# HEART RATE VARIABILITY IN THE PATIENTS WITH CORONARY ARTERY DISEASE DURING SESSION OF HYPERBARIC OXYGENATION THERAPY

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#### **SUMMARY**

Prior trials detected benefits from hyperbaric oxygenation therapy (HBOT) for patients with coronary artery diseases (CAD) and acute myocardial infarction. The aim of this study was to assess the changes in ANS in patients with CAD during session of HBOT by using the technique of HRV. The patients with CAD were subdivided into three groups in dependence of atmosphere pressure and contents of oxygen. We measured the total power (TP), low frequency component (LF) reflecting sympathetic and high frequency (HF) reflecting vagal activity, autonomic balance (LF/HF ratio) and LF and HF in normalized units (LFn, HFn). We observed significant increase under HBOT of TP, decreased LF/HF ratio because of changing in both branch of AHS and parasympathetic activity increased more significant than decreased sympathetic activity. In our point of view the changes in ANS depend of proportionally from oxygen tension in tissues coursed by HBOT. Our preliminary results showed that measurement of HRV is helpful in monitoring not only the circulation but also the common status of patients during the sessions of HBOT and it will be possible in the future to modulate the protocols of HBOT individually for certain patient. Increasing of vagal activity and total power with decreasing of sympathetic tone during of HBOT is the evidence of "relaxation" of circulation and ANS which less stressed by monitoring the body oxygenation. Adjunctive HBOT can improve prognosis in patients with CAD in various ways: the positive modifying of HRV is a sign of favorable changing in ANS; increasing of cardiac electrical stability; prevention of left ventricular dysfunction, progressing in Killip class and ventricular ectopic activity and presence of late potentials; restores of sinus nodal cells to neural modulations.

**KEY WORDS:** hyperbaric oxygenation therapy, coronary artery disease, heart rate variability, autonomic nervous system

#### INTRODUCTION

Hyperbaric oxygenation therapy (HBOT) is inhalation of pure oxygen at great then 1 atmosphere absolute pressure (abs). Prior trials detected benefits from HBOT for patients with coronary artery diseases (CAD) [5] and acute myocardial infarction [4]. HBOT increases plasma concentration of dissolved oxygen, and this effect may normalize or even increase oxygen tension to hyperoxic levels in ischemic tissue [2]. HBOT is a useful modality for treatment of diseases in which tissue oxygen availability is decreased. HBOT reduces the ischemic effects of coronary artery occlusion in animal and clinical studies [3]. But a little is known about the influence of HBOT on autonomic nervous system (ANS). The changes in ANS have a high relation with cardiac function and mortality [9, 10, 11, 13]. The heart rate variability (HRV) as the one of potential prognostic value of markers of autonomic activity has gained progressive popularity [6.7]. Now HRV is a proven tool for examining the ANS [12].

### **OBJECTIVES**

The aim of this study was to assess the changes in ANS in patients with CAD during

session of HBOT by using the technique of HRV.

#### **MATERIAL AND METHODS**

The study's patients received HBOT as adjunctive therapy of CAD and they were drawn from the Cardiology Department of Central Clinical Hospital N5, Kharkov. All patient were in sinus rhythm and had CAD (stable angina pectoris I–III class NYHA), none had history of diabetes mellitus or acute myocardial infarction and receiving usual treatment. They were 28 patient (15 men and 13 women) in mean age 52±10 year. The patients were subdivided into three groups.

The first group (9 patients) were pressurized in hyperbaric chamber in 100% oxygen atmosphere during 15-20 minute up to 1,5 abs and remained at this pressure for 40 minutes (it was isopression) and then depressurized during 15 minute period to normal atmosphere pressure. Total time of HBOT was 70 - 80 minutes. Every patient received 7-10 HBOT sessions in the same time every day.

