PRELIMINARY RESEARCH OF NEUROPROTECTIVE EFFECTS OF RECOMBINANT HUMAN ERYTHROPOIETIN IN PEDIATRIC OPEN-HEART SURGERY

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Background: Erythropoietin(EPO) has been widely used in different clinical conditions. Recent studies have demonstrated that EPO may play a role in the development of the brain and subsequently in the maintenance of cerebral homeostasis. Evidences have established that EPO offers promise as a treatment for brain injury. The purpose of this study was to evaluate the neuroprotective effects of EPO on children scheduled for open-heart surgery.

Materials & Methods: 45 children scheduled for VSD and/or ASD repairment were randomly divided into control group and two study groups(n=15). The patients in study groups received single dose of recombinant human erythropoietin(rHuEPO) 50IU/kg(EPO1) or 100IU/kg(EPO2) intravenously before anesthesia induction, respectively. Cerebral oxygenation was monitored continuously and non-invasively using near-infrared spectrometry(NIRS) during surgery. Blood samples were taken intravenously before anesthesia induction(t1), 1h(t2) and 20h(t3) after CPB. Serum concentrations of neuron specific enolase(NSE) and S100 protein were detected.

Methods: After the preparation and maintenance of the slices as well as electrophysiological and pharmacological techniques are used, Near steady-state, voltage-current relationships were obtained by applying ramp commands during voltage-clamp condition (and AP were obtained during current-clamp condition). According to the different kinds of ion channels, the slices were divided into the sodium channels group, the potassium channels group and the AP group. Each group contains control group and the experiment group. The control group was perfused with normal ACSF; the experiment group was perfused with ACSF containing different concentrations of Et. Then by applying various protocols, we investigated if the Et could dose-dependently affect the activation process, the deactivation process and the de-inactivation process of the sodium channels; the activation process of the potassium channels; and the electronic portrait of single AP.

Results: Intracranial oxygenation status at different time point showed significant difference within each group($P<0.01$). But there wasn't significant difference among three groups($P>0.05$). After pretreatment with rHuEPO 50IU/kg, all of the parameters provided by NIRS showed ameliorated tendency but with no statistical significance. Among those, ScO2 representing for the balance of oxygen supply and consumption decreased less compared with that of control group. ΔHHb representing for oxygen extraction changed to a relatively less extent than control group. ΔO2Hb representing for cerebral arterial blood flow recovered relatively faster after ischemia and ΔcHb representing for cerebral blood volume decreased relatively slower. Increasing the dosage of rHuEPO didn't bring further improvement of these parameters. Serum concentrations of NSE and S100 protein at different time point had significant differences within each group and among three groups($P<0.01$). The serum concentrations of these two neurobiochemical markers increased significantly at 1h after CPB compared with basic level and remained higher at 20h after CPB in control group, while in EPO1 group the serum concentrations increased significantly at 1h after CPB and recovered to basic level at 20h after CPB. Giving high dosage(100 IU/kg) didn't show any further improvement.

Conclusions: rHuEPO could ameliorate neurobiochemical markers of children undergoing open-heart surgery. The results of cerebral oxygenation could also be improved to some extent. rHuEPO might play a role of neuroprotection in CNS ischemic-hypoxic injury.

References

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2. *Juul S. Erythropoietin in the central nervous system, and its use to prevent hypoxic-ischemic brain damage. Acta Paediatr Suppl. 2002;(438):36-42.*

