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# Evaluation of Immunologic and Virologic Data in Patients with Infective Endocarditis, Infected by Hiv, Operated Upon with the Use of Total Controlled Hyperthermic Perfusion

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The peculiarities of immunological and virological status of 11 patients with IE, with lesions of the right heart valves, which were examined and operated on at the National N.M. Amosov Institute of Cardiovascular Surgery AMS of Ukraine during 01.01.1990 – 01.10.2013, were studied. In all cases, the patients were infected with hepatitis C virus and human immunodeficiency virus. Study of changes in immunological and virological status of patients was carried out on the basis of perioperative dynamics of the cellular and humoral immunity, as well as the degree of viral load for HIV and hepatitis C. After completing the main stage of surgical correction protocol of the total controlled hyperthermic perfusion (TCHP) was used, which included warming the patient to 39,0 єC with an exposure 30 min. It was proved that the use of TCHP in patients with IE, which were infected with HIV, was associated with lower degree of viral load in the early postoperative period. Differences in the dynamics of the degree of viral load of hepatitis C and human immunodeficiency were associated with different viral resistance to temperature and with the choice of diverse cellular targets.

**Key words:** *infective endocarditis of the right heart, total controlled hyperthermic perfusion (TCHP), immunology, virology.*

Decreased host immunity among HIV-infected patients places them at increased risk of infection and is associated with poor outcomes [1].

Conducted studies suggest that HIV patients are also at increased risk of CA-MRSA infections from community's networks in which there is high prevalence of intravenous drug use. Independent factors described as risks for MRSA bacteremia within HIV-infected patients: intravenous drug use, hemodialysis and CD4 counts < 200. Clinical outcomes suggest that incidence of re-infection and one-year mortality in this group are high [3].

Recent data from the study by Kempker et al. showed that CA-MRSA bacteremia was associated with advanced age, black race and AIDS infection/ risk of increased mortality compared to other strains also observed in this group [2].

The occurrence of HIV-infection among patients with infective endocarditis (IE), associated with drug abuse, ranges 1,5–100% [1]. The main indications for cardiac surgery in this group of patients are: heart failure; embolic complications; persistent bacterial infection on the background of adequate antibiotic therapy.

Initial immunologic and virologic status influences the results of surgical treatment and rate of postoperative complications.

This study **aimed** to investigate immunologic and virologic status of HIV-infected patients in surgical treatment of IE with the use of hyperthermic cardiopulmonary bypass(CPB).

**Methods.** The study included 11 patients with infective endocarditis of the right part of the heart, operated upon from 01.01.1990 to 01.01.2013. In all cases IE was associated with drug abuse. The mean patients age was 26,2±1,7 years. All patients were initially infected with hepatitis C (HCV) and HIV viruses.

Comparative analysis was carried out with reference to the cellular and humoral immunity (T-cells, T-helpers, T-suppressors, helpers/suppressors coefficient, NK-cells, IgA, IgG, IgM). Determination of HIV viral load (HIV-RNA copies/ml) and HCV(HCV-RNA copies/ml) was performed.

Surgical technique included middle sternotomy, heparinization, cannulation of aorta, separate cannulation of vena cava superior and inferior with subsequent use of standard technique of extracorporeal circulation.

Patients were operated upon with the use of total controlled hyperthermic perfusion. After moderate hypothermia (t=28 °C) was reached, surgical correction of the heart lesion was carried out, patients were warmed up to initial temperature. Then total controlled hyperthrmic perfusion (TCHP) began: body temperature was raised to 39 °C with the exposure 30 min. Cooling of the patients to normothermia was performed in passive way.

**Results.** The process of summing up the research revealed changes in cellular and humoral immunity. HIV-infected patients were characterized with: decrease in phagocytic activity of the macrophages – 87,04±1,9%, absolute and relative levels of T-helpers/T-inductors (CD3+, CD4+): 393 cells/μL and 20,1±2,7% correspondingly; increase of absolute and relative numbers of immature T-lymphocytes (CD4+,CD8+)- 0,028±0,01 cells/μL and 1,02±0,5% correspondingly; decrease of T-helpers/T-suppressors index – 0,4±0,06; increased level of circulating immune complexes C1q and C3q composed 178±20,3 mkg/ml and 71,6±31,2 mkg/ml correspondingly; decreased level of IgG and IgA – 262,5±18,6mg/dl and 71,6±31,2 mg/dl.

In postoperative period immunologic screening was performed on the 3,10 and 14 days. Analysis of the dynamics of a number of immunologic and virologic indices showed following changes in immunologic status of patients: significant decrease in phagocytic activity – 80,3±10,7%; decrease in lymphocytes level – 840±21 cells/μL; decrease in T-lymphocytes level( CD3+) –718±12,6 cells/μL; decrease in T-lymphocytes level( CD3+,CD4+) – 295±8,3 cells/μL; increase of T-helpers/T-suppressors index – 0,6±0,1; decrease in level of circulating immune complexies C1q and C3q composed 132±10,6 mkg/ml and 19,2±8,5 mkg/ml correspondingly; increased level of IgG and IgA – 1373±400,7 mg/dl and 257,3±143,2 mg/dl.

Maximum decrease in cellular and humoral immunity was registrated on the 3–4 postoperative days with consequent restoration to initial levels by 14 postoperative days. Thus, studied patients are most sensitive to development of postoperative infectious complications beginning from the 3–4 day after surgery.

It was proved that the use of TCHP in patients with IE, infected by HIV, is associated with lower degree of viral load in the early postoperative period. Maximum decrease of HIV viral load was observed on 6 day of postoperative period with consequent restoration to initial levels by 14 postoperative days. This fact may be explained by the temperature influence on the HIV, and on the other way by temperature influence on the cellular immunity indices.

