

Haemodynamics During Liver Transplantation in Familial Amyloidotic Polyneuropathy: Study of the Intraoperative Cardiocirculatory Data of 50 Patients [75]

JOAQUIM DA SILVA VIANA*, CARLOS BENTO**, HELENA VIEIRA**, SÍLVIA NEVES**, CARLOS SECO**,
LUÍS ELVAS***, LOURENÇO COELHO****, JOSÉ FERRÃO*****, LUÍS TOMÉ*****, RUI PERDIGOTO*****,
ANTÓNIO LOPES CRAVEIRO*****, LUÍS AUGUSTO PROVIDÊNCIA*****,
ALEXANDRE LINHARES FURTADO*****
University Hospitals of Coimbra. Coimbra, Portugal.

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SUMMARY

Background: Circulatory instability frequently complicates liver transplantation for familial amyloidotic polyneuropathy (FAP) and may be a source of surgical morbidity and mortality.

Objective: To evaluate FAP intraoperative haemodynamic data and their relation to the duration of surgery, and need for anaesthetic drugs, RBC and sympathomimetic amines.

Setting: Clinical study during a four year period.

Patients (mean \pm SD): Group I included 50 consecutive FAP ATTR Met 30 recipients of first transplantation. Age was 35.3 ± 7.1 years, neurological score 34.3 ± 13 in 100 and time elapsed from first symptom 5.0 ± 2.7 years. Group II (control), not different concerning age and sex, included 51 patients transplanted during the same period with other pathologies.

Method: Anaesthetic protocol, monitoring

RESUMO

Hemodinâmica Durante Transplante Hepático em Doentes com Polineuropatia Amiloidótica Familiar: Estudo de Aspectos Cardiocirculatórios do Intraoperatório de 50 Doentes

O transplante hepático em doentes com polineuropatia amiloidótica familiar (PAF) é frequentemente complicado por uma severa instabilidade circulatória, a qual pode ser fonte de morbidade e mortalidade cirúrgica.

Concepção do estudo: Estudo clínico com a duração de quatro anos.

Objectivo: Estudar aspectos cardiocirculatórios do intraoperatório de transplante hepático em doentes com PAF de tipo português.

Doentes: O grupo I foi constituído por 50 doentes com PAF ATTR Met 30, sujeitos a primeiro transplante hepático nos Hospitais da Universidade de Coimbra, com $35,3 \pm 7,1$ anos de idade, $5,0 \pm 2,7$ anos de evolução da doença e de $34,3 \pm 13,0$ em 100 de

* Assistente Hospitalar de Anestesiologia, responsável pela Anestesia e Cuidados Intensivos de Transplante Hepático.

** Assistente Hospitalar de Anestesiologia.

*** Assistente Hospitalar de Cardiologia.

**** Interno de Cardiologia.

***** Assistente Hospitalar de Medicina Interna.

***** Professor da Faculdade de Medicina de Coimbra, Assistente Hospitalar de Gastro-enterologia.

***** Professor de Faculdade de Medicina de Coimbra, Assistente Hospitalar de Medicina Interna.

***** Director do Serviço de Anestesiologia dos HUC.

***** Professor Catedrático da Faculdade de Medicina de Coimbra, Director do Serviço de Cardiologia.

***** Professor Catedrático da Faculdade de Medicina de Coimbra, Director da Unidade de Transplantação.

and surgical techniques were similar in both groups. Data of the two groups were compared either by the Student's t-test or Fisher's exact test.

Results: Low values of systemic vascular resistance index were observed in both groups, with no differences between them.

Systemic arterial pressures were usually lower in group I, because cardiac index and heart rate were also significantly lower, although within normal values. However, in group I, isoflurane (a vasodilator anaesthetic) was used during less time ($p < 0.05$) and in lower concentrations ($p < 0.01$) and phenylephrine was necessary in 26% of patients *vs* 0 patients in group II ($p < 0.001$).

Conclusion: FAP patients presented a different intraoperative behaviour when compared to other patients submitted to liver transplantation. From a clinical point of view, the authors stress: 1 – As a result of autonomic dysfunction, the administration of anaesthetic drugs to FAP patients always presents the risk of producing significant hypotension; even the use of ketamine does not prevent hypotension; 2 – Safety is ensured by beat-to-beat surveillance of arterial pressures and the capacity to act immediately to support circulation; 3 – These patients seem to be very sensitive to decreases in the pre-load; 4 – Hypotension is also frequent with an adequate pre-load, usually as the result of low SVR; an infusion of a vasoconstrictor drug emerges as the most frequent treatment requested and our experience supports it as an effective one.