The second group (8 patients) had the same protocol except pressure inside of chamber that remained on normal atmosphere level. These patients stayed in HBOT chamber under 1,0 abs in the atmosphere of 100% oxygen during 70 - 80

minutes. Every patient received 2 such oxygenation therapy sessions in the same time of the day.

The third group (11 patients) stayed in supine position like in HBOT chamber, but breathed usual atmosphere air (20,9% oxygen under 1,0 abs) during 70 - 80 minutes. Each patient had one investigation.

We used monoplace chamber "OKA-MT" with 1m³ volume inside. Monitoring of electrocardiogram (ECG), noninvasive blood pressure (before and after HBOT in supine position) was performed during HBOT sessions.

HRV was calculated in general agreement with the standards of measurement proposed by Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [1]. The HRV was recorded using computer based electrocardiograph system "Cardiolab 2000". In the first group HRV was recorded during sessions before HBOT, on the first minute of isopression under the 1,5 abs and on 40th minute under 1,5 abs. In the second group the HRV was recorded before HBOT, on 15 and 55 minutes of the sessions. In the third group the HRV was recorded on 6 minute after taking supine position and than on 15 and 55 minutes of the investigation. HRV was analyzed on 5-minute period of stable ECG recording for the frequency domain measures with the use of fast Fourier transform. We measured the total power (TP) of the R - Rinterval (0–0.5 Hz) as overall heart rate variability. The frequency ranges were subdivided into 0.03 - 0.15 Hz as a low frequency component (LF) reflect sympathetic and 0.15 - 0.5 Hz as a high frequency (HF) reflect vagal activity. TP, LF, HF was expressed in absolute values (ms<sup>2</sup>). We measured also the autonomic balance (LF/HF ratio) and LF and HF in normalized units (LFn, HFn respectively calculated as a percentage of TP of the R - R interval, from which the power of any component with a

frequency of less than 0.03 Hz was removed) [1]. The results are given as mean  $\pm$  standard deviation (SD). A p-value <0.05 was considered significant.

#### RESULTS

Table 1 shows the HRV measurement for the groups before and during investigation.

In the first group (HBOT) on the first minute under 1,5 abs we observed significant increase of TP by 99,3%, LF by 138%, HF by 67.6%. Increase of LFn by 0.8% (p=0.26) and decrease of HFn by 1.4% (p=0.32) and LF/HF ratio by 34,8% (p=0,176) was not significant. The changes on the 40<sup>th</sup> minute under 1,5 abs were significant in all values compared with values before HBOT. We observed significant increase of TP by 153,3%, LF by 155%, HF by 252%, HFn by 39.6%, and decrease of LFn by 25.9% and LF/HF ratio by 61.1%.

In the second group (clean oxygen without pressure) we found the same tendency with the first group but less in values. On the 15<sup>th</sup> minute of session significant increased the TP by 113%, LF by 145%, HF by 63%, HFn by 18% and decreased the LFn by 13% and LF/HF ratio by 52%. The changes on the 55<sup>th</sup> minute under 1,5 abs were following: TP increased by 136%, LF by 142%, HF by 64%, HFn by 11% (not significant), LFn decreased by 10% (not significant) and LF/HF ratio by 48%.

In the third group (atmosphere air) on the 15<sup>th</sup> minute of session the TP increased by 51%, LF by 67%, HF by 96%, HFn by 23%, LFn decrease by 19%, LF/HF ratio by 43%. The changes on the 55<sup>th</sup> minute was not significant but we found opposite tendency in changes, compared with the first and second groups: LF increase of by 13% and HF decrease by 12%, LF/HF ratio increase by 19%.

