Title
A novel therapeutic strategy improves functional recovery after MCAo stroke in rats

Journal
STROKE, 38(2)

ISSN
0039-2499

Authors
Belayev, Ludmila
Khoutorova, Larissa
Zhao, Karen L
et al.

Publication Date
2007

60

A Novel Therapeutic Strategy Improves Functional Recovery After MCAo Stroke in Rats

Ludmila Belayev, Larissa Khoutorova, Karen L Zhao, Fang M Zuo, Andrew Salzman, Inotek, Beverly, MA; Allen W Davidoff, Alan F Moore, Stem Cell Therapeutics Corp, Calgary, Canada; Steven C Cramer, Univ of California, Irvine, Irvine, CA

INTRODUCTION: Human chorionic gonadotropin (hCG) and erythropoietin (EPO) have been postulated to contribute to neuroprotection and neuroregeneration by influencing endogenous adult neural stem cells. The current study tested the hypothesis that administration of this two compound regimen, initiated 24 hours after MCAo stroke, improves long-term behavioral outcome. METHODS: Long-Evans rats received 90 min MCