



Intraoperative Management of Liver Transplantation for Familial Amyloid Polyneuropathy Met30: What Has Changed in the Last 10 Years?

J.S. Viana, H. Vieira, C. Bento, S. Neves, C. Seco, and A.L. Furtado

FAMILIAL amyloid polyneuropathy (FAP) is a genetic disorder inevitably lethal without liver transplantation. This procedure has been performed for FAP since 1990¹ and this disease is now, by far, the most frequent metabolic indication for liver transplantation, with more than 700 patients having undergone transplantation worldwide. In the last years, results improved significantly, and FAP Met30 1-year survival rates reached 90% to 98%.

Because these patients had no liver insufficiency, their livers have been used as grafts in transplantation of other patients, since October 1995, in the so-called “domino” or sequential liver transplantation.²

PURPOSE

The purpose of this study was to evaluate changes in intraoperative management of FAP Met30 patients during liver transplantation in three successive time periods from 1992 to 2002, and to compare these changes with the intraoperative management of non-FAP adult patients who underwent transplantation in similar periods.

PATIENTS

This study included all 140 patients with FAP Met30 submitted to first liver transplantation in our institution from October 1992 to May 2002. Group IA included 49 patients who underwent transplantation from 1992 to 1996, Group IIA included 44 patients who underwent transplantation from 1997 to 1999, and Group IIIA included 47 patients who underwent transplantation from 2000 to 2002. We used as control the 184 non-FAP patients submitted to first liver transplantation in our institution to 18 years of age or older, divided into Group IB (1992 to 1996, 58 patients), Group IIB (1997 to 1999, 64 patients), and Group IIIB (2000 to 2002, 62 patients).

Within the patients with FAP no group differences were observed concerning age, sex, weight, and duration of clinical disease pretransplantation, although the outcomes were different with 1-year actuarial survival rates of 79.6% in Group IA, 95.5% in Group IIA, and 98.0% in Group IIIA ($P = .010$). Groups also were different concerning donation for domino transplantation as the livers of 5 Group I patients (10%), 19 Group IIA patients (43%), and 27 Group IIB patients (57%) were harvested as grafts for other patients ($P < .001$).

METHODS

The groups were compared with nonparametric tests (Mann-Whitney U test, Kruskal-Wallis test, or chi-square test as appropriate). Kaplan-Meier curves were compared using Cox regression. Data as mean \pm SD.

RESULTS

The anesthetic technique was similar for patients with and without FAP and during all study periods: induction with thiopental, succinylcholine, and fentanyl, maintenance with isoflurane (in oxygen/air), fentanyl, and vecuronium or pancuronium, depending on the heart rate. Immunosuppression also was the same: methylprednisolone and azathioprine in the operating room, and cyclosporine exclusively in the postoperative period. In both FAP and non-FAP, a progressive decrease was observed in use of blood products. For FAP, red blood cells (RBC), needs decreased from 5.8 ± 10.7 U per transplantation in 1992 to 1996 to 4.2 ± 7.4 in 1997 to 1999 to 2.0 ± 2.0 in 2000 to 2002 ($P = .013$). In patients without FAP, the use of decreased RBC fell from 12.5 ± 11.2 U per transplantation in 1992 to 1996, to 14.4 ± 5.5 in 1997 to 1999 to 5.5 ± 5.3 in 2000 to 2002 ($P < .001$). Greater reductions were observed in the use of fresh frozen plasma ($P < .001$ either in FAP or non-FAP), and of platelet concentrates ($P = .046$ in FAP and $P < .001$ in non-FAP). During the last years, albumin was less frequently employed as a plasma expander, with an increase in synthetic solutions, particularly hydroxyethylstarches.

Major differences were observed in vasoactive drugs to support circulation; phenylephrine infusions were used in 12.2% of FAP transplantation in 1992 to 1996, 54.5% in 1997 to 1999, and 53.5% in 2000 to 2002 ($P < .001$). Low-dose dopamine ($<3 \mu\text{g}/\text{kg}/\text{min}$) was used in all patients. Rates equal or higher than $10 \mu\text{g}/\text{kg}/\text{min}$ were used only in 16.3% of Group IA, 8.5% of Group IIA, and 8.5%

From the Departments of Transplantation and Anaesthesiology, Coimbra University Hospitals, Coimbra, Portugal.