There is a significant correlation between level of RNA-HIV (PCR) and immunologic indices (table 1).

Received results showed specific relationship between HIV level and cellular immunity indices.

Analysis of the dynamics of viral load for HCV: minimal level was registrated on 10 day and by 14 postoperative days its level increased considerably, over initial value. Differences in the dynamics of the viral load degree of hepatitis C and human immunodeficiency is possibly associated with different viral resistance to temperature and choice of diverse cellular targets.

There is a significant correlation between level of RNA-HCV (PCR) and immunologic indices (table 2).

*Table 1*

**Correlation between level of RNA-HIV (PCR) and immunologic indices**

| Immunologic indicies | r | p |
|---|---|---|
| Leucocytes | 0,784 | 0,012 |
| Lymphocytes (%) | 0,633 | 0,037 |
| Lymphocytes (abs) | 0,851 | 0,007 |
| Monocytes(%) | - 0,602 | 0,050 |
| CD3+ (abs) | 0,924 | 0,001 |
| CD3+, CD4+ (abs) | 0,939 | 0,001 |
| CD3+, CD8+ (abs) | 0,987 | 0,001 |
| CD19+ (abs) | 0,927 | 0,001 |
| NK-cells (abs) | 0,842 | 0,001 |
| T-activeted (abs) | 0,937 | 0,001 |

*Table 2*

**Correlation between level of RNA-HCV (PCR) and immunologic indices**

| Immunologic indices | r | p |
|---|---|---|
| NKT-cells (%) | - 0,726 | 0,041 |
| NK-cells (%) | 0,775 | 0,024 |
| T-activeted (abs) | - 0,751 | 0,032 |

Analysis of immunologic and virologic data has showed different reaction of HIV and HCV to the TCHP. Also differences in correlations between levels of viral load and immunologic indices for HIV and HCV were revealed.

Application of TCHP allowed to decrease HIV viral load on 6 day of postoperative period in surgical treatment of patients with IE, infected by HIV.

**Conclusions**

1. In the group of patients, infected by HIV, maximum decrease in cellular and humoral immunity was registrated on the 3–4 postoperative days.
2. It was proved that the use of TCHP in patients with IE, infected by HIV, is associated with lower degree of viral load in the early postoperative period.
3. Differences in the dynamics of the viral load degree of hepatitis C and human immunodeficiency virus is possibly associated with different viral resistance to temperature and choice of diverse cellular targets.

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## Динаміка імунологічних і вірусологічних показників у хворих на інфекційний ендокардит, інфікованих вірусами імунодефіциту людини та гепатиту С, оперованих в умовах загальної керованої гіпертермічної перфузії

**Книшов Г.В., Максименко В.Б., Колтунова Г.Б., Крикунов О.А.**

Були вивчені особливості імунологічного і вірусологічного статусу 11 хворих ІЕ, з ураженнями клапанів правих відділів серця, які пройшли обстеження і хірургічне лікування в Національному інституті серцево-судинної хірургії імені М.М. Амосова НАМН з 01.01.1990 по 01.10.2013 рр. У всіх випадках пацієнти були інфіковані вірусами гепатиту С та імунодефіциту людини. Вивчення змін імунологічного і вірусологічного статусу пацієнтів проводилося на основі періопераційної динаміки показників клітинного і гуморального імунітету, а також ступеня вірусного навантаження для ВІЛ і гепатиту С. Після завершення основного етапу хірургічної корекції протокол ЗКГП включав зігрівання пацієнта до 39 єС з експозицією 30 хв. Доведено, що використання ЗКГП у хворих ІЕ, інфікованих вірусом імунодефіциту людини, супроводжувалося зниженням ступеня вірусного навантаження в післяопераційному періоді. Відмінності в динаміці ступеня вірусного навантаження гепатиту С та імунодефіциту людини пов'язані з різною резистентністю вірусів до температурного впливу і вибором інших клітинних мішеней.

**Ключові слова:** *інфекційний ендокардит правих відділів серця, загальна керована гіпертермічна перфузія (ЗКГП), імунологія, вірусологія.*

## Динамика иммунологических и вирусологических показателей у больных инфекционным эндокардитом, инфицированных вирусами иммунодефицита человека и гепатита С, оперированных в условиях общей управляемой гипертермической перфузии

**Кнышов Г.В., Максименко В.Б., Колтунова А.Б., Крикунов А.А.**

Были изучены особенности иммунологического и вирусологического статуса 11 больных ИЭ, с поражениями клапанов правых отделов сердца, которые прошли обследование и хирургическое лечение в Национальном институте сердечно-сосудистой хирургии им. Н.М. Амосова НАМН с 01.01.1990 по 01.10.2013 гг. Во всех случаях пациенты были инфицированы вирусами гепатита С и иммунодефицита человека. Изучение изменений иммунологического и вирусологического статуса пациентов проводилось на основе периоперационной динамики показателей клеточного и гуморального иммунитета, а также степени вирусной нагрузки для ВИЧ и гепатита С. После завершения основного этапа хирургической коррекции протокол ОУГП включал согревание пациента до 39 єС с экспозицией 30 мин. Доказано, что применение ОУГП у больных ИЭ, инфицированных ВИЧ, сопровождается снижением степени вирусной нагрузки в раннем послеоперационном периоде. Различия в динамике степени вирусной нагрузки гепатита С и иммунодефицита человека связаны с различной резистентностью вирусов к температурному воздействию и выбором других клеточных мишеней.

**Ключевые слова:** *инфекционный эндокардит правых отделов сердца, общая управляемая гипертермическая перфузия (ОУГП), иммунология, вирусология.*