

**Conclusion:** The absence of decreasing of the  $pCO_2$  tissue hypoxia marker at the A-V difference after microcirculatory - mitochondrial recruitment, rejects the necrosis / apoptosis, cellular hypo- (an) ergic and proves the mitochondrial eu-energetic metabolic remodeling with the elimination of the hypo (an) ergic mitochondria performed by clearance lysosomal (mitophagy), thus demonstrating eu-ergic mitochondria with the normalization of mitochondrial uniporter- $Ca^{++}$  and mitochondrial permeability pore transition, which productively inactivate the toxic forms of oxygen and nitrogen.

## REZUMAT

Instalarea centralizării macro - circulației în declanșarea MODS în stări critice de obstetrică cauzate de coagularea intravasculară, HELLP, șoc, SIRS, septicemie, CARS, embolie a arterei pulmonare, cerebrală și altele; - microcirculația va fi de asemenea grav afectată, iar perfuzia fluxului sanguin afectează revenirea venoasă pentru a elimina deșeurile de metabolism celular, unde un marker al hipoxiei tisulare este creșterea dioxidului de carbon, la diferența A-V. Această tulburare generează sindromul detresei microcirculator - mitocondriale (MMDs), colapsul energetic mitocondrial, care poate fi de-instalat (recuperat) prin recrutarea microcirculator - mitocondrială odată cu optimizarea presiunii de perfuzie sistemică, în dependență de tensiunea arterială medie și rezistența capilară. Recrutarea microcirculator - mitocondrială descentralizează macrocirculația și ameliorează microcirculația în spațiul metabolic capilar - celulă. În cazurile de manifestare a  $\uparrow CO_2$ -dependent respirator-pulmonar, confirmat  $\downarrow PaO_2 / FiO_2 \downarrow 300$  pentru ARDS, sindromul de detresă respiratorie acută (definiția de la Berlin, 2012), agravează de asemenea, și sindromul detresei microcirculator-mitocondriale, colapsul mitocondrial iar recrutarea microcirculator - mitocondrială este suplimentată cu terapia de sprijin multi-organ (MOST). 1. Recrutarea alveolară prin suport respirator în moduri de ventilație specifice preponderent APRV, cu hipercapnie permisivă la un pH normal. 2) MOST - extracorporeal cu suport tehnic în managementul vital prin sprijin extracorporeal - ELSO. 3) modelarea fluidului pulmonar extra-vascular; 4) Blocul epidural T4-Th5 toracic.

Reducerea markerului hipoxiei tisulare  $pCO_2$  la diferența A-V după recuperarea microcirculator - mitocondrială, respinge necroza / apoptoza, hypo- (an) ergicul celular și dovedește remodelarea metabolică eu-energetică mitocondrială prin eliminarea hypo (an) mitocondriilor ergice efectuate prin clearance-ul lizosomal (mitofagie), demonstrând astfel mitocondriile eu-ergice cu normalizarea tranziției porilor permeabilității mitocondriale și canalului uniporter- $Ca^{++}$ , care inactivează productiv formele toxice de oxigen și azot.



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## HORMONE REPLACEMENT THERAPY USED FOR CORRECTION OF MENSTRUAL DYSFUNCTION ASSOCIATED WITH LIVER PATHOLOGY

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The problem of viral hepatitis and menstrual dysfunctions stays present, being determined by the high incidence and severity of physiopathological abnormalities, specific to these associations. In Republic of Moldova 9% of population are chronic carriers of HVB, HVC affects 1.5-5% of population.

**The purpose of this work** was to study the therapeutic effect of hormone therapy in women with menstrual dysfunctions caused by chronic viral hepatitis.

**Materials and methods:** The controlled randomized study evaluated the treatment results of 80 patients with menstrual dysfunctions in association with liver pathology, randomly picked out from 319 women suffering from chronic viral hepatitis. The selection of the hormonal therapy was made depending on the menstrual irregularities, hormonal profile and results of the genitals sonography:

- 1<sup>st</sup> group (26 patients) – hepatoprotectors,
- 2<sup>nd</sup> group (23 patients) – Didrogesteron 10 mg (Duphaston) + hepatoprotectors,
- 3<sup>rd</sup> group (31 patients) – Estradiol 2mg + Didrogesteron 10 mg (Femoston) + hepatoprotectors. The control group included 15 healthy women of reproductive age with normal menstrual cycle.

**Results:** The examined patient's age varied between 18 and 40 years, mean age -  $26.0 \pm 5$  years. Bilirubin level in patients with HVB was 3 times higher compared with control group, but in mix-hepatitis -10 times. Transaminases were elevated 10-40 times, especially in mixed viral hepatitis. Alkaline phosphatase ( $27.81 \pm 1.3$  UI/l), prothrombin, total protein, and albumin were considerably decreased. Similar changes have been observed in **cholesterol level (dropped till  $2.60 \pm 0.21$  mmol/l) and  $\beta$ -lipoprotein ( $195.0 \pm 25.3$  Un)**, which are evidently decreased in all patients with all types of viral hepatitis. Regular menstrual cycle was present only in  $7.5 \pm 2.48$ .

