

COMPARISON OF LISINOPRIL AND BISOPROLOL INFLUENCES ON REGULATORY SYSTEMS OF THE ORGANISM IN BIOFEEDBACK SERIES IN HEALTHY VOLUNTEERS

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In 15 conditionally healthy volunteers aged from 18 to 22 years influence of Lisinopril and Bisoprolol on the biofeedback in the loop of paced breathing under control of heart rate variability parameters was compared. Every volunteer underwent 3 everyday biofeedback series with 5 session in each with a 5 months gap between the series, adding oral drugs application to the 2nd and 3rd series. During the 2nd series biofeedback sessions was conducted one hour after oral application of 2,5 mg Lisinopril. During the 3rd series biofeedback sessions was conducted one hour after oral application of 2,5 mg Bisoprolol. In used protocol, it was found that Bisoprolol promotes earlier and more substantial optimization of regulatory systems in comparison with Lisinopril.

KEY WORDS: biofeedback, paced breathing, HRV, regulatory systems, BQI, Lisinopril, Bisoprolol

ПОРІВНЯННЯ ВПЛИВУ ЛІЗИНОПРИЛУ І БІСОПРОЛОЛУ НА РЕГУЛЯТОРНІ СИСТЕМИ ОРГАНІЗМУ В БІОЛОГІЧНОМУ ЗВОРОТНОМУ ЗВ'ЯЗКУ У ЗДОРОВИХ ДОБРОВОЛЬЦІВ

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На 15 умовно здорових добровольцях від 18 до 22 років порівняли вплив лізиноприлу і бісопрололу на якість біологічного зворотного зв'язку (БЗЗ) в контурі метрономізованого дихання під контролем параметрів варіабельності серцевого ритму (ВСР). Кожному випробуваному провели по 3 серії щоденних сеансів БОС на протязі 5 днів з часовим інтервалом у 5 місяців між ними, доповнюючи 2-у та 3-ю серії пероральним прийомом препаратів. В 2-й серії сеанси проводили через час після перорального прийому лізиноприлу в дозі 2,5 мг, в 3-й серії – через час після перорального прийому бісопрололу в дозі 2,5 мг. В використаному протоколі бісопролол, в порівнянні з лізиноприлом, сприяє більш ранній та суттєвій оптимізації регуляторних систем.

КЛЮЧОВІ СЛОВА: біологічний зворотній зв'язок, метрономізоване дихання, ВСР, регуляторні системи, BQI, лізиноприл, бісопролол

СРАВНЕНИЕ ВЛИЯНИЙ ЛИЗИНОПРИЛА И БИСОПРОЛОЛА НА РЕГУЛЯТОРНЫЕ СИСТЕМЫ ОРГАНИЗМА В БИОЛОГИЧЕСКОЙ ОБРАТНОЙ СВЯЗИ У ЗДОРОВЫХ ДОБРОВОЛЬЦЕВ

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На 15 условно здоровых добровольцах в возрасте от 18 до 22 лет сравнили влияния лизиноприла и бисопролола на качество биологической обратной связи (БОС) в контуре метрономизированного дыхания под контролем параметров вариабельности сердечного ритма (ВСР). Каждому испытуемому провели по 3 серии ежедневных сеансов БОС в течении 5 дней с временным интервалом в 5 месяцев между ними, дополняя 2-ю и 3-ю серии пероральным приёмом препаратов. Во 2-й серии сеансы проводили через час после перорального приёма лизиноприла в дозе 2,5 мг, в 3-й серии – через час после перорального приёма бисопролола в дозе 2,5 мг. В использованном протоколе бисопролол, по сравнению с лизиноприлом, способствует более ранней и существенной оптимизации регуляторных систем.

КЛЮЧЕВЫЕ СЛОВА: биологическая обратная связь, метрономизированное дыхание, ВСР, регуляторные системы, BQI, лизиноприл, бисопролол

RESEARCH URGENCY

The function of circulatory system is under control of regulatory systems of the organism [1]. Distress, especially chronic, has an influence on pathological states development of circulatory system that overstrains regulatory systems and causes disbalance of regulation [2].

Lisinopril (angiotensin-converting enzyme (ACE) inhibitor) and Bisoprolol (beta-blocker) have a protective effect during distress through alteration of regulatory systems of the organism [3-5]. Lisinopril and Bisoprolol are widely adopted in cardiologists practice [4-5].