Key-Words

Amyloid; Amyloidosis: familiar;
Anaesthesia: complications: arrhythmias, hypotension;
Transplantation: liver

pontuação neurológica. O grupo II (controle) foi constituído por 51 doentes transplantados no mesmo período devido a outras patologias, que não diferiam do grupo I quanto à idade, sexo e altura.

Método: O protocolo anestésico e a monitorização foram semelhantes em ambos os grupos. Os dados foram comparados pelo teste t de Student para duas amostras ou pelo teste exacto de Fisher, consoante apropriado.

Resultados: Observaram-se valores baixos de resistências vasculares sistémicas em ambos os grupos, não se observando diferenças entre eles quanto ao seu índice. As pressões arteriais foram geralmente mais baixas no grupo I, porque as frequências cardíacas e os índices cardíacos foram igualmente mais baixos neste grupo, embora dentro dos valores da normalidade. Observaram-se estas diferenças apesar de, no grupo I, se usar isoflurano (um anestésico inalatório com efeitos vasodilatadores) durante menos tempo de cirurgia ($p < 0,05$) e em menores concentrações ($p < 0,01$) e ter sido necessário usar fenilefrina em 26% dos doentes deste grupo *vs* 0 do grupo II ($p < 0,001$).

Discussão: Os doentes com PAF apresentam um comportamento circulatório durante o transplante hepático diferente dos outros doentes sujeitos a esta cirurgia. Quanto à segurança intraoperatória, os autores ressaltam: 1 – Devido à disautonomia, os anestésicos apresentam sempre um risco de provocar uma hipotensão importante; mesmo o recurso à *ketamina* não garante que não se observe hipotensão; 2 – São aspectos importantes uma vigilância cardiocirculatória apertada e a capacidade de intervir, de forma rápida, para suporte da circulação; 3 – Estes doentes são normalmente muito sensíveis a reduções da pré-carga; 4 – Mesmo na presença de uma pré-carga adequada, a hipotensão é frequente como resultado de quedas nas resistências vasculares sistémicas; na nossa prática, foi frequentemente necessário o uso de vasoconstritores, os quais se mostraram eficazes para o seu tratamento.

Palavras-Chave

Amilóide; Amiloidose familiar;
Anestesia: complicações: hipotensão, arritmias;
Transplantação: hepática

Familial amyloidotic polyneuropathy (FAP) is a genetic disease, reported by Corino de Andrade⁽¹⁾, which is systemic and the nervous damage is simultaneously sensitive, motor and neurovegetative. It is endemic in Portugal, relatively frequent in Sweden and Japan and sporadic cases have been reported in many other countries^(1,2).

Different clinical presentations are included under the denomination of FAP, type I, or Portuguese type, is by far the most frequent and is characterized by its onset in the lower extremities and autonomic failure⁽²⁾. Different biochemical anomalies are included within the clinical diagnosis of FAP and even within the clinical diagnosis of FAP type I. With very rare exceptions, all cases observed in Portugal are FAP Met 30, identified by the abnormal replacement of a valine by a methionine in position 30 of the transthyrin protein, leading to the amyloid substance responsible for the characteristic lesions⁽³⁾.

The clinical setting begins with neurologic and gastrointestinal symptoms, usually during the third or fourth decade of life, which lead to death about ten years after the initial signs⁽²⁾. The circulatory system is always involved at some point during its evolution. The cardiovascular disturbances of this pathology have been the source of several studies^(1,9) including hundreds of patients. The main conclusions can be summarized as follows:

- orthostatic hypotension and disturbances of rhythm and intracardiac conduction are the most important and frequent circulatory findings;
- circulatory symptoms are the final result of two distinctive mechanisms: autonomic dysfunction and amyloid infiltration of the structures of the cardiocirculatory system, the infiltration of intracardiac conduction tissues being particularly important;
- cardiac failure is a rare event as a direct result of amyloid myocardial infiltration, contrary to findings observed in other types of amyloidosis;

Since transthyretin (either normal or amyloidotic abnormal variants) is produced almost exclusively by the liver, hepatic transplantation arose as a logical treatment for an otherwise terminal disease and, in what concerns FAP patients, it was performed for the first time in Sweden in 1990. It has now been proved that hepatic transplantation in these patients result-

ed in the immediate disappearance of circulating amyloidotic substances^(10,11) and halted the evolution of the disease⁽¹¹⁾. Although liver transplantation is a procedure with relevant mortality and morbidity, it constitutes the only proven treatment with these effects. In November 1997, the FAP World Transplant Registry reported 247 liver transplantations in FAP patients at 34 transplantation centers in 16 countries⁽¹²⁾.