Table 1

Values of HRV in the groups expressed in mean  $\pm$  SD

HF<sub>2</sub> TP (ms²) LF<sub>2</sub> (ms<sup>2</sup> LFn HFn LF/HF Groups (nu) (nu) 378<u>±20</u> 1170±584 248±18 35±16 3.39±2.06 63±15 2332±91 0 90<u>4±</u>49 2 419±13 34±10\* П First (HBOT) 64±11\*  $2.21 \pm 1.09$ 6 2966±14 969±72 879±40 47±13 49±14  $1.32\pm0.62$ 352±19  $2.9 \pm 2.1$ 62±22 414±15 38±19 1215±62 Second 2584±10 94 863±37 54±12 673±31  $1.4 \pm 0.7$ 45±12 П (oxygenation) 42±8\* 852<u>±</u>56  $1.5 \pm 0.7$ 56±11\* 0 1246±69 259±18 337<u>±2</u>5 Third 54±19  $2.1 \pm 2.5$ 43±18 (atmosphere's air) 1885±83 563<u>±</u>41 П 44±19 507±25 53±18  $1.2 \pm 1.3$ 38±19\* 501±35 61±20\* 2 4\*

Values before investigation.

1 - Values in the first group on the first minute under 1,5 abs, in the second and third group on the 15<sup>th</sup> minute of investigations.
 1 - Values in the first group on the 40<sup>th</sup> minute under 1,5 abs, in the second and third group on the 55<sup>th</sup> minute of investigations.
 Not significantly changed compared with values before HBOT and investigation

#### **DISCUSSION**

As confirmed by other investigators, we found HRV to be reduced in the patient with CAD and with the signs of increased sympathetic activity [8]. It has been hypothesized that influences can make impairment of HRV may predict acute myocardial infarction and sudden cardiac death. This is the first study of record changes in frequency domain measures of HRV during HBOT. The analysis of HRV in the

patients of the first group during a HBOT session showed significant changes. We observed significant increase of TP and it components -LF and HF. But if analyze LF/HF as marker of sympathovagal balance and LFn and HFn we could note that the LF/HF ratio decreased because of changing in both branch of AHS and parasympathetic activity increased significant (on 40%) than decreased sympathetic activity (on 25%).

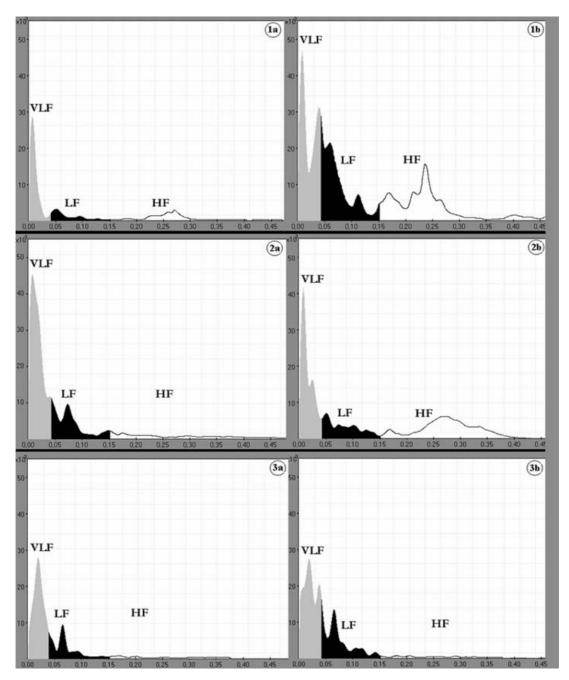


Fig. 1 - 3. Examples of changes of HRV status in some patients under affecting of different procedures. Gray, black and white colors of different fields reflect VLF, LF and HF components respectively.

1a - HRV status in the patient of the first group before HBOT.

<sup>1</sup>b - Changes in HRV status after HBOT under 1,5 abs on 40th minute for the same patient showed increase of TP, LF and significant increase of HF component.

- 2a HRV status in the patient of the second group before oxygenation without pressure.
- 2b Changes in HRV status on 55th minute after oxygenation without pressure for the same patient of the second grope showed the same tendency with the first group (Fig. 1b) but less in values.
- **3a** HRV status in the patient of the third group at breathing of usual atmosphere air.
- 3b Changes in HRV status on 55th minute for the same patient of the third grope showed the opposite tendency in changes, compared with the first and second groups.

