Safe use of induced hypotension in a patient with cirrhotic liver disease

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Induced hypotension was used in a patient with chronic active hepatitis and cirrhosis presenting for clipping of an intracranial aneurysm. A mean arterial pressure of 50 mmHg was produced with a combination of sodium nitroprusside and labetalol. The patient sustained no postoperative changes in hepatic function. Previous studies have examined the effects of induced hypotension on the function of the normal liver, but there is relatively little information available on its effects in the presence of liver disease. The lack of an adverse outcome in this patient does not prove the safety of this technique in patients with liver disease; further studies of this patient group are required.

Induced hypotension, often to profound levels, is indicated for clipping of intracranial aneurysms, both to facilitate surgery and to prevent intraoperative aneurysm rupture. Information is available concerning brain, kidney, and cardiac function during induced hypotension.[1] Hepatic disease is commonly listed as a relative contraindication to its use. Since the liver has little or no ability to autoregulate,[2] blood flow may decline passively with systemic blood pressure, and in an already diseased liver, one would be concerned about the possible risk of hepatic ischaemia. We report the successful use of sodium nitroprusside-induced hypotension in a patient with chronic active hepatitis and cirrhosis for intracranial aneurysm surgery.

Case report

A 36-year-old, 80 kg woman was scheduled to undergo craniotomy for clipping of a right internal carotid artery

Key words

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aneurysm. Her past history included hepatitis B infection at age 12, with subsequent biopsy-proven chronic active hepatitis and cirrhosis. Several bouts of upper gastrointestinal bleeding and hepatic encephalopathy had occurred within five years of the current admission. Angiograms showed portal hypertension and oesophageal varices. The patient's medications included cimetidine 300 mg q.i.d., spironolactone 100 mg b.i.d., and lactulose 20 ml b.i.d. Preoperative physical examination revealed jaundice, finger clubbing, palmar erythema, and spider angiomata. A grade III/VI systolic ejection murmur was audible at the left sternal border and mild ascites was present.

The haemoglobin was $11.9 \text{ g} \cdot \text{dl}^{-1}$, platelet count $120,000 \text{ mm}^{-3}$, prothrombin time (PT) 15.8 sec (control 10–13) and partial thromboplastin time (PTT) 35.4 sec (control 21–31). The abnormal PT and PTT failed to reverse with vitamin K administration. The serum albumin was $2.6 \text{ g} \cdot \text{dl}^{-1}$, total protein $6.2 \text{ g} \cdot \text{dl}^{-1}$, and total bilirubin $5.6 \text{ mg} \cdot \text{dl}^{-1}$. Lactate dehydrogenase (LDH) was $310 \text{ IU} \cdot \text{L}^{-1}$ (normal 100–185), serum glutamic oxaloacetic transaminase (SGOT) $74 \text{ IU} \cdot \text{L}^{-1}$ (normal 7–40) and alkaline phosphatase $172 \text{ IU} \cdot \text{L}^{-1}$ (normal 20–110). Hepatitis B surface antigen and core antibody were positive. The chest x-ray showed a prominent pulmonary artery and the heart size and pulmonary vasculature were at the upper limits of normal. The ECG was within normal limits. An echocardiogram showed hypertrophy of both atria and of the left ventricle. A cerebral angiogram showed an aneurysm at the right carotid bifurcation. Although the aneurysm was not producing symptoms, the patient was a candidate for liver transplantation and it was considered most appropriate to repair the aneurysm as the initial procedure.

The morning of surgery, two units of fresh frozen plasma were administered following which the PT was 14.2 sec. In the operating room, a 7F balloon-tipped thermodilution Swan-Ganz catheter was placed via the right external jugular vein and a radial arterial catheter was placed, both under local anaesthesia. Haemodynamic values and blood gases pre-, intra-, and postoperatively are shown in Table 1. Anaesthesia was induced with sufentanil 100 μg and droperidol 2.5 mg. Lidocaine 100 mg IV and pancuronium 10 mg were administered prior to

