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Short Communication

Urea-secreting Function of the Liver and Urea-Secreting Function of the Kidneys after Liver Resection and Hyperbaric Oxygenation

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Introduction

Previous studies have shown the ability of hyperbaric oxygen to regulate the glutamine cycle in the liver, depending on its condition during oxygenation [1,2]. It is known that the glutaminase unit of this cycle participates in the synthesis of urea, which is subsequently excreted in the urine. Therefore, the question arises as to how the urea-secreting function of the liver and the urea-secreting function of the kidneys will change in case of liver damage and the use of Hyperbaric Oxygenation (HBO) in the treatment regimen against this background.

Goal

Study of the effect of liver resection and its combination with Hyperbaric Oxygenation (HBO) on the kinetics of urea in the liver and kidneys of rats.

Methods

Experimental studies were conducted on 30 female white rats weighing 180-220 g. Liver Resection (LR) was performed under diethyl ether anesthesia, removing part of the left lobe of the liver (15% - 20% of the organ mass). HBO was performed with medical oxygen in an experimental pressure chamber 4-8, 24 and 48 hours after RP in the 3 ata (303.6 kPa) mode. Compression time was 5 min, isopressure time was 50 min, decompression time was 5 minutes . The work with experimental animals was carried out in accordance with the regulations of the EU declaration of 22 September 2010 on the use of laboratory animals for scientific purposes. The study was approved by the Ethics Committee of the Voronezh State Medical University.

The object of the study was the left and middle lobes of the liver (LDP and SDP, respectively), kidneys, choledochal bile, urine, blood: a. femoralis, v. porta, v. hepatica, v. renalis, v. hepatica blood was obtained from the interlobular (left and middle lobes of the liver) sinus after its isolation from the posterior vena cava *in situ*. Operated animals were euthanized under ethaminal anesthesia on the 3rd day after LR; oxygenated animals - immediately after the end of the third session of HBO. The urea content in the tissue and biological fluids was determined by the diacetyl monooxime method [3]. The research results were processed statistically using the parametric Student *t* - test and the nonparametric Mann–Whitney test after preliminary verification of the hypothesis of the normality of the sample distribution. The results were considered significant at a *p* value of < 0.05. Statistical analysis was performed using the packages "Microsoft Excel", Statistica 5.0 (StatSoft) " and "Biostat".

Results

Normally, the urea content in the blood from the v. hepatica significantly exceeded that in arterial blood and v. porta blood, which made the hepatic arterio-venous (hAVDu) and porto-venous (PVDu) differences in urea negative (Table 1). This indicates the incretion of urea from the intact liver into the central bloodstream. Arterio-portal (APDu) and renal arterio-venous (rAVDu) differences in urea were positive (Table 1). This indicates the excretion of "arterial" urea into the lumen of the gastrointestinal tract and renal tubules, respectively. The concentrations of urea in LLL and MLL did not significantly differ (Table 1). On the 3rd day after LR, the urea content in LLL, bile, and arterial blood did

Table 1: Urea content in the liver, kidneys (mmol/kg wet tissue) and biological fluids (mmol/l) on the 3rd day after liver resection and a three-day course of hyperbaric oxygenation (M ± m).

Object of study	Norm N = 10	Liver Resection N = 10	Liver Resection + HBO N = 10
	1 series of experiments	2 series of experiments	3 series of experiments
LLL	4.82 ± 0.14	4.34 ± 0.21	6.57 ± 0.41*▲
MLL	4.64 ± 0.16	3.91 ± 0.22*	6.01 ± 0.39*▲
Bile	2.78 ± 0.10	2.92 ± 0.13	5.32 ± 0.3*
Blood a. femoralis	3.4 ± 0.12	3.55 ± 0.37	5.78 ± 0.22*▲
Blood v. porta	2.7 ± 0.11	3.91 ± 0.37*	7.23 ± 0.62*
Blood v. hepatica	4.25 ± 0.13	3.07 ± 0.13*	4.74 ± 0.32
Blood v. renalis	2.63 ± 0.19	3.39 ± 0.23*	5.83 ± 0.16*▲
hAVDu	-0.83 ± 0.11	nrd	-0.43 ± 0.07*
PVDu	-1.22 ± 0.38	0.92 ± 0.11	nrd
APDu	0.74 ± 0.14	-0.42 ± 0.12	nrd
rAVDu	0.77 ± 0.08	nrd	nrd
Kidneys	11.2 ± 1.01	12.5 ± 0.77	11.0 ± 0.73
Urine	34.6 ± 3.3	24.3 ± 3.1*	46.6 ± 3.8*▲

