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Levosimendan in septic cardiac failure

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Cardiac failure in septic shock is not always corrected by vasoactive-inotropic drugs and fluid therapy [1]. Levosimendan is a new inodilator for primitive cardiac failure acting by sensitising troponin-C to calcium and opening the adenosine-triphosphate-sensitive potassium channels. In addition, it has phosphodiesterase-inhibiting properties [2]. Animal data (in vitro [2] and pre-treatment in vivo [3]) showed a positive effect when used in septic shock, as well as in different types of shock in humans, some of which were septic [4]. The drug's mode of action in septic cardiac failure could also be different from calcium sensitivity [2].

We used levosimendan in two cases of septic shock with cardiac failure unresponsive to standard treatment (Table 1). Patient A was a 26-year-old, previous healthy female, admitted in shock due to bacterial pneumonia. Day 1: mechanical ventilation, fluid loading and continuous infusion of vasopressors improved the hemodynamic status but myocardial competence was getting worse with anuria, gut ischemia, intestinal bleeding, and cutaneous necrosis (Day 2).

Patient B was a 79-year-old male, with dilated cardiomyopathy, admitted in shock due to acute cholangitis. Day 1: despite mechanical ventilation, fluid loading and continuous infusion of vasopressors, a severe hypo-dynamic state was present. Day 2: we tried to adjust vasopressor dosages without significant clinical change. In both cases, on day 3, a loading dose of levosimendan (12 μg/kg, but not in patient B because of atrial fibrillation at high frequency) followed by a 24-h continuous infusion at 0.1 μg·kg·min was administered.

A clinical improvement of shock was recorded at 2 h of levosimendan administration. There was improvement of pulmonary venous oxygen saturation and a decline in serum lactate levels. The peak of the hemodynamic effect was reached between 6–18 h allowing a concomitant de-

Table 1 Best hemodynamic parameters found in the selected days in patient A and B. Days 1–2: standard septic-shock therapy. Day 3: before levosimendan infusion (pre-) and during 24-h treatment. Day 8 (patient A), day 6 (patient B): withdrawal of amine infusion. (*NE* norepynephrine, *DB* dobutamine).

Patient A												
Day	Vasoactive Drugs	HR (bpm)	MAP (mmHg)	CVP (mmHg)	PAPm (mmHg)	WP (mmHg)	SvO2 (%)	CI/SI (l·min·m^2)/(ml/m^2)	SVR (dyne·s/cm^5·m^2)	Shunt (%)	Lactate (mmol/l)	pH
1	NE 12 μg/min DB 10 μg·kg·min	143	59	14	28	19	75	4. 7/33	497	48	4. 6	7. 36
2	NE 10 μg/min DB 12 μg·kg·min	108	56	22	29	25	50	1. 9/17	850	20	7	7. 35
3 (pre-)	NE 10 μg/min DB 12 μg·kg·min	106	60	22	28	25	51	2. 1/19	948	18	6. 6	7. 35
3 (2 h)	NE 8 μg/min DP 12 μg·kg·min	110	60	15	26	22	61	2. 6/23	900	22	5. 7	7. 37
3 (6 h)	NE 8 μg/min DP 11 μg·kg·min	114	63	14	23	14	67	3. 1/27	765	24	4. 8	7. 38
3 (12 h)	NE 3 μg/min DP 10 μg·kg·min	116	65	18	25	19	63	2. 6/24	857	22	1. 6	7. 39
3 (18 h)	NE 3 μg/min DB 8 μg·kg·min	106	71	16	24	19	70	3. 4/32	692	22	1. 4	7. 41
8	Stop	91	71	15	23	16	74	3. 5/38	726	19	0. 9	7. 4
Patient B												
Day	Vasoactive Drugs	HR (bpm)	MAP (mmHg)	CVP (mmHg)	PAPm (mmHg)	WP (mmHg)	SvO2 (%)	CI/SI (l/min·m^2)/(ml/m^2)	SVR (dyne·s/cm^5·m^2)	Shunt (%)	Lactate (mmol/l)	pH
1	NE 30 μg/min DB 6 μg/kg/min	125	50	15	33	21	63	2. 6/20	620	14	7. 4	7. 37
2	NE 15 μg/min DB 10 μg/kg/min	128	51	21	30	26	66	2. 9/24	413	8	5. 5	7. 47
3 (pre-)	NE 15 μg/min DB 10 μg/kg/min	105	54	18	31	24	65	3. 0/29	523	7	5. 1	7. 44
3 (2 h)	NE 15 μg/min DB 5 μg/kg/min	104	57	14	26	23	75	3. 3/31	531	10	1. 4	7. 46
3 (6 h)	NE 15 μg/min DB 4 μg/kg/min	100	62	17	26	21	75	3. 8/38	466	13	0. 6	7. 47
3 (12 h)	NE 15 μg/min DB 4 μg/kg/min	103	64	19	28	21	74	3. 9/38	440	11	0. 9	7. 40
3 (18 h)	NE 12 μg/min	95	61	15	25	17	70	3. 8/40	479	9	0. 8	7. 41
6	Stop	99	67	8	24	15	76	3. 9/39	615	7	0. 6	7. 45

crease of vasoactive dosages until suspension on days 8 and 6 respectively, strongly suggesting a causal relationship. Of note, there was a trend toward pulmonary artery decrease as suggested by experimental data [3], not associated with worsening of pulmonary shunt. Patient A died from brain haemorrhage on day 23 after resolution of septic shock and severe pneumonia. Patient B was discharged to the ward after 14 days.

Our report confirms the effectiveness of levosimendan in human septic shock [4], supporting a potential application in a definite scenario (severe septic cardiac failure) and timing (unresponsiveness to standard therapy).

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