. Further in 1, 6 and 12 months VLF and remained in all groups of the therapy in both classes of complex duration. In 12 months of the therapy VLF prevailed the initial indices in 14 %, 11 % and 15 % in IACE, BB and IACE +BB groups, consequently, in class ≤

100 ms and in 8 %, 10 % and 11 % in IACE, BB and IACE +BB groups, consequently, in class > 100 ms (p < 0,05). In 12 months of the therapy LF prevailed the initial indices in 9 %, 8 % and 12 % in IACE, BB and IACE +BB groups, consequently, in class  $\leq$  100 ms and in 10 %, 12 % and 11 % in IACE, BB and IACE +Bb groups, consequently, in class > 100 ms (p < 0,05).

<sup>\*</sup> p < 0.05, \*\* p < 0.01 in current indices between subgroups on the research stages;

<sup>#</sup> p < 0,05, ## p < 0,01 between the meanings in subgroups on the research stages;

L – lizinopril group of therapy,

B – bisoprolol group of therapy,

L + B - combination;

Table 3 Indices of BCP, AP and HFR in patients with AH in 6 and 12 months of lizinopril, bisoprolol and their combinations therapy in classes of QRS ECG complex (M±sd, ms)

| Stag           | ges of therapy /      | Class of ECG QRS complex duration, ms |                |                |               |               |               |  |  |
|----------------|-----------------------|---------------------------------------|----------------|----------------|---------------|---------------|---------------|--|--|
| indices        |                       |                                       | ≤ 100          |                | > 100         |               |               |  |  |
|                |                       | L                                     | В              | L+B            | L             | В             | L+B           |  |  |
|                | TP, ms <sup>2</sup>   | $1269 \pm 481$                        | $1318 \pm 679$ | $1231 \pm 591$ | 1011 ± 642*   | 1103 ± 561*   | 1134 ± 624*   |  |  |
|                | VLF, ms <sup>2</sup>  | $549 \pm 297$                         | 497 ± 145      | $511 \pm 207$  | $792 \pm 299$ | $795 \pm 215$ | $812 \pm 299$ |  |  |
| s <sub>q</sub> | LF, ms <sup>2</sup>   | $558 \pm 217$                         | $562 \pm 189$  | $534 \pm 114$  | $546 \pm 149$ | $551 \pm 185$ | $621 \pm 207$ |  |  |
| 6 months       | HF, ms <sup>2</sup>   | 181 ± 25*                             | 194 ± 21*      | 199 ± 19*      | 187 ± 17**    | 211 ± 21**    | 242 ± 19**    |  |  |
| 9              | LF/HF, dimensionless. | $1,7 \pm 1,3$                         | 1,9 ±1 ,3      | $1,8 \pm 1,3$  | $1,9 \pm 2,3$ | $2,0 \pm 2,3$ | $1,8 \pm 2,3$ |  |  |
|                | SAP, mm Hg            | 136 ± 13*                             | 140 ± 17*      | 138 ± 16*      | 139 ± 15**    | 140 ± 15**    | 137 ± 15**    |  |  |
|                | DAP, mm Hg            | 87 ± 12*                              | 88 ± 12*       | 86 ± 12*       | $86 \pm 12$   | 87 ± 12       | 81 ± 12       |  |  |
|                | TP, ms <sup>2</sup>   | 1375 ± 481*                           | 1331 ± 679*    | 1298 ± 591*    | 1019 ± 642*   | 1106 ± 561*   | 1141 ± 624*   |  |  |
|                | VLF, ms <sup>2</sup>  | 559 ± 297*                            | 545 ± 145      | $565 \pm 207$  | $800 \pm 299$ | $815 \pm 215$ | 823 ± 299*    |  |  |
| 12 months      | LF, ms <sup>2</sup>   | 485 ± 217**                           | 480 ± 189**    | 498 ± 114**    | 585 ± 149**   | 596 ± 185**   | 590 ± 207**   |  |  |
|                | LF/HF, dimensionless. | 1,7 ± 1,3*                            | 1,9 ± 1,3*     | 1,8 ± 1,3*     | $1,9 \pm 2,3$ | 1,8 ± 2,3*    | $1,8 \pm 2,3$ |  |  |
|                | SAP, mm Hg            | 128 ± 13*#                            | 131 ± 17*#     | 130 ± 16*#     | 139 ± 15**#   | 139 ± 15**#   | 136 ± 15**#   |  |  |
|                | DAP, mm Hg            | 88 ± 12*                              | 88 ± 12*       | 84 ± 12*       | 86 ± 12*      | 87 ± 12*      | 81 ± 12*      |  |  |

