

AUTHOR
PROOF

Changes in Peripheral Blood Levels of Platelet-Activating Factor After Orthotopic Liver Transplantation

P. Moreno, M.A. Gijon, R. Fradera, J. Fabregat, A. Rafecas, S. Biondo, J. Figueras, M. Sánchez-Crespo, and E. Jaurrieta

PLATELET-ACTIVATING factor (PAF) is a phospholipid mediator structurally characterized as 1-alkyl-2-acetyl-*sn*-glycero-3-phosphocholine with a broad range of biological activities. PAF has been implicated as a mediator of the acute allergic and inflammatory response as well as in the pathogenesis of hyperacute rejection in organ transplantation, which is mediated by antibodies and complement.¹

High levels of PAF have been detected in the peripheral blood of patients suffering from hepatic cirrhosis²; moreover, as PAF has been implicated in the pathogenesis of hyperacute graft rejection, PAF receptor antagonists have been shown to improve the survival of grafts in animal models with hyperacute rejection.³ Up to now there has been no definite evidence of the role of PAF in acute organ rejection. The purpose of this study was to evaluate blood PAF levels in liver transplant patients in order to ascertain its possible role in the pathogenesis of acute rejection episodes.

PATIENTS AND METHODS

Seventeen patients (13 males, 7 females) underwent orthotopic liver transplantation (OLT); the mean age was 49 years (range, 21 to 61 years). The preoperative diagnosis was end-stage liver cirrhosis in 11 patients, 3 patients had hepatocellular carcinoma (HCC) on liver-compensated cirrhosis, 2 patients had HCC without cirrhosis, and 1 patient had cholangiocarcinoma. Peripheral blood PAF levels were measured in the preoperative period and during the immediate reperfusion phase (at 5 and 60 minutes) and monitored during rejection episodes. In 4 patients blood samples from the suprahepatic veins were drawn during the immediate reperfusion phase. The control group was formed by 10 healthy age-matched volunteers. PAF was measured following well-established procedures, including extraction of lipids by the Bligh-Dyer procedure,⁴ straight-phase high-performance liquid chromatography, and bioassay on rabbit platelets.⁵

Statistical analysis was performed using the Student's *t* test. Data were expressed as the means \pm SD.

RESULTS

The levels of PAF in peripheral blood were significantly higher in cirrhotic patients than in those diagnosed of primary hepatic tumor (0.16 ± 0.078 and 0.04 ± 0.077 ng/mL, respectively; $P < .05$). In a group of age-matched normal controls PAF levels were either lower than 0.04 ng/ml or undetectable (Fig 1).

Following successful OLT in cirrhotic patients, blood PAF levels diminished to values similar to those of normal

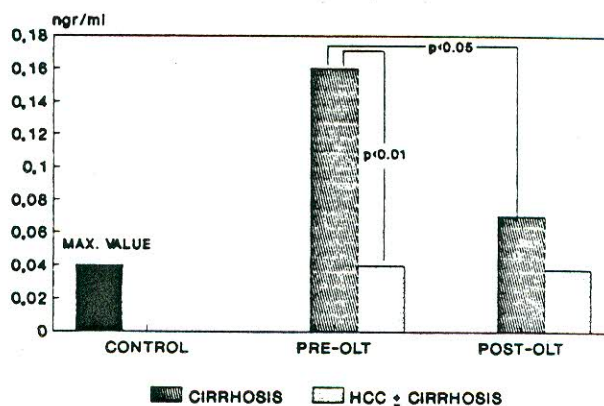


Fig 1. PAF levels in patients with end-stage liver cirrhosis are significantly higher than those measured in the control group and in patients with primary hepatic tumor. Following OLT, in cirrhotic patients, blood PAF levels diminished to values similar to those of normal controls.

controls. The decrease in PAF levels was parallel to the decrease in prothrombin time observed after recovery of graft function. Blood PAF levels were not modified during the immediate reperfusion phase, either in peripheral blood or in blood from the hepatic veins. Measure of peripheral blood PAF during nine rejection episodes in 6 patients also failed to show significant variation as compared to previous values.

CONCLUSIONS

PAF levels in peripheral blood are higher in cirrhotic-decompensated patients than in primary hepatic tumor patients with or without compensated cirrhosis. Successful OLT normalizes blood PAF levels in cirrhotic-decompensated patients as early as 2 days after completion of surgery. The measure of PAF in peripheral blood seems unrelated to the onset of acute liver rejection episodes;

From the Liver Transplant Unit, Hospital de Bellvitge, Universidad de Barcelona, Barcelona, and Laboratorio de Nefrología, Fundación Jimenez Diaz-CSIC, Madrid, Spain.

Supported by a 1990 grant from Fondo de Investigaciones de la Seguridad Social.

Address reprint requests to Pablo Moreno Llorente, Hospital de Bellvitge, Unidad de Trasplante Hepático, Feixa Llarga s/n, 08907 Hospitalet de Llobregat, Barcelona, Spain.

© 1993 by Appleton & Lange
0041-1345/93/\$3.00/+0

Au: Spell
out CSIC
Au: Match
authors
to their
respective
affiliation

PLATELET-ACTIVATING FACTOR

2659

accordingly, the use of PAF antagonists in clinical liver transplantation deserves future investigations.

REFERENCES

1. Braquet P, Shen TY, Touki L, et al: *Pharmacol Rev* 39:97, 1987
2. Caramelo C, Fernandez-Gallardo S, Santos JC, et al: *Eur J Clin Invest* 17:7, 1987
3. Camussi G, Salvidio G: *Prog Biochem Pharmacol* 22:106, 1988
4. Bligh EG, Dyer WJ: *Can J Biochem Physiol* 37:911, 1959
5. Caramelo C, Fernandez-Gallardo S, Marin-Cao D, et al: *Biochem Biophys Res Commun* 120:789, 1984