Cardiac and circulatory pathology is always an important risk factor for surgical patients. The involvement of the cardiocirculatory system in FAP can be a potential source of serious intraoperative hazards and it has been reported that anaesthesia and surgery in these patients are frequently complicated by severe hypotension and arrhythmias, even during minor surgical procedures.

Liver transplantation in FAP patients has allowed teams to gain important knowledge on the circulatory behaviour of these patients when submitted to anaesthetics and surgical stress. In other settings, it would certainly be difficult for a single anaesthetic team to manage such a considerable number of patients and use the extensive monitoring conditions that are standard in liver transplantation, in which surgery and post-operative period takes place with pulmonary artery catheterization and monitoring of cardiac output and related haemodynamic values⁽¹³⁾.

The aim of this study was to evaluate the experience of the Liver Transplantation Unit of the University Hospital of Coimbra in what concerns the intraoperative circulatory aspects of liver transplantation performed in FAP patients. It was our purpose to do this in a way that our conclusions could be useful, not only in the environments of liver transplantation, but also as a contribution to the safety of these patients during general anaesthesia performed for any type of surgical procedure.

PATIENTS

In this study we evaluated the circulatory intraoperative aspects of the first 50 consecutive patients, with clinical symptoms of FAP type I and positive to transthyretin Met 30, submitted to first liver transplantation in the University Hospitals of Coimbra during a 50 month period between November 1992 and January 1997 (Group I). Twenty six were male and 24 female aged from 25 to 53 years

(35.3 ± 7.1 years), 163.7 ± 8.8 cm in height, 54.5 ± 11.3 kg in weight (10 ± 15% less than ideal weight), 1.58 ± 0.18 m² of body surface, 20.3 ± 3.4 kg/m² of body mass index (BMI) and 34.3 ± 13.2 in 100 of neurological score on the scale of E. Macedo and col.¹⁰. One to 11 years (5.0 ± 2.7 years) had elapsed from the date of the first symptom until transplantation. Four patients had a definitive pacemaker inserted weeks or months before the surgery.

As a control (Group II), we evaluated adults with other pathologies submitted to first liver transplantation during the same period. To prevent age differences between the two groups we considered the age of 55 years or more as an exclusion factor in this group. Therefore, group II included 51 patients - 34 with cirrhosis, 4 with fulminant liver failure, 3 with sclerosing cholangitis and 10 with miscellaneous liver diseases. Thirty two were male and 19 female, ranging in age from 17 to 54 years (38.5 ± 11.3 years), 165.0 ± 9.8 cm in height, 62.8 ± 11.9 kg in weight (3 ± 18% more than ideal weight), 1.69 ± 0.18 m² of body surface and 23.0 ± 4.1 kg/m² of body mass index (BMI).

METHOD

Anaesthetic and monitoring protocols were similar in both groups.

Anaesthetic induction was performed with 1 to 2 µg/kg of fentanyl, followed by intravenous thiopental in a dosage determined by the loss of eyelid reflexes. For orotracheal intubation, 1 mg/kg of succinylcholine was used. Anaesthesia was maintained with fentanyl and isoflurane vaporized in an air/oxygen mixture and neuromuscular blockade achieved with vecuronium or pancuronium, selection based on the heart rate. In the case of hypotension (sustained systolic arterial pressure below 100 mm Hg) isoflurane was stopped and anaesthesia guaranteed with intravenous ketamine combined with diazepam.

Electrocardiographic monitoring included two leads (DII and V5). According to standards in this kind of surgery, the procedure was performed with an intra-arterial catheter (radial artery) and Swan-Ganz catheter, usually inserted after anaesthetic induction. Four cases with definitive pacemakers were exceptions and in these cases our option was not to use a pulmonary catheter and pre-load monitoring was confined to central venous pressure. Cardiac output was measured by thermodilution in the majority of cases. In a small number of the most recent

cases, a continuous method (Vigilance monitor, Edwards Laboratories) was utilized.

