Translational Research: May Transplantation of Human Umbilical Cord Blood Mononuclear cells Become an Adjuvant Therapy For Delayed Thrombolysis in Brain Ischemia?

Ramli Y.1, Alwahdy A.S.1, Kurniawan M.2, Juliandi B.2, Wuyung P.E.3
1Neurology Department, Medical Faculty University of Indonesia, 2Institut Pertanian Bogor, Biology Department, 3Pathology Anatomy Department, University of Indonesia/Ciptomangunkusumo National Hospital, Jakarta, Indonesia.
Correspondence: ule842002@yahoo.com, telephone no: +628176636381

ABSTRACT

Introduction
Cerebral ischemia is among the most common type of stroke seen in patients. Thrombolysis (rt-PA) is the only United States Food and Drug Administration (FDA) approved drug available. For regeneration of death neurons are remain questionable. Human umbilical cord blood mononuclear cell (cbMNC) is one of the option treatments for ischemia stroke through their various advantages; availability, pluripotency and immaturity.

Method
One group for healthy rat and three groups (n=6 per group) of male wistar rats were undergone permanent middle cerebral artery occlusion (MCAO). Rats were allowed to recover for 7 days before intraarterial (IA) and intravenous (IV) injection of $3 \times 10^5$ human cbMNC. Behavioural tests were performed before MCAO, 1 week after MCAO and at 3, 9 and 14 days after cbMNC injection. Neurogenesis (TUJ1), gliosis (GFAP) and angiogenesis (VEGF) marker were evaluated.

Results
Behavioral test in sensoricmotor evaluation revealed no significant differences between all groups. Spontaneous activity of stroke rats have significantly improved compared to placebo group P<0.05 (Graphic 1a and 1b). Neurogenesis (TUJ1) in IA and IV route have better result compare to placebo, P<0.05 (Table 1a). There were no significant differences in reducing gliosis amount (GFAP) in treating rats compare to placebo (Table 1b). Perivascular edema reduced qualitatively and angiogenesis in IA showed significant differences. P<0.001 (Table 1c) compare to IV and placebo respectively.

Conclusion
IA and IV human cbMNC transplantation provides post stroke functional recovery and spontaneous activity. Human cbMNC as hematopietic stem cells showed their pluripotency effect. The existence of more neovascularization in periflaxin area and reduced perivascular edema in the administration of cbMNC intraarterially provides hope for the possibility of blood vessels repair so as to reduce the occurrence of blood brain barrier leakage, edema and bleeding after delayed thrombolysis when it passes its therapeutic time window or even after mechanical thrombectomy procedure.

Keywords: Human umbilical cord blood, Mononuclear cells, Middle cerebral artery occlusion, Monofilm, Rats

References