Menstrual dysfunction in the evaluated patients was depend on the type of HV. Hypermenstrual syndrome and uterine bleeding were found in 2,4% patients. But  $22.6 \pm 1.48\%$  patients revealed a hypomenstrual syndrome and 67,5% was with amenorrhea. The disorder was more manifest in patients with HVC ( $35,3 \pm 2,3\%$ ) and in those with mix-hepatitis ( $28,58 \pm 1,08\%$ ). Analysis of hormone's reflects a wide range of variations in the content of estradiol (from 70.3 to 670 nmol / l) and progesterone (from 1.42 to 5.5 nmol / l). Hyperestrogenemia prevail in patients with severe HVB and those with mixed forms (in  $63.75 \pm 3.1\%$  cases). Progesterone was dropped in  $67,5 \pm 2,9\%$  patients and varied from 1,42 to 7,42 nmol/l, thus indicating an essential hypoprogesteronemia ( $p > 0,05$ ). FSH seric concentrations ( $6,62 \pm 0,3$  mME/ml) and LH ( $2,7 \pm 0,08$  mME/ml) slightly exceeded the maximal tolerated limit. High levels of Prolactin ( $505,3 \pm 46,3$  ng/ml ( $p < 0,05$ )) were registered in the majority of cases.

At the ultrasound investigation performed in the 13<sup>th</sup> day of the menstrual cycle, it has been observed a decreased M-echo till  $4.0 + 0.9$  mm, in patients with HVB,  $3.0 + 1.1$  mm – with HVC, and  $3.2 + 0.8$  mm – with mix- hepatitis.

The results of the study reveal serious disturbances in all hepatic functions in patients with viral hepatitis with direct repercussions over the ovaries, which lead to derangements in ovarian hormone biosynthesis. The correction of menstrual abnormalities depends on the activity degree of the viral hepatitis activity and the length of these dysfunctions.

In the 1<sup>st</sup> group a gradual normalization of hepatic function after 3 months of traditional treatment was observed, a full recuperation of the menstrual function using only hepatoprotectors is not possible. Duphaston is a selected treatment for correcting the menstrual function at women with the minimum and moderate hepatitis activity degree, contributed to menstrual cycle adjustment, thus decreasing menstrual cycle dysfunction's incidence with 52% compared with 1-st group (RR=0,246; IC=0,52 $\pm$ 0,098; ( $p < 0,001$ )). Femoston is recommended for the recovery of serious hormonal dysfunctions, caused by viral the mixed hepatitis, moderate or severe forms. The high efficiency of the Femoston therapy was observed in 67.74% of cases (RR=0.51, IC=0.34 $\pm$ 0.098, ( $p < 0.05$ )).

**Conclusions.** The clinical researches showed the lack of adverse effects of the Femoston and Duphaston therapies over the hepatic function.



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#### **PREECLAMPSIA AND FUTURE CARDIOVASCULAR RISK**

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**Key Words:** preeclampsia, maternal morbidity, complications

**Introduction:** Preeclampsia is a pregnancy-specific disorder resulting in hypertension and multiorgan dysfunction. There is growing evidence that these effects persist after pregnancy. We aimed to systematically evaluate and quantify the evidence on the relationship between preeclampsia and the future risk of cardiovascular diseases. The goal of this review is to determine the association of preeclampsia and future cardiovascular risk and to explore the potential management options for these high-risk women.

**Materials and methods:** Study of obstetrical history of patients with a ischemic cardiovascular diseases. The study performed in the Cardiology department of IMSP SCM-3 mun. Chișinău during 2014-2016. The study also included 98 pregnant women whose pregnancy was complicated by preeclampsia of various degrees of severity during 2010-2012, analyzed after 5 years.

**Discussion results** The study found that 29 patients out of 52 had complicated pregnancies with preeclampsia, accounting for 56%, 13 patients having complicated pregnancies - 25%, and 19% - 10 patients had a physiological pregnancy. Preeclampsia is a major risk factor for developing cardiovascular complications 3 times more frequently than uncomplicated pregnancies (OR 17.62; 95% CI 6.65 to 46.4)  $P < 0.001$ . Women with a history of preeclampsia have a double risk of subsequent ischemic heart disease, stroke and thromboembolic events within the next 5-15 years after pregnancy. None of the 98 women after birth complicated with preeclampsia was not monitored, and so they developed complications.

**Conclusion:** Preeclampsia is associated with a 4-fold increase in future incident heart failure and a 2-fold increased risk in coronary heart disease, stroke, and death because of coronary heart or cardiovascular disease. This important association can be used to screen for women with an increased risk to better target counselling on lifestyle modifications such as weight loss, exercise, and a healthier diet.