TABLE I   Haemodynamics

	Prior to induction	Post-induction	Hypotension	Post-hypotension	Post-op (ICU)
BP (mmHg)	120/76	120/70	70/40	122/72	130/70
MAP (mmHg)	90	86	50	88	88
PAP (mmHg)	42/27	45/31	39/23	38/26	43/16
PCWP (mmHg)	25	18	14	14	10
CO ($L \cdot min^{-1}$)	12.5	11.0	9.1	8.1	12.5
SVR ($dyne \cdot s \cdot cm^{-5}$)	460	524	330	750	525
Arterial blood gases					
pH	7.41	7.47	7.46	7.45	7.39
$PaCO_2$ (mmHg)	41	35	35	36	42
PaO_2 (mmHg)	61	268	199	319	85
FiO_2	0.21	1.0	1.0	1.0	0.35
$P\bar{v}O_2$ (mmHg)	46	59	52	54	
$S\bar{v}O_2$ (%)	80	88	84	87	

BP = blood pressure; MAP = mean arterial pressure; PAP = pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; CO = cardiac output; SVR = systemic vascular resistance; FiO_2 = fractional inspired O_2; $P\bar{v}O_2$ = mixed venous PO_2; $S\bar{v}O_2$ = % mixed venous O_2 saturation.

tracheal intubation. Anaesthesia was maintained with sufentanil (total dose 200 μg), isoflurane 0.20 per cent end-tidal, and oxygen 100 per cent. Additional monitoring included an ECG, mass spectrometer (providing end-tidal and inspired analysis of O_2, N_2O, CO_2, and isoflurane), ECG and a neuromuscular transmission monitor. Sodium nitroprusside, $3-5 \mu g \cdot kg^{-1} \cdot min^{-1}$ and labetalol 30 mg were used to lower mean arterial pressure (MAP = 2/3 diastolic BP + 1/3 systolic BP) to 50 mmHg for 45 minutes during dissection and clipping of the aneurysm. Blood loss was estimated to be 800 ml. Four units of fresh frozen plasma and two units of packed red blood cells were administered intraoperatively. Neuromuscular relaxation was reversed with neostigmine 3.0 mg and glycopyrrolate 0.6 mg. The patient awakened immediately postoperatively and was fully alert and responsive. In the postoperative period, no new neurological deficits developed and there was no significant change in transaminase values (Table II) and no clinically evident alterations in hepatic function. The patient was discharged home on the tenth postoperative day. Two months later a successful liver transplant was performed.

Discussion
Conflicting data exist on liver blood flow and metabolism during induced hypotension. In dogs, Gelman and Ernst,[3] using sodium nitroprusside (SNP), $10-20 \mu g \cdot kg^{-1} \cdot min^{-1}$, decreased MAP to 70 mmHg (a 40 per cent change). While hepatic and portal blood flows sustained decreases, there were no changes in liver oxygen consumption or the liver lactate:pyruvate ratio. At higher concentrations of SNP (above $25 \mu g \cdot kg^{-1} \cdot min^{-1}$), blood pressure declined more than 50 per cent, portal and hepatic flows decreasd 80 and 40 per cent respectively, and portal and

hepatic venous oxygen contents declined $5 ml O_2 \cdot dl^{-1}$ blood. Unfortunately, the authors eliminated this latter data set and did not analyze it in their report.

In contrast, Lagerkranser et al.[4] decreased MAP in dogs to 50 mmHg, a 60 per cent change, using SNP at an average dose of $14 \mu g \cdot kg^{-1} \cdot min^{-1}$. Portal venous flow initially decreased 16 per cent, then by 60 minutes returned to control, while hepatic arterial flow decreased 39 per cent over the study period. Oxygen uptake in the preportal tissues and the liver was unchanged, while hepatic oxygen extraction increased from both the hepatic arterial and portal venous systems. No significant alteration in hepatic lactate extraction was found. The authors concluded that SNP-induced hypotension to MAP 50 mmHg resulted in a reduction in hepatic blood flow, but this change was balanced by increased hepatic oxygen extraction resulting in overall unchanged hepatic metabolism.