For subsequent comparisons, we used haemodynamic data registered one hour after the beginning of surgery (pre-anhepatic phase), one hour after the removal of the receptor liver (anhepatic phase) and one hour after the complete reperfusion of the graft (post-anhepatic phase).

An infusion with 3 µg/mg/minute of dopamine was administered during the whole procedure. In the case of hypotension with an adequate pre-load, the dose was increased from 5 to 15 µg/kg/minute. In the case of sustained hypotension, an infusion of dobutamine or phenylephrine was used, depending on the aetiology: low cardiac output or low systemic vascular resistances. Significant arrhythmias were treated according to standards.

A venovenous bypass was performed with a centrifugal biopump (Biomedicus) from the inferior vena cava and portal vena to the axillary vena in 10 patients of group I and 17 of group II (p = ns). Antibiotic treatment and immunosuppression protocols were similar in both groups, the latter with methylprednisolone and azathioprine. Ciclosporine was never used in the operating room. An infusion of aprotinin (Hammersmith regimen) was used during all surgery in 18% of patients in group I and 68.6% in group II (p < 0.001).

Thirty patients in each group had complete computer records of partial pressures of oxygen, carbon dioxide and isoflurane in inhaled and exhaled gases during the surgery. These records were used to evaluate intraoperative use of isoflurane in particular.

Data about doses of intravenous anaesthetics, amounts of blood products and use of circulatory drugs were acquired from the manually written anaesthetic records.

STATISTICS

Depending on the type of data, the groups were compared either by two-sample Student's t-test or Fisher's exact test. A probability below 0.05 was considered statistically significant. Values are presented as mean ± standard deviation.

RESULTS

The groups were not different in what concerns age (p = ns), sex (p = ns) and height

($p=ns$), but group II presented greater body weight than group I ($p<0.001$) and consequently greater body surface ($p<0.01$) and BMI ($p<0.001$).

The duration of anaesthesia (from induction until operating room discharge) was shorter in group I: 599.5 ± 160.3 minutes *vs* 667.7 ± 171.7 minutes in group II ($p<0.05$).

The consumption of red blood cells was less in FAP patients: 5.7 ± 10.7 units in group I and 12.2 ± 10.1 units in group II ($p<0.01$). The median was 3.0 units in group I and 8.5 units in group II.

The dose of thiopental used for anaesthetic induction was similar in both groups ($p=ns$), but, in what concerns the whole anaesthesia time, it was necessary to administer more fentanyl in group II ($p<0.001$) (Table I).

Haemodynamic instability lead to the cessation of isoflurane administration during significantly more time in group I when compared to group II ($p<0.05$). In what concerns the period of utilization exclusively, inhaled and exhaled isoflurane concentrations were higher in group II ($p<0.01$). Ketamine was used to maintain anaesthesia during sustained hypotension in 20 patients (40.0%) in group I and 4 patients (7.8%) in group II ($p<0.001$) (Table II).

With regard to circulatory drugs, a dobutamine infusion was used in 2 patients (4.0%) in group I and 7 patients (13.7%) in group II ($p=ns$) and phenylephrine in 13 patients (26.0%) in group I and 0 patients in group II ($p<0.001$) (Table I).

In spite of the different utilization of these drugs – less isoflurane and more ketamine and phenylephrine in group I – blood pressures in most cases were lower in this group, basically as the result of lower cardiac indices as no differences were observed in systemic vascular resistance indices (Table II).

Lidocaine was used for the treatment of ventricular arrhythmias in 6 patients (12.0%) in group I and in one patient (2.0%) in group II ($p=ns$). Propranolol was used in one case in group I and verapamil in one case in group II ($p=ns$) for supraventricular arrhythmia treatment.

DISCUSSION

Our study shows that, in what concerns haemodynamics during liver transplantation, FAP patients are quite different from the remaining patients submitted to this surgery.