Lisinopril point of application is renin-angiotensin-aldosterone system (RAAS). Blocking angiotensin I to angiotensin II conversion, Lisinopril lowers not only angiotensin II level in blood, but aldosterone level as well, lowering arginine-vasopressin and endothelin-I formation that have, in particular, vasoconstriction effect [6-7]. Additional vasodilation effect is achieved through bradykinin level saving and endogenic prostaglandins level increasing [7]. Bisoprolol, blocking beta-1 adrenergic receptors of heart, provide inhibition of sympathetic part of vegetative nervous system and, in addition, lowers renin secretion [8-9].

One of perspective ways of investigation, estimation, status and subsequent intervention in regulatory systems with the purpose of restoration their balance in organism is biofeedback series in the loop of paced breathing under control of heart rate variability (HRV) parameters [10-12].

Earlier we showed that systematic biofeedback series in the algorithm of optimal frequency of paced breathing lookup starting from physiological norm and from free breathing in healthy volunteers [10-12] and patients with hypertension [13] optimize regulatory systems of the organism through restoration sympathovagal and neurohumoral balances of regulation with a long-term (up to 3 months) saving of the results [14].

Therefore, it is interesting to compare Lisinopril and Bisoprolol influences on alterations of regulatory systems of the organism in combination with biofeedback series in the loop of paced breathing under HRV parameters control on one contingent of volunteers.

The study is conducted as a part of research project of V.N. Karazin Kharkiv National

University «Development and Research of Automatic Control of Heart Rate Variability», registration No. 0109U000622.

RESEARCH OBJECTIVE

To compare Lisinopril and Bisoprolol influences on alterations of regulatory systems of the organism in combination with biofeedback series in the loop of paced breathing under HRV parameters control on one contingent of volunteers.

OBJECT AND METHODS OF THE RESEARCH

The study involved 15 conventionally healthy volunteers aged from 18 to 22 years (average age is $19,53 \pm 1,55$). Exclusion criteria: pernicious habits, medication taking last 3 months, heart rate less than 60 bpm at rest, blood pressure lower than 100/60 mmHg.

The study is conducted with computer diagnostic complex «CardioLab 2009» («KhAI-Medica») with special module «Biofeedback» that contains programmatically connected aural-visual breathing metronome and algorithm of HRV parameters estimation.

Biofeedback technology in the loop of paced breathing under HRV parameters control optimizes regulatory systems of the organism with a long-term (up to 3 months) saving of the results [14]. It gives an opportunity to evaluate influences of biofeedback both singly and in combination with Lisinopril and Bisoprolol on alterations of regulatory systems of the organism on one contingent of volunteers through conducting of 3 series of biofeedback sessions with a more than 3 months interval between series.

In compliance with research objective, volunteers were conducted 3 series of everyday biofeedback sessions in the loop of paced breathing under HRV parameters control for 5 days with a 5 months interval between them, adding to the 2nd and 3rd series oral intake of medications. Taking into account that experiment was conducted in healthy volunteers, Lisinopril and Bisoprolol was added to the 2nd and 3rd series of biofeedback sessions in minimal therapeutic dose. The sessions of the 2nd biofeedback series were conducted 1 hour after oral intake of 2,5 mg Lisinopril. The sessions of the 3rd biofeedback series were conducted 1 hour after oral intake of 2,5 mg of Bisoprolol.

HRV parameters were estimated in slide buffer for 1 minute through dynamic spectral HRV parameters were estimated in slide buffer for 1 minute through dynamic spectral decomposition by fast Fourier transform of R-R intervals sequence of lead I ECG records with 1000 Hz digitization frequency during 7-minute biofeedback session [11]. Powerfulness of low (V, up to 0,05 Hz), medium (L, 0,05-0,15 Hz) and high (H, 0,15-0,40 Hz) HRV parameters were estimated [12], then they were transformed into two-dimensional coordinate space with L/H and V/(L+H) axes, which correspond to powerfulness of sympathovagal and neurohumoral balances of regulation [15].

