High-dose insulin therapy in a case of subarachnoid hemorrhage-related severe cardiodepression with ischemic-like electrocardiographic changes

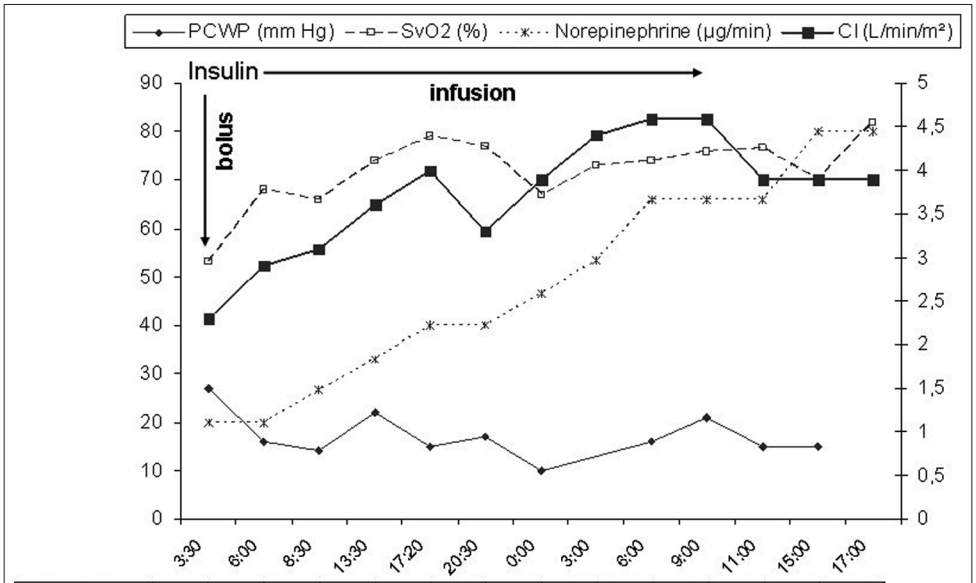
Sir,

A significant myocardial dysfunction may occur

during subarachnoid hemorrhage (SAH).[1] Since, catecholamines are thought to represent one of the potential mechanisms, the treatment of acute heart failure with catecholamines as first-line inotropic agent could be potentially harmful.[2] We describe a case for which high-dose insulin therapy was considered as a preferred option.

A 53-year-old woman (60 kg weight) was admitted with a Glasgow Coma Score at 3/15 after evidence of a major subarachnoid bleeding (Fisher scale 4) on brain computed tomography. Angiography confirmed the presence of two aneurysms located on the intracranial part of the left internal carotid artery. On admission, arterial blood pressure was only 83/58 mm Hg. The first electrocardiogram (ECG) showed a marked elevation of the ST-segment in the inferior and lateral territories, mimicking acute myocardial infarction (AMI). Heart rate was 110/min. Echocardiography confirmed a marked and diffuse alteration of the left ventricular (LV) function (ejection fraction <20%). Right ventricular contractility was normal, with also no evidence of pulmonary hypertension or valvular disease. The peak troponin-I concentration was 11.05 ng/mL (<0.08), while the peak B-type natriuretic peptide value was 2234 pg/mL (<100). Due to the risk of low cerebral perfusion pressure in the presence of intracranial hypertension, vasopressors (norepinephrine) were started immediately. Superior vena cava venous saturation ($ScvO_2$) was measured at 50%. A Swan-Ganz catheter was inserted and measurements confirmed a low cardiac output with high central venous pressure, high capillary wedge pressure, and high systemic vascular resistances [Figure 1]. Inotropic support was considered; however, because of tachycardia with ischemic-like changes on the ECG, high doses of insulin were preferred over dobutamine or epinephrine. A bolus of 60 IU (1 IU/kg) insulin together with 30 g intravenous glucose was given. This was immediately followed by a continuous infusion of insulin at the rate of 1 IU/kg/hour, together with 30% glucose infusion (rate ranging from 100 to 150 mL/hour), for the next 30 h. Blood glucose and potassium levels were checked hourly, and glucose and potassium perfusion were adapted to avoid any metabolic side effects of the treatment. Hemodynamic changes are shown in Figure 1. Heart rate was not modified during therapy. At the end of insulin infusion, a mild decrease of cardiac index was noted but followed by a progressive rise up to 4.5 L/min/m^2 21 h later. Echocardiography normalized 10 days after this acute heart failure episode, with LV ejection fraction more than 50%. Further neurological evolution was characterized by hydrocephalus, intraventricular catheter insertion complicated by intraparenchymal bleeding, rising intracranial pressure and finally death on day 30. Cardiac examination at autopsy revealed normal coronary arteries.

Acute ECG changes are particularly frequent following SAH and may mimic AMI in patients who have typically



HR (bpm)	107	110	111	111	120	104	110	105	112	110	104		95
SBP (mmHg)	101	100	82	114	102	98	98	98	107	111	88	101	106
DBP(mmHg)	66	64	58	70	67	56	54	23	57	62	62	54	63
SVRI (dyne*s/cm^5)	2783	2207	1781	1911	1460	1697	1395	1218	1270	1357	1477	1456	1600

Figure 1: Hemodynamic data. HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PCWP: Pulmonary capillary wedge pressure; CI: Cardiac index; SVRI: Systemic vascular resistances index; SvO_2: Pulmonary artery oxygen saturation

normal coronary arteries.[3] These abnormalities may be associated to transient LV dysfunction usually reported as "neurogenic stunned myocardium." The true incidence is not known but may reach up to 10% of SAH patients. Pathophysiology of this entity includes high doses circulating catecholamines usually observed in those patients as well as direct release of cathecholamines immediately within the myocardium through direct innervations.[4] There is probably an overlap between typical takotsubo cardiomyopathy (apical ballooning) and variants characterized by diffuse ventricular dysfunction leading to cardiogenic shock. The treatment of these severe forms usually includes catecholamines administration or even intraaortic balloon pump. There is, however, an increasing interest for the myocardial metabolic and inotropic properties of insulin. High doses of insulin may have potential benefits in situations where the use of drugs increasing myocardial oxygen consumption is not warranted (possible worsening of myocardial ischemia by catecholamines-induced tachycardia). High-dose insulin infusion has been shown to have positive inotropic effects in experimental models and in humans with altered or normal LV function while preserving heart rate.[5] The positive inotropic effects of insulin result from at least three actions:myocardial metabolic switch from free fatty acids oxidation to glucose, systemic vasodilation, improvement of calcium-dependent contractility.[6] The insulin-mediated positive inotropy is not related to catecholamine release and is partially independent from glucose. Because the calcium ion is known to play a crucial role in excitation-contraction coupling, it is possible that insulin-induced positive inotropy may be mediated through changes in calcium movements in the cells.[6] That insulin has also vasodilatory properties is illustrated by the fact that we had progressively to increase norepinephrine infusion rate during insulin therapy. However, after the improvement of cardiac output and withdrawal of high-dose insulin infusion, high requirement for norepinephrine persisted for several hours, suggesting some degree of vasoplegia that could not be related to insulin.

Conclusion

We suggest that the inodilator properties of high doses of insulin should be further explored in SAH patients with severe LV dysfunction.

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