The changes of HRV in the patients of the second group had the same tendency with the first group but less in values. It seems to us natural, because the quantity of oxygen in the blood have a linear dependence from partial pressure in breathing air according to the law of Genre-Dalton. The main "job" of blood and circulation is the transportation of oxygen to the all tissues of the body and oxygen level in the plasma monitoring very precisely, but in the tissues because of infections and diseases this vital tissue oxygen level can drop down to almost zero! Oxygen transport is determined by the percentage respired and the barometric pressure. In usual air under 1 abs approximately patients (people) receiving 20,9% of O<sub>2</sub> with oxygen plasma tension about 95mm Hg. In hyperbaric conditions the oxygen plasma tension increases from values of 95 mm Hg to 673 mm Hg in 100% O<sub>2</sub> under 1 abs till 1053 mm Hg in 100% O<sub>2</sub> under 1,5 abs, and this is increasing the gradient or the transfer of oxygen into tissues. Thus it is possible to suspect that extent of changes in ANS within 1 hour HBOT depend proportionally from oxygen tension in tissues. Of course the vital importance of oxygen level can obviously influent on status of ANS in common and on the both it brunch. The changes of HRV in the patients of the third group had statistically insignificant negative tendency as to increasing LF, LF/HF ratio and decreasing HF. We think that changes in third groups reflect the normal, usual variations in time and the first reaction in supine position to the vagal activity changed by hypersympathetic activity. >From this point of view the use of HBOT for patient with CAD is useful modality as adjunctive increasing of activity. parasympathetic The studies influence of HBOT on organism is not finished

and well understanding the changes in ANS will help in management the patient that received HBOT for a long time (it was reported about more than 900 sessions for one patient). In some patients that were not included in this study we observed decreasing the TP and increasing the LF/HF ratio and it was close correlated with problems during the sessions claustrophobia, pain in ears etc.

#### **CONCLUSION**

- 1. Our preliminary results showed that values of HRV increasing during the sessions of HBOT and it measurement are helpful in monitoring not only the circulation but also the common status of patients.
- 2. The HRV measurement reflected effectiveness of the complex treatment of patients with CAD.
- 3. Based on values of HRV it will be possible in the future to modulate the protocols of HBOT individually for certain patient.
- 4. Increasing of vagal activity and total power with decreasing of sympathetic tone during of HBOT is the evidence of "relaxation" of circulation and ANS which less stressed by monitoring the body oxygenation.
- 5. Adjunctive HBOT can improve prognosis in patients with CAD in various ways: the positive modifying of HRV is a sign of favorable changing in ANS (neurogumoral and sympato-vagal interaction) [1]; increasing of cardiac electrical stability; prevention of left ventricular dysfunction, progressing in Killip class [14] and ventricular ectopic activity and presence of late potentials [1]; restores of sinus nodal cells to neural modulations [15].

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#### ВАРІАБЕЛЬНІСТЬ СЕРЦЕВОГО РИТМУ У ПАЦІЄНТІВ ХВОРОБОЮ СЕРЦЯ ІШЕМІЧНОЮ ПРОТЯГОМ ГІПЕРБАРИЧНОЇ ОКСИГЕНАЦІЇ

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Попередні дослідження виявили позитивні ефекти гіпербаричної оксигенації (ГБО) у пацієнтів зі стенокардією та гострим інфарктом міокарда. Мета даного дослідження - оцінити характер змін в автономній нервовій системі (АНС) у пацієнтів з ІХС протягом сесії ГБО, за даними динаміки показників варіабельності

пацієнтів з ГАС протягом сесп і во, за даними динаміки показників варіаослівності серцевого ритму.