Address reprint requests to J.S. Viana, Department of Anaesthesiology, University Hospitals, Pct. Mota Pinto, 3000-075 Coimbra, Portugal. E-mail: jviana@huc.min-saude.pt

of Group IIIA ($P =$ not significant). No statistical differences were observed among non-FAP patients concerning the use of vasoactive drugs. High-dose aprotinin (Hammer-smith regimen) was employed only in the initial 8 (5.7%) FAP transplantation. For non-FAP patients, aprotinin which remained the rule for those with coagulopathies and portal hypertension, was used in 79.2% of transplantation.

Veno-venous porto-caval-axillary bypass with a Biomedicus pump was used in the initial two patients with FAP and the initial 10 patients without FAP before the piggyback technique became the rule. Donation to domino liver transplantation imposed the interruption of the inferior vena cava for patients with FAP and the return to the original technique with bypass. In non-FAP patients, bypass was used occasionally (24.7%) to decompress the venous pressure in the surgical field.

The policy of previous pacemaker insertion in patients with FAP was progressively more defensive. Initially, the rules for pacemaker insertion in patients with FAP waiting liver transplantation were similar to those applied to the general population. Since 1995, the indications include Classes I and II of the classification of the American College of Cardiology and the American Heart Association, resulting in 18% of patients with FAP with an intracavitary pacemaker on the date of transplantation. Recently, preoperative pacemaker insertion was extended to any patient with FAP with a conduction disturbance (even intermittent and asymptomatic) or also history of syncope (even when a cardiac cause was not proved). Overall, 23 patients with FAP (16.1%) had a permanent pacemaker on the date of transplantation. The tendency to earlier transplantation counteracted the increased indications for a pacemaker, the percentage of patients who underwent transplantation with a pacemaker has decreased over time. In control (non-FAP) patients, no one had a pacemaker on the date of transplantation.

DISCUSSION

The major differences in intraoperative management of patients with FAP Met30 for liver transplantation were a progressive increase in the use of pure vasoconstrictors (our choice was phenylephrine), and a progressive decrease in the consumption of blood products (including albumin) with a compensatory increase in synthetic plasma expanders. The reduced consumption of blood products, which may represent better surgical technique or low values of transfusional triggers, was similar to non-FAP patients. The tendency to less extensive use of albumin, which reflects the

general trend of the 1990s, also was common to FAP and non-FAP patients. On the other hand, the changes in vasoactive drugs deserve special comment because they were specific for patients with FAP. When liver transplantation started in FAP, it was known that these patients exhibited remarkable hemodynamic instability during anesthesia and surgery,³ their cardiac risk was soon recognized to be an important factor in transplantation outcome.^{4,5} The causes for hemodynamic instability were not completely clear. The few available reports laid particular emphasis on rhythm disturbances.³ The increased use of vasoconstrictors is a consequence of the understanding that low vascular resistance was the main intraoperative problem⁴⁻⁶ and that these drugs are effective to restore arterial pressures.⁴⁻⁶ Obviously, their increased use in patients with FAP had no parallel in non-FAP patients because deregulation of the autonomic circulatory control was not of special significance in FAP.

On the contrary, the use of dopamine did not increase in FAP and, when used, the tendency was not to use high doses. This practice was a consequence of preliminary reports that dopamine use in patients with FAP did not increase vascular resistance, but rather decreased its frequently being ineffective to support the circulation.^{5,7}

To what extent the changes in intraoperative management have played a role in improving the results of FAP liver transplantation, is a question with no easy answer. It is recognized that the experience achieved in liver transplantation for FAP has increased the safety in anesthetic management of these patients, independent of the kind of surgery and the environment, but the increased posttransplantation survival is probably more related to better patient selection than differences in intraoperative management.

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