During biofeedback session, initialization of adaptation algorithm of biofeedback module was conducted in first 2 minutes, while volunteer breathe in his normal rhythm. After that for each following minute exact frequency of paced breathing was set through frequency rearrangement of aural-visual breathing metronome. Adaptation algorithm consists in automatic seeking of such frequency, when current L/H and V/ (L+H) values are maximally approximate to optimum zone [12].

Biofeedback quality estimation was based on optimality (O, estimation of farness of regulatory systems from optimal state during whole period of session), sensitivity (S, estimation of receptivity of regulatory systems to paced breathing), effectiveness (E, estimation of approaching range of HRV parameters to optimal physiological state during execution of optimal bioreverse control algorithm) parameters both for whole regulatory system (D) and its parts, and also on BQI integral index (parameter that reflects all qualitative changes of biofeedback process) [15]. Estimation of all values were carried out using PTC MathCad computer software.

Statistical analysis of the results for each subject was carried out using Microsoft Excel computer software. Average values (M) and standard deviation (sd) of O, S, E parameters for D, L/H, V/ (L+H) indicators of first and last records of each subject were put down in spreadsheet.

The differences reliability of each parameter between first and second sessions and in each session was determined by Wilcoxon signed-rank test.

RESULTS AND DISCUSSION

O, S, E parameters values for D, L/H, V/(L+H) indicators of 1st and 5th sessions of 1st, 2nd and 3rd biofeedback series in conventionally healthy volunteers are shown in the table. Systematic biofeedback series in the loop of paced breathing under HRV parameters control optimized regulatory systems state. Biofeedback series with Lisinopril and Bisoprolol application allowed optimization process accelerating of biofeedback parameters. Optimization in biofeedback series with Bisoprolol was more expressed than with Lisinopril.

BQI values alterations of 1st, 2nd and 3rd biofeedback series in every volunteer, that are shown on the picture, confirm earlier and more rapid optimization of regulatory systems with Lisinopril and Bisoprolol application with a more positive influence of Bisoprolol.

These results show optimization of regulatory systems of the organism by conducting systematic biofeedback series that proofs the literature data [10-16]. Founded more effective biofeedback influence on regulatory systems of the organism with a Bisoprolol application in comparison with Lisinopril should be explained by direct Bisoprolol influence on sympathetic part of vegetative regulation, whereas Lisinopril influence is mediated through number of mechanisms of humoral systems [6-9].

In compliance with derived results, biofeedback series with supplemented application of properly selected medication should be considered as important instrument of improvement of therapeutic measures effectiveness in clinical practice not only of cardiology but other fields of medicine as well.

CONCLUSIONS:

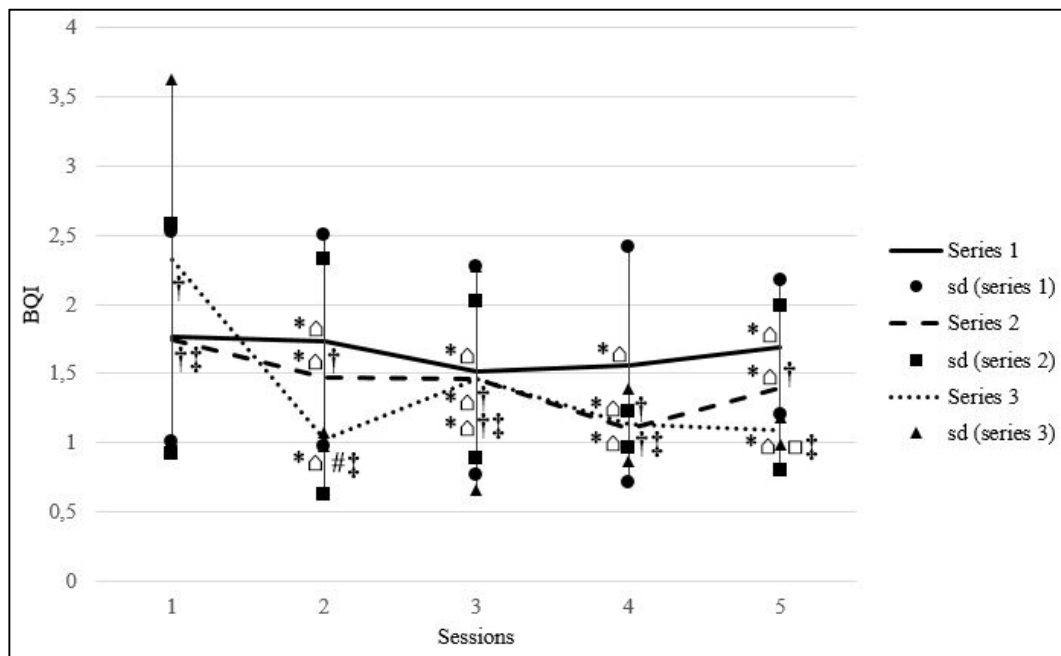
1. Systematic biofeedback sessions in the loop of paced breathing under HRV parameters control optimize regulatory systems state of the organism.
2. Biofeedback series with Lisinopril and Bisoprolol application allow achieving earlier and more rapid optimization of regulatory systems state.
3. In used protocol, it was found that Bisoprolol promotes earlier and more substantial optimization of regulatory systems in comparison with Lisinopril.