Table I

Utilization of anaesthetic and cardiocirculatory intravenous drugs in two groups. Data are reported from all patients in the study. Only for thiopental, were four patients in group II pre-operatively intubated and this drug not used

	Group I	Group II
Thiopental dose ($p=ns$)	339 ± 64 mg	360 ± 85 mg
Fentanyl dose ($p<0.001$)	419 ± 210 μ g	868 ± 537 μ g
Patients with dopamine infusions ($p=ns$)	50 (100%)	51 (100%)
Patients with beta doses of dopamine ($p=ns$)	21 (42.0%)	18 (35.3%)
Patients with alpha doses of dopamine ($p=ns$)	8 (16.0%)	6 (11.8%)
Patients with dobutamine infusions ($p=ns$)	2 (4.0%)	7 (13.7%)
Patients with adrenalin infusions ($p=ns$)	0	1 (2.0%)
Patients with phenylephrine ($p<0.001$)	13 (26.0%)	0
Patients with lidocaine ($p=ns$)	6 (12.0%)	1 (2.0%)
Patients with beta-blockers ($p=ns$)	1 (2.0%)	0
Patients with amiodarone ($p=ns$)	0	1 (2.0%)
Patients with verapamil ($p=ns$)	0	1 (2.0%)

This is clearly visible in two different aspects: firstly, the need for vasoconstrictors is significantly greater in Group I, although the surgical procedure is technically easier and performed in patients without coagulation disorders and, consequently, shorter and less haemorrhagic; secondly, a reduced tolerance to the depressive effects of anaesthetic drugs was also observed in group I, a fact that is perceived in the lower time of utilization of inhalation

Table II

Utilization of isoflurane in the two groups. Data are reported from 30 patients in each group (patients with complete computerized records of the anaesthetic concentrations). Mean exhaled and inhaled concentrations were calculated during the period in which this anaesthetic was utilized and not for the total duration of the surgical procedure

	Group I	Group II
Surgical time without isoflurane ($p<0.05$)	28 ± 30 %	16 ± 24 %
Inhaled concentration of isoflurane ($p<0.01$)	0.41 ± 0.13 %	0.55 ± 0.20 %
Exhaled concentration of isoflurane ($p<0.01$)	0.34 ± 0.11 %	0.46 ± 0.16 %

nal anaesthetics and the lower concentrations when they were used.

Severe hepatoopathies, acute or chronic, are characterized by hyperdynamic circulation with high cardiac output (CO) and low systemic vascular resistances (SVR)⁽¹⁵⁻¹⁶⁾. The values observed in group II could not be considered abnormal considering the pathologies observed in these patients, and are similar to the data previously reported by several authors as haemodynamic values during liver transplantation^(16, 17).

Contrary to liver patients, it is expected that FAP patients present normal preoperative values of CO and SVR. No published data exist against this assumption and our own preoperative haemodynamic studies, although including only a short number of cases, support this⁽¹⁸⁾. Therefore, it is rather uncommon to find low intraoperative values of SVR in group I, in general not different or with small differences compared to the values of group II. This fact must be considered, in our opinion, as a consequence of particular sensitivity to the vasodilation effects of one or more drugs used during the intraoperative period. On reviewing the pre-

viously described circulatory effects of each one of the drugs used, the main suspicion obviously goes to the anaesthetic drugs.

Isoflurane is the most commonly used anaesthetic in clinical practice and it does not usually produce a significant drop in blood pressure. A certain degree of systemic vasodilation could be found with its use, but it is normally compensated by a reflex increase in cardiac output.

Nevertheless, its direct myocardial effects are depressive and they could be clinically relevant and a matter of particular concern in severely ill patients with cardiac disease and abnormal circulatory status⁽¹⁹⁻²¹⁾.

Fentanyl is an opioid analgesic with an almost universal use in anaesthesia. It produces a minimal decrease in heart rate, usually without effects in arterial pressures, CO or SVR. However, in situations where adequate blood pressures are sustained by an increased sympathetic outflow, the administration of fentanyl can produce a lisis in this outflow and be followed by a drop in arterial pressures and SVR⁽²²⁾.

Due to the possible hypotensive effects of the anaesthetic drugs, it is a routine, in gene-

Table III

Haemodynamic data observed in two groups. Initial values were registered before anaesthetic induction, pre-anhepatic phase values were registered one hour after the beginning of surgery, anhepatic phase values were registered one hour after the removal of the receptor liver and post-anhepatic phase values are registered one hour after the complete reperfusion of the graft