### Comment:

L – lizinopril group of therapy,

B – bisoprolol group of therapy,

L+B – combination

Growth of HF in all groups in both classes of ECG QRS complex duration was observed in 2 weeks, 1, 6 and 12 months of the therapy. In 12 months of the therapy HF prevailed the initial indices in 19 %, 18 % and 21 % in IACE, BB and IACE +BB groups, consequently, in class  $\leq$  100 ms and in 15 %, 14 % and 18 % in IACE, BB and IACE +BB groups, consequently, in class  $\rangle$  100 ms (p  $\langle$  0,01).

Lowering of LF/HF in all groups of the therapy was observed in 2 weeks of the therapy and in both classes of ECG QRS complex duration (19 %, 27 % and 35 % in IACE, BB and IACE +BB groups, consequently, in class  $\leq$  100 ms and in 4 %, 14 % and 4 % in IACE, BB and IACE +BB groups, consequently, in

class > 100 ms). Lowering of LF/HF to the meanings of control group in all groups of the therapy and classes of complex duration was revealed on the stages of the therapy (in 12 months of the therapy LF/HF decreased in comparison with initial indices in 4 %, 3 % and 4 % in IACE, BB and IACE +BB groups, consequently, in class  $\leq$  100 ms and in 4 %, 2% and 3% in IACE, BB and IACE +BB groups, consequently, in class  $\geq$  100 ms) (p < 0,05).

Decrease of AP in all groups of therapy and classes of ECG QRS complex duration were observed in 2 weeks of the therapy (for SAP in 11%, 9 % and in 10 % in IACE, BB and IACE +BB groups, consequently, in class  $\leq$  100 ms and in 11 %, 8 % and 13 % in IACE, BB and

<sup>\*</sup> p<0,05, \*\* p<0,01 in current indices between subgroups on the research stages;

<sup>#</sup> p < 0,05, ## p < 0,01 between the meanings in subgroups on the research stages; Note:

IACE +BB groups consequently in class > 100 ms) (p < 0,05). Further in 1, 6 and 12 months decrease of both SAP and DAP remained (in 12 months in 12 % for SAP, 10 % and 11 % in IACE, BB and IACE +BB groups consequently, in class  $\leq$  100 ms and in 16 %, 16 % and 17 % in IACE, BB and IACE +BB groups, consequently, in class > 100 ms) (p < 0,05).

Low level of AD, HF, big indices of VLF, LF and LF/HF and levels of SAP, DAP revealed in our work are typical for the patients with AH [12-14] and connected with the deprivation of humoral link of regulation and activation of symphatic system. Positive growth of AD, VLF, HF, decrease of LF, LF/HF, DAP and mostly SAP no matter classes of ECG QRS duration found in IACE, BB and IACE +BB groups of therapy in patients with AH correspond to the given ones [15-20].

The received lower meanings of HRV AD HF, LF/HF in patients with AH in the class of ECG QRS complex >100 ms and higher — LF, SAP, DAP, than in the class of ECG QRS  $\leq$  100 ms, are new. The best response and HRV AD growth during the therapy were typical for patients in IACE therapy group in the class  $\leq$  100 ms, and in IACE +BB group in the class  $\geq$  100 ms in comparison with the corresponding therapy groups and classes of ECG QRS. Optimal levels of AP were reached

in all groups of therapy and classes of complex duration with the best indices in IACE group in the class  $\leq 100$  ms, in IACE +BB group in the class > 100 mms in comparison with the corresponding therapy groups and classes of ECG QRS. They can be stipulated for initially more significant misbalance of sympathoparasympathetic regulation with corresponding electrophysiological changes of myocardium with big levels of SAP and DAP in patients in the class of ECG QRS >100 ms, which defined their stronger response on prolonged combined antihypertensive therapy with lizinopril and bisoprolol.

# **CONCLUSIONS**

- 1. In patients with AH in IACE group the best response of HRV indices on therapy was indicated in the class of ECG QRS complex duration  $\leq$  100ms and in group IACE+ B B-> 100 ms.
- 2. In patients with AH of ECG QRS complex duration ≤ 100 ms in antihypertensive therapy IACE lizinopril is preferable with ECG QRS complex duration >100 ms combination of IACE lizinopril and BB bisoprolol.

The study of the meaning of ECG QRS complex duration is perspective in the therapy of the patients with AH by antihypertensive preparations of other pharmacotherapeutic groups.

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