Note : LLL: Left Lobe of the Liver; MLL: Middle Lobe of the Liver; hAVDu: Hepatic Arteriovenous Urea Difference; PVDu: Porto-Venous Urea Difference; APDu: Arterioportal Urea Difference; rAVDu: Renal Arteriovenous Urea Difference; HBO: Hyperbaric Oxygenation; * ($p < 0.05$) – Reliability of Differences Compared To The Norm.▲ ($p < 0.05$) – Reliability of Differences Compared to LR (2 series), nrd: Not a Reliable Difference.

not differ from the norm. In non-operated MLL and blood v. hepatica decreased by 16% and 28%, respectively. In the blood of v. porta, it increased by 45% (Table 1). hAVDu was unreliable, PVDu was positive, and APDu was negative. In the kidneys, the concentration of urea remained within the normal range, decreased by 30% in the urine and increased by 29% in the blood of v. renalis, as a result, the urea level became statistically insignificant (Table 1).

On the 3rd day of the postoperative period, oxygenated rats that underwent LR showed a significant increase in the concentration of urea in LDP and LDP, both compared with the norm and with non-oxygenated animals with LR (Table 1). In the blood of v. hepatica, its content was within the normal range, exceeding the same indicator of animals of the 2nd series by 54% (Table 1). Compared with the norm, the urea content in arterial blood, v. porta blood, and bile was increased by 70%, 167%, and 91%, respectively; while compared with the 2nd series of experiments, it was increased by 84%, 63%, and 82%, respectively (Table 1). The negative hAVDu was restored, but was 48% below normal, PVDu and APDu were unreliable (Table 1). In the kidneys, the urea content did not change, but it was increased in the blood of v. renalis relative to the norm and the 2nd series, respectively, by 122% and 78%. This was accompanied by an increase in the concentration of urea in the urine relative to the norm and the 2nd series, respectively, by 34% and 92%. rAVDu was reliable (Table 1).

Discussion

The decrease in urea incretion from the operated liver into the central bloodstream on the 3rd day after LR did not lead to a similar change in the arterial blood. This was accompanied by retention in the liver of urea, which was supplied in excess with the blood v. porta, as indicated by a positive PVDu . However, this was not sufficient to prevent a decrease in the concentration of urea in the MLL. This may be attributed to a decrease in its formation by hepatocytes of the operated organ [4]. At the same time, the excretion of urea from the operated liver with bile did not change. A negative APDu indicated a decrease in the secretion of "arterial" urea into the lumen of the gastrointestinal tract, which led to an increase in its content in the blood v. porta. At the same time, there was a decrease in the excretion of urea in the urine as a result of an increase in its reabsorption in the renal tubules. This is indicated by an increase in its concentration in the blood of v. renalis, while in arterial blood it was within normal limits.

A three-day course of HBO restored the urea-increting function of the liver, impaired by LR. A comparison of the degree of increase in urea concentration in the operated liver, in the blood flowing into and out of it, with literature data [4] allows us to say that HBO stimulated the formation of urea in the operated liver and its entry into the bile capillaries. This was evidenced by an increased concentration in bile. During HBO, the decrease in excretion of "arterial" urea into the lumen of the gastrointestinal tract, triggered by LR persisted. At the same time, the hepatic-intestinal circulation of urea was activated. This is indicated by the positive correlation between the urea content in the bile and blood of the v. porta ($r = 0.89$). Under HBO conditions, the LR-induced increase in renal urea reabsorption was reversed , which was accompanied by an increase in its concentration in the urine. The discrepancy between the increase in urea content in arterial blood and blood of the v. renalis compared to the norm allows us to speak about the stimulation by hyperbaric oxygen of the formation of urea in the cells of the renal tubules with its subsequent incretion into the renal bloodstream.

Conclusion

Hyperbaric oxygen eliminates the disturbance of the urea-increting function of the operated liver, thus removing the need for increased renal urea reabsorption . An increase

in the excretion of urea in urine in oxygenated animals with LR is accompanied by an increase in its content in the blood flowing from the kidneys. Together with the restoration of the uric acid secreting function of the liver, this explains the increase in arterial metabolite levels, which is not seen in animals operated on with LR without HBO.

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