		HR (beats/min)		AP syst (mmHg)		AP diast (mmHg)		AP mean (mmHg)	
Initial values	Group I	86.2 ± 14.3	p=ns	138 ± 22	p=ns	74 ± 15	p < 0.05	92 ± 13	p=ns
	Group II	89.3 ± 17.0		140 ± 21		67 ± 14		90 ± 15	
Pre-anhepatic phase	Group I	92.8 ± 15.9	p < 0.05	111 ± 16	p < 0.01	56 ± 9	p=ns	74 ± 10	p < 0.05
	Group II	101.3 ± 17.5		120 ± 15		60 ± 9		79 ± 10	
Anhepatic phase	Group I	93.1 ± 14.4	p < 0.001	114 ± 14	p=ns	59 ± 7	p < 0.01	77 ± 9	p < 0.01
	Group II	105.2 ± 14.1		119 ± 18		66 ± 13		83 ± 14	
Post-anhepatic phase	Group I	93.7 ± 13.6	p < 0.001	110 ± 13	p < 0.01	55 ± 9	p < 0.05	72 ± 10	p < 0.001
	Group II	107.2 ± 12.4		122 ± 16		60 ± 13		79 ± 14	
		PAP syst (mmHg)		PAP diast (mmHg)		PAP mean (mmHg)		PAP wedge (mmHg)	
Pre-anhepatic phase	Group I	22.1 ± 6.1	p < 0.05	9.3 ± 3.0	p < 0.05	14.7 ± 4.0	p < 0.01	9.2 ± 3.5	p=ns
	Group II	25.3 ± 7.0		11.0 ± 3.6		17.4 ± 4.8		9.8 ± 4.2	
Anhepatic	Group I	20.9 ± 6.0	p=ns	8.7 ± 3.1	p=ns	13.7 ± 3.5	p < 0.05	8.4 ± 3.3	p=ns
	Group II	23.0 ± 5.9		9.2 ± 4.2		15.2 ± 4.3		8.7 ± 3.6	
Post-anhepatic phase	Group I	23.3 ± 5.3	p < 0.01	10.3 ± 3.8	p < 0.05	15.8 ± 4.5	p < 0.01	10.0 ± 3.4	p=ns
	Group II	26.1 ± 5.3		11.8 ± 4.4		18.1 ± 4.0		11.2 ± 3.6	
		CVP (mmHg)		CI (L/m ²)		SVR (dyn/sec/cm ⁵ /m ²)		SVRI (dyn/sec/cm ⁵ /m ²)	
Pre-anhepatic phase	Group I	7.9 ± 2.7	p=ns	1.2 ± 0.8	p < 0.001	821 ± 233	p < 0.01	1280 ± 305	p=ns
	Group II	8.4 ± 3.5		5.2 ± 1.3		689 ± 254		1153 ± 388	
Anhepatic phase	Group I	7.2 ± 2.2	p < 0.05	1.2 ± 1.0	p < 0.05	876 ± 283	p=ns	1368 ± 390	p=ns
	Group II	8.5 ± 3.1		4.7 ± 1.4		840 ± 341		1413 ± 540	
Post-anhepatic phase	Group I	8.8 ± 3.0	p=ns	4.5 ± 0.9	p < 0.001	726 ± 203	p=ns	1149 ± 307	p=ns
	Group II	9.5 ± 3.3		5.6 ± 1.4		638 ± 290		1068 ± 439	

ral anaesthesia practice, to reduce or suspend the delivery of volatile anaesthetic and to avoid the administration of fentanyl in situations where hypotension is observed. This means that one can estimate the degree of circulatory stability of any anaesthetic procedure by the evaluation of the periods of time without isoflurane, their duration, the concentrations used and also the total amount of opioid drugs.

In our results, the doses of fentanyl are clearly lower in FAP patients when compared with those in liver patients, and isoflurane is also used during less time and in small concentrations. This must be understood as a clear sign that the tendency of hypotensive episodes during liver transplantation is much greater in FAP patients than in liver patients.

However, based on previous knowledge of the autonomic dysfunction that characterizes the disease, we are likely to assume that these abnormal responses may not be the result of a direct action on the circulatory system, but, on the contrary, the result of a reduction or suppression of the compensatory neurovegetative reflexes. With regard to values registered in heart rate, it is necessary to consider the finding that group I patients have lower heart rate despite longer periods with no isoflurane and lower arterial pressures as relevant. In our opinion, this is the consequence of a certain degree of inability of FAP patients to increase heart rate and therefore cardiac output has compensatory mechanisms in the presence of hypotension and low SVR.

The use of intravenous ketamine in some patients must be discussed. In several aspects, including the mechanism of action and circulatory and respiratory effects, this drug is unique among anaesthetic drugs. In what concerns circulation, it is the only one that produces tachycardia and hypertension. Due to its clinically relevant side effects, its role in clinical anaesthetic practice is, in general, of a second line drug, reserved to situations where hypotension and haemodynamic instability is observed. In our liver transplantation anaesthesia protocols, ketamine is used to maintain the patient unconscious during the situations where isoflurane administration was ceased due to low arterial pressures.