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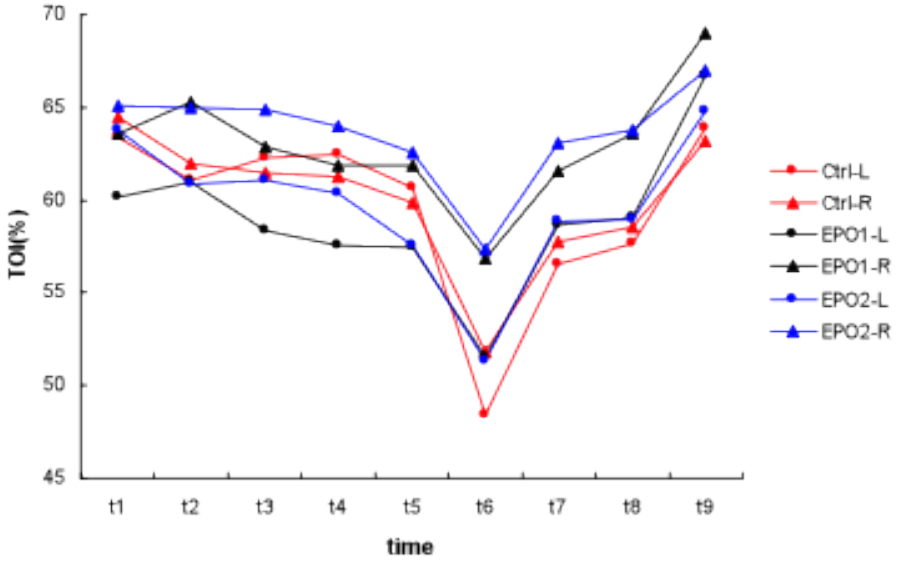

Figure 1. Changes in bilateral TOI (%)

