Changes in Liver Polar Lipid Fatty Acid Composition After Partial Hepatectomy in Mice

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Summary

The purpose of this study was to assess changes in the liver polar lipid fatty acid composition after 1/3 partial hepatectomy (PHx). The fatty acid composition of liver phospholipids was significantly influenced by liver regeneration. The significant differences were found in the arachidonic and palmitooleic acid contents, and in unsaturation during all examined post-operative periods. Simultaneously, the content of saturated fatty acids was higher and polyunsaturated lower than in the control group. Negative correlations between n-6 and n-3 fatty acids (r=-0.69), arachidonic acid content and eicosanoid precursor ratio (r=-0.77) and positive between unsaturation and docosahexaenoic acid content (r=0.82) were found during PHx.

Introduction

Partial hepatectomy (PHx) leads to proliferation of all population of cells within the liver, including hepatocytes, biliary epithelial cells and endothelial cells[1]. Regenerating liver is an ideal model system in which to study the mechanisms that control cell proliferation. The biochemical changes that occur during liver regeneration also occur during tumor growth, therefore, will lead to a better understanding of the mechanisms of neoplastic and some liver diseases. Fatty acids can regulate lipid metabolism at three levels[2]. The structures and composition of fatty acids in the phospholipids are important, because they are, together with cholesterol content in biomembranes, basic determinants of physical properties of membranes. Arachidonic acid

is the major precursor for eicosanoids and are to be released from membrane lipids at first step. The saturated fatty acids in the residual liver are intensively converted to unsaturated acids, which are essential for the synthesis of phospholipids and for the esterification of cholesterol[3].

In this study, we extended the analysis of changes in the phospholipid fatty acids to day 7 after 1/3 PHx in the mice liver tissues.

Materials and Methods

Four different groups of adult male Balb/C mice, divided into groups of eight, were studied. All animals were kept under a 12-h light:12-h dark cycle and fed with a standard diet (Faculty of Biotechnology, Domzale, Slovenia). When the mice reached a weight of at least 25 g (around the age of 2-3 mo), they were assigned to four different groups (control, 1st-, 2nd- and 7th day). All operations were performed between 09:00 h and noon under ether anaesthesia. Animals were sacrificed 1st, 2nd and the 7th days after the operation. Liver tissues were removed with plastic instruments, washed several times with saline solution to remove blood, weighed and stored at −80°C until further analysis.

Total lipids were extracted according to *Folch et al.*, and polar lipids were separated and purified by solid-phase extraction and fatty acids of polar lipids analysed in the form of fatty acid methyl esters by gas chromatographic analysis[4].

The significance of difference was assessed using the Statistica software package for Windows 1997 by Statsoft, Inc. All values were expressed as the means±SD. A statistical analysis was performed using the nonparametric *Kruskal-Wallis* one-way analysis of variance by rank and the *Mann-Whitney* U-test to assess significant differences among the hepatectomized groups. Statistical significance was assumed with a $P < 0.05$.

Results

Relative percentages of fatty acids in the polar lipid fraction isolated from the examined liver tissue samples are shown in Table 1. The fatty acid composition of liver phospholipids was significantly influenced by liver regeneration. Unsaturation reached a minimum on day 7 after PHx, as well as eicosanoid precursor ratio. A high negative correlation (r=-0.77) in the liver polar lipids was found between the eicosanoid precursor ratio and arachidonic acid content, and a high positive correlation between unsaturation and the docosahexaenoic acid content. Comparing to the control, a significant difference was in arachidonic acid during all examined postoperation times as showed in Figure 1. The C18:2/C20:4 and C22:6/C20:4 ratios reached the minimum on the 1st day and maximum on the 7th day. The importance of the C20:4 content linked with desaturases activity. The highest saturation (SFA) during liver regenera-

Table 1. Fatty acid composition (%) of the total phospholipids in the mice liver tissue samples in the untreated control and 1, 2 and 7 days after PHX