It is also rather curious that, although ketamine was used in 40% of group I patients and only in 7.8% of group II patients; we still found low SVR values in group I patients (and had to use phenylephrine in 26% of patients in this group and no phenylephrine in group II patients).

This leads us to think that ketamine may not have a hypertensive effect on FAP patients and not exclude the possibility that it may produce hypotensive action.

The explanation for these findings should be sought in its mechanisms of action. The ketamine stimulation of the circulatory system is mainly a central one, transmitted to the effect organs by the autonomic nervous system and resulting in an increase in noradrenalin levels in sympathetic receptors. Some evidence exists suggesting that the direct effects of ketamine on the circulatory organs are depressive, usually not clinically visible because they are overcome by central increase in sympathetic activity^(23, 24).

FAP patients present autonomic compromise and low noradrenalin levels^(6, 8). In the laboratory, tyramine, a drug that promotes noradrenalin release, does not produce a normal increase in this mediator⁽⁸⁾ and during liver transplantation noradrenalin levels of FAP patients are about one third to one half of the levels measured in liver patients⁽²⁵⁾. In these settings, we are able to admit that ketamine, at least in some FAP patients, lacks its hypertensive action and can even have a hypotensive effect.

Another important subject for discussion is the problem of intraoperative rhythm and conduction disturbances since, in the past, severe intra-operative bradyarrhythmia associated to hypotension were reported in patients with no rhythm problems detected pre or post-operatively⁽²⁶⁾. Amyloid infiltration of intracardiac conduction and autonomic dysfunction are frequent findings in FAP and it was considered that they could be a source of particular sensitivity to arrhythmias during anaesthesia. Some authors assumed that these patients should always be submitted to the insertion of a transitory pacemaker⁽²⁶⁾ before any anaesthetic procedure, a practice still maintained in some transplantation centers⁽²⁷⁾. Some recent data support the tendency to consider that attitude overzealous and to reserve the preoperative insertion of pacemakers to patients with documented alterations in conduction⁽²⁸⁻³⁰⁾. Our experience supports these findings since our data show that only four patients had a definitive pacemaker, and we have no records of any therapeutic manoeuvres for correction of bradyarrhythmias, including the use of emergency pacemaker (always available in the operating room) or isoprenaline infusions.

However, in this study we only evaluate the number of therapeutic interventions and

not the incidence of arrhythmias. With regard to the number of therapeutic interventions requested, we can refute that severe arrhythmias are frequent complication in FAP liver transplantation, but we can not prove that they are not a rare, but severe complication. Therefore it is our opinion that subsequent studies need to be done on this point, including intraoperative Holter as standard material.

Summarising the most important goals for general anaesthetic practice, we consider the key-points for the safety of FAP patients submitted to anaesthesia and surgical procedures to be as follows:

Firstly – It is necessary to bear in mind that the administration of anaesthetic drugs to FAP patients always presents a substantial risk of severe hypotension, and requires a beat-to-beat surveillance of the circulatory data. This is probably true with all anaesthetic techniques available and even the use of ketamine does not prevent hypotension.

Secondly – The high frequency of situations that require pharmacological interventions to support circulation implies that these situations must be anticipated and prepared for in advance. It is important to be able to give a rapid response in the frequent circumstances where hypotension presents a severe degree.

Thirdly – These patients seem to be very sensitive to decreases in the pre-load and require careful surveillance and correction in this aspect.

Fourthly – Hypotension is also frequent with an adequate pre-load, a drop in low systemic vascular resistances being the most relevant implicated mechanism. There could be several therapeutic interventions, but if the purpose is to restore the normality in haemodynamic values, the most logical approach is the administration of a pure vasoconstrictor. Trying to increase the cardiac output to compensate the low SVR could be another approach to treat hypotension even changing the pre-load to supra-normal values or increasing heart rate and contractility with inotropic drugs.

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Pedido de separatas para
JOAQUIM DA SILVA VIANA
Serviço de Anestesiologia
Hospitais da Universidade de Coimbra
3049 Coimbra Codex – Portugal

VI Reunião da Associação Portuguesa de Hipertensão

HOTEL DOS TEMPLÁRIOS
TOMAR

4 a 6 de Fevereiro
de 2000