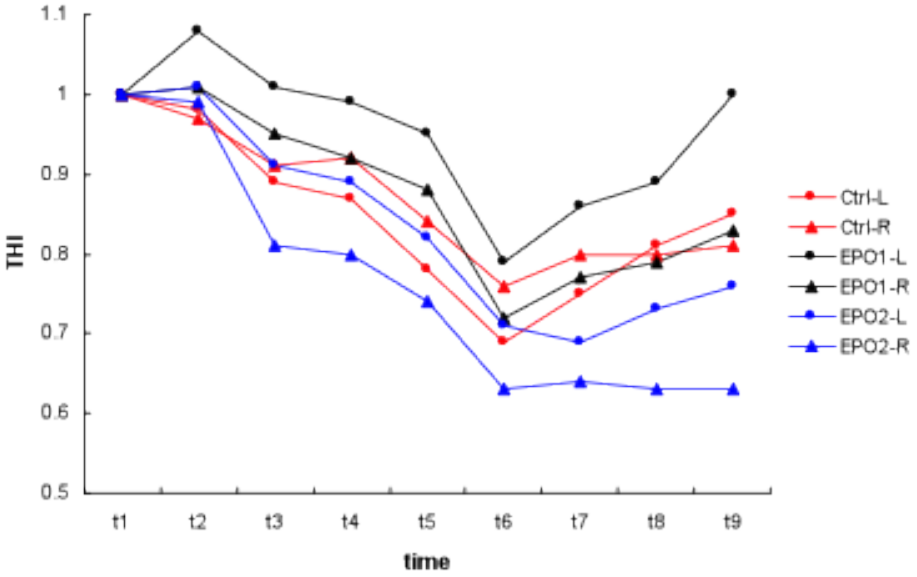

Figure 2. Changes in bilateral THI

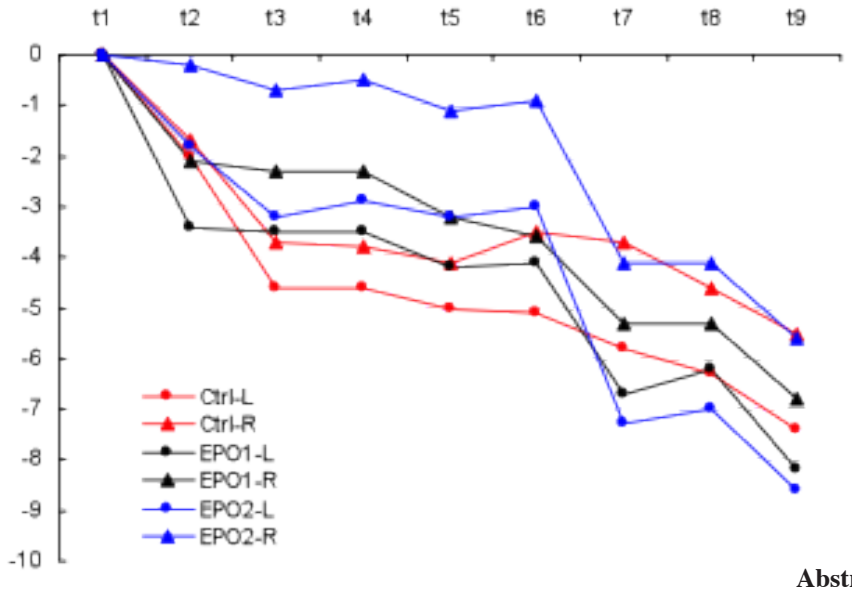

Figure 3. Changes in bilateral ΔHHb

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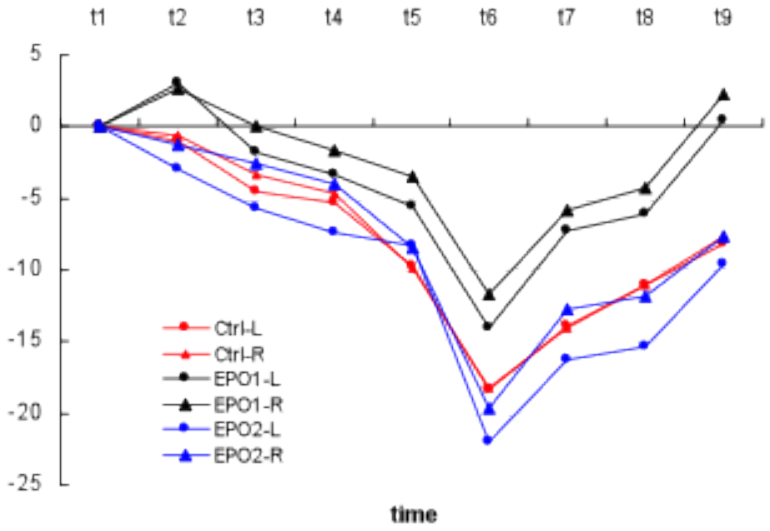

Figure 4. Changes in bilateral ΔO_2Hb

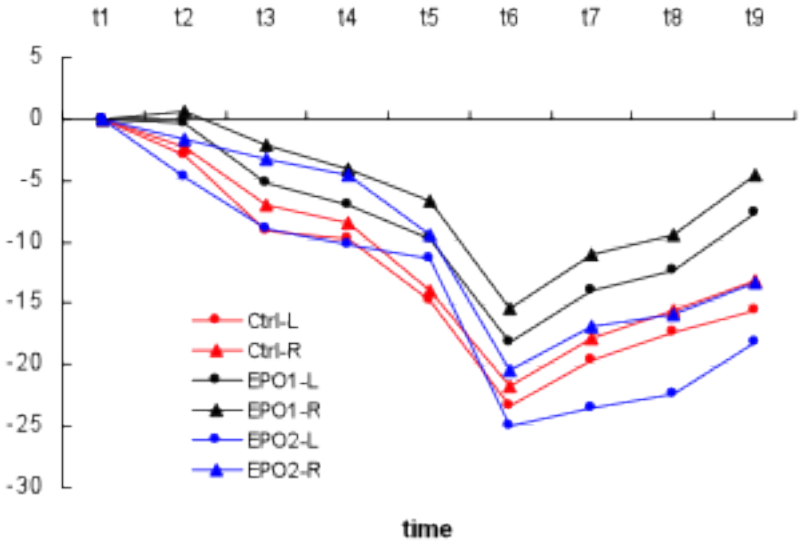

Figure 5. Changes in bilateral ΔcHb

Table 1. Changes in NSE and S100 protein (μg/L) (x±s)

		NSE			S100		
	n	t_1	t_2	t_3	t_1	t_2	t_3
Ctrl group	15	6.5±2.0	35.3±14.5**	23.4±7.3**	0.55±0.11	1.20±0.43**	0.85±0.47
EPO1	15	5.4±1.6	27.7±7.4**	9.8±5.3$^{\Delta\Delta\#\#}$	0.62±0.07	0.91±0.11**$^{\#\#}$	0.70±0.12$^{\Delta\Delta}$
EPO2	15	6.3±2.3	29.7±10.9**	17.4±12.8	0.62±0.13	1.09±0.33**	0.74±0.17$^{\Delta\Delta}$

**P<0.01, compared with t1; ΔΔP<0.01, compared with t2; ##P<0.01, compared with control group