Пацієнти з ІХС були розподілені на три групи залежно від тиску у барокамері. Вимірювалися загальна потужність спектру (ТР), низькочастотний компонент спектру (LF) як відображення симпатичного і високочастотний компонент спектру (НF), як відображення вагусної активності, баланс АНС (LF/HF відношення) і LF та HF у нормалізованих одиницях (LFn, HFn).

ГБО істотно збільшувала ТР, зменшувала LF/HF відношення внаслідок зменшення парасимпатичного тонусу

ня симпатичного і більш істотного збільшення парасимпатичного тонусу.

На наш погляд, ці зміни пропорційні збільшенню напруги кисню в тканинах організму під впливом ГБО. Попередні результати показали, що зміни ВСР відображають не тільки стан кровообігу, але також і загальний, інтегральний стан організму протягом сесії ГБО, що, можливо, дозволить індивідуально змінювати протокол ГБО. Збільшення вагусної активності і загальної потужності спектру з одночасним зменшенням симпатичного тонусу протягом ГБО - свідоцтво "релаксації" кровообігу і АНС в умовах гіпероксигенації.

ГБО, на додаток до стандартної терапії, може покращувати прогноз у пацієнтів з ІХС внаслідок декількох механізмів: сприятлива зміна АНС; збільшення електричної стабільності міокарда; попередження розвитку лівошлуночкової дисфункції і недостатності кровообігу; відновлення чутливості клітин синусового вузла до

нейрональної модуляції.

*СЛОВА*: гіпербарична оксигенація, ішемічна хвороба серця, варіабельність серцевого ритму, автономна нервова система

## ВАРИАБЕЛЬНОСТЬ СЕРДЕЧНОГО РИТМА У ПАЦИЕНТОВ С ИШЕМИЧЕСКОЙ БОЛЕЗНЬЮ СЕРДЦА В ТЕЧЕНИИ СЕАНСА ГИПЕРБАРИЧЕСКОИ ОКСИГЕНАЦИИ

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#### **РЕЗЮМЕ**

Предшествующие исследования выявили положительны эффект гипербарической оксигенации (ГБО) у пациентов со стенокардией и острым инфарктом миокарда. Цель данного исследования - оценить характер изменений в автономной нервной системы (АНС) у пациентов с ИБС в течение сессии ГБО, по данным динамики по-

казателей вариабельности сердечного ритма.

Пациенты с ИБС были подразделены на три группы в зависимости от рабочего давления в барокамере. Измерялись общая мощность спектра (TP), низкочастотый компонент спектра (LF), как отражение симпатическего и высокочастотый компонент спектра (HF), как отражение вагусной активности, баланс АНС (LF/HF отношение) и LF и HF в нормализованных единицах (LFn, HFn). ГБО существенно увеличивала TP, уменьшала LF/HF отношение вследствие уменьшения симпатическего и значительно более существенного увеличения парасимпатическего тонуса. С нашей точки зрения эти изменения пропорциональны увеличению напряжения кислорода в тканях под воздействием ГБО. Предварительные результаты показали, что изменения ВСР отражают не только состояние кровообращения, но также и общее, интегральное, состояние организма в течение сессий ГБО, что, возможно, позволит индивидуально модулировать протокол ГБО. Увеличение вагусной активности и общей мощности спектра с одновременным уменьшением симпатическего тонуса в течение ГБО - свидетельство "релаксации" кровообращения и АНС в условиях гипероксигенации.

ГБО в дополнение к стандартной терапии может улучшать прогноз у пациентов с ИБС вследствие нескольких механизмов: благоприятное изменение в АНС; увеличение электрической стабильности миокарда; предотвращение развития левожелудочковой дисфункции и недостаточности кровообращения; восстанавление чувствительности клеток синусового узла к нейрональной модуляции.

*КЛЮЧЕВЫЕ СЛОВА*: гипербарическая оксигенация, ишемическая болезнь сердца, вариабельность сердечного ритма, автономноая нервная система