Dong et al.[5] produced extreme hypotension (MAP 12–25 mmHg) in 20 dogs. Eight died, but among the

TABLE II   Enzymes and bilirubin

Day	LDH	SGOT	ALKP	Bilirubin
Day prior to surgery	310	74	172	5.6
Post-op				
Day 1	256	64	119	6.0
Day 2	273	61	113	6.8
Day 3	349	56	113	8.2
Day 5	273	56	95	6.4
Day 8	257	47	138	7.9

LDH = lactate dehydrogenase, $IU \cdot L^{-1}$, normal 100–185; SGOT = serum glutamic oxaloacetic acid transaminase, $IU \cdot L^{-1}$, normal 7–40; ALKP = alkaline phosphatase, $IU \cdot L^{-1}$, normal 20–110; Bilirubin, $mg \cdot dl^{-1}$, normal = 0.5–1.0.

survivors, nearly all showed elevations in SGOT, serum glutamic pyruvic transaminase (SGPT), and alkaline phosphatase, as well as histological evidence of hepatic necrosis. CNS function, by neurological, behavioural and histological examinations, remained intact. These authors concluded that the liver was more susceptible to ischaemic damage from profound hypotension than the brain. None of these studies specifically addressed the significance of duration of hypotension.

In a large group of patients undergoing total hip arthroplasty, MAP of 50 mmHg was produced with halothane or SNP.[6] No difference between postoperative SGPT, SGOT, serum bilirubin or alkaline phosphatase were detected in hypotensive versus non-hypotensive controls. In patients undergoing gynaecological surgery,[7] liver blood flow was assessed by clearance of indocyanine green (ICG) under normotensive and hypotensive conditions. At a MAP or 52–57 mmHg produced either by SNP or lumbar epidural blockade, no changes in ICG clearance were noted. Two recent abstracts[8,9] also reported no changes in ICG clearance at MAP ranging from 35–55 mmHg produced by SNP or isoflurane. The data from these human studies show no apparent adverse effects of induced hypotension upon the liver in normal patients.

In our patient, labetalol, a combined alpha and beta-adrenergic antagonist, was used as an adjuvant for induced hypotension. No information is available on its effects on hepatic blood flow and therefore its use may be questioned. Propranolol $0.1 \, mg \cdot kg^{-1}$ antagonizes the hepatic arterial or vasodilator response to isoproterenol but does not alter hepatic arterial or portal venous resistances.[10] When given intraportally ($1 \, mg \cdot kg^{-1}$), in the rat, it constricts hepatic sinusoids.[10] The effects of alpha-adrenergic antagonists are more difficult to assess, but in rats, phenoxybenzamine, $1 \, mg \cdot kg^{-1}$ intraportally, dilates the liver sinusoids.[10] The combined effects on the liver of alpha and beta blockade are not known.

It remains to be determined if the information known concerning liver blood flow and metabolism under hypotensive conditions in normal livers can be applied to patients such as ours. However, intraoperatively no evidence of impaired organ perfusion occurred, and postoperatively there was no clinical or laboratory evidence of any alteration in hepatic function.

While many agents are available for inducing hypotension, SNP was chosen because of the previously cited evidence, albeit limited, that it produces minimal changes in hepatic blood flow and metabolism. Labetalol was chosen as an adjunct both to decrease heart rate and to maintain MAP at a stable value of 50 mmHg. It is entirely possible that other agents, alone or in combination, could have been used successfully as well. Comparative studies in humans or animals would be necessary to clarify this issue.

In summary, we have shown the apparent safety of induced hypotension to MAP 50 mmHg for 45 minutes using SNP and labetalol, in a patient with cirrhosis. It must be emphasized, however, that one does not know how representative this patient was of other patients with hepatic injury. Factors such as the presence of acute inflammation or the metabolic rate of the injured liver may modify the response to hypotension. Further studies of liver blood flow and metabolism in diseased livers during induced hypotension are needed in an animal model or in humans in order to define the safe limits of hypotension in this patient population.

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Résumé

L'hypotension contrôlée fut utilisée chez un patient atteint de cirrhose et d'une hépatite chronique active se présentant pour clampage d'un anévrysme intracrânien. Une pression artérielle moyenne de 50 mmHg était induite avec du nitroprussiate et du labétolol. Le patient n'a démontré aucun changement post-opératoire dans sa fonction hépatique. Des études antérieures ont examiné les effets de l'hypotension contrôlée sur la fonction hépatique normale. Relativement peu d'information est disponible sur les effets de l'hypotension contrôlée en présence d'une atteinte hépatique. L'absence d'effets secondaires chez ce patient n'est cependant pas une preuve de la sécurité de cette technique chez les patients atteints de maladie hépatique. D'autres études sur ce groupe de patients sont requises.