Table

O, S, E parameters values for D, L/H, V/(L+H) indicators of 1st and 5th sessions of 1st, 2nd and 3rd biofeedback series in healthy volunteers (M±sd)

Parameter		Series 1		Series 2		Series 3	
		Session 1	Session 5	Session 1	Session 5	Session 1	Session 5
D	O	-0,30 ± 4,84	-0,96 ± 2,74*	-0,71 ± 4,23†	-3,15 ± 6,10*†	-2,77 ± 4,13‡	-0,06 ± 1,88*†‡
	S	0,91 ± 0,26	0,94 ± 0,49*	1,10 ± 0,35†	1,00 ± 0,35*†	0,62 ± 0,27†Δ	0,83 ± 0,30*†‡
	E	0,27 ± 0,25	0,46 ± 0,16*	0,43 ± 0,31†	0,31 ± 0,32*†	0,32 ± 0,26†‡	0,05 ± 0,10*□‡
L/H	O	-8,84 ± 10,84	-3,78 ± 4,03*	-5,62 ± 6,10†	-50,57 ± 49,90*†	-9,17 ± 12,66†‡	-0,51 ± 2,10*†‡
	S	6,39 ± 1,04	7,93 ± 1,88○	6,68 ± 2,04†	5,09 ± 2,39○#	4,18 ± 1,43□Δ	5,43 ± 2,83*†‡
	E	0,99 ± 0,02	1,00 ± 0,00*	0,97 ± 0,05†	0,91 ± 0,13*#	0,95 ± 0,06#‡	0,75 ± 0,50*†‡
V/(L+H)	O	-1,43 ± 1,08	-1,34 ± 0,99*	-1,08 ± 1,25†	-0,80 ± 1,28*†	-4,21 ± 0,71□◇	-3,88 ± 1,65*#Δ
	S	1,44 ± 2,14	0,60 ± 0,31*	1,65 ± 2,31†	2,18 ± 2,63*†	0,40 ± 0,04†‡	0,23 ± 0,15○#
	E	0,37 ± 0,37	0,23 ± 0,16*	0,41 ± 0,33†	0,51 ± 0,39*†	0,07 ± 0,08†‡	0,07 ± 0,05*†Δ

Notes: - p > 0,05 on sessions against base values of one series;
 ○ - p < 0,05 on sessions against base values of one series;
 † - p > 0,05 on same session against base series;
 # - p < 0,05 on same session against base series;
 □ - p < 0,01 on same session against base series;
 ‡ - p > 0,05 on same session against adjacent series;
 Δ - p < 0,05 on same session against adjacent series;
 ◇ - p < 0,01 on same session against adjacent series.



Pic. BQI values alterations of 1st, 2nd and 3rd biofeedback series in every volunteer

Notes: * - p > 0,05 on sessions against base values of one series;
 △ - p > 0,05 on adjacent sessions of one series;
 † - p > 0,05 on same session against base series;
 # - p < 0,05 on same session against base series;
 □ - p < 0,01 on same session against base series;
 ‡ - p > 0,05 on same session against adjacent series.

Biofeedback series with supplemented application of properly selected medication should be considered as important instrument of improvement of therapeutic measures

effectiveness in clinical practice. It is interesting to study the influence of used biofeedback method in patients with different diseases of circulatory system.

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