Fatty acid	Control	Day 1	Day 2	Day 7
Myristic ($C_{14:0}$)	0.05±0.03	0.05±0.01	0.07±0.03	0.07±0.02
Myristoleic ($C_{14:1n-5}$)	0.00	0.00	0.00	0.00
Palmitic ($C_{16:0}$)	24.87±0.50	28.13±1.78	26.43±1.40	25.22±1.05
Palmitoleic ($C_{16:1n-7}$)	0.83±0.20	1.37±0.50	1.18±0.20	1.36±0.24
Stearic ($C_{18:0}$)	15.98±1.99	17.09±2.01	17.22±0.57	16.48±1.21
Oleic ($C_{18:1n-9}$)	9.52±1.50	8.95±1.72	8.13±0.67	11.65±2.39
Linoleic ($C_{18:2n-6}$)	13.68±1.23	15.78±1.60	16.25±0.51	16.06±1.18
Arachidic ($C_{20:0}$)	0.31±0.15	0.11±0.09	0.12±0.06	0.19±0.07
γ-linolenic ($C_{18:3n-6}$)	0.54±0.50	0.27±0.10	0.31±0.15	0.25±0.11
Eicosenoic ($C_{20:1n-9}$)	0.00	0.21±0.10	0.32±0.12	0.11±0.03
Behenic ($C_{22:0}$)	0.00	0.00	0.00	0.00
Eicosadienoic ($C_{20:2n-6}$)	0.22±0.11	0.16±0.04	0.17±0.04	0.25±0.06
Homo-γ-linolenic ($C_{20:3n-6}$)	1.11±0.40	1.02±0.29	1.28±0.28	1.37±0.20
Arachidonic ($C_{20:4n-6}$)	11.03±0.55	7.77±1.03	9.25±1.05	13.55±0.75
Eicosapentaenoic ($C_{20:5n-3}$) (EPA)	1.08±0.40	0.87±0.37	0.96±0.14	0.53±0.14
Lignoceric ($C_{24:0}$)	0.31±0.27	0.10±0.06	0.06±0.03	0.09±0.04
Docosahexaenoic ($C_{22:6n-3}$) (DHA)	20.50±1.57	18.10±0.73	18.25±1.27	12.83±1.11
Σ Saturated (SFA)	41.50±2.41	45.49±1.36	43.90±0.99	42.04±1.11
Σ Monounsaturated (MUFA)	10.35±1.64	10.52±2.14	9.63±0.73	13.12±2.53
Σ Polyunsaturated (PUFA)	47.04±2.81	42.96±2.83	45.19±1.81	43.46±1.80
PUFA/SFA	1.14±0.13	0.95±0.08	1.03±0.06	1.03±0.03
PUFA/MUFA	4.63±0.78	4.22±0.84	4.72±0.53	3.44±0.79
$C_{18:2}/C_{20:4}$	1.24±0.13	2.04±0.21	1.77±0.19	1.19±0.10
Unsaturation[a]	2.15±0.11	1.90±0.07	1.98±0.07	1.84±0.04
Eicosanoid precursor ratio[b]	0.19±0.02	0.25±0.09	0.25±0.05	0.14±0.03

Data are means ±S.D. (n=8 per group).

[a] Unsaturation was calculated according Kishino et al.[5]

[b] Eicosanoid precursor ratio was calculated according Palombo et al.[6]

tion was found on the 1st day after PHx and then returned nearly to the preoperative level.

The highest content of polyunsaturated fatty acids (PUFA) was found at the preoperative level and reached the minimum on the 1st day. The highest content of monounsaturated fatty acids (MUFA) was found on the 7th day and reached the minimum on the 2nd day. PUFA, unsaturated fatty acids (UFA), UFA/SFA and PUFA/SFA ratios, followed the same tendency.

Changes in the lipid composition in plasma membranes in regenerating liver would have an effect on membrane fluidity and together with the changes in the protein composition may be significant in the altered growth of the hepatoma.

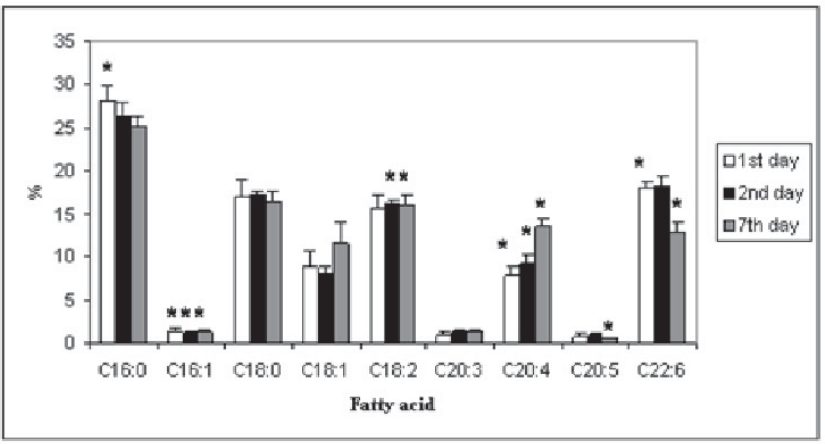

Figure 1. The fatty acid composition major FA of the liver PL during PHx given as the mean ±SD.
**p < 0.05 compared to the control and day 1, 2 and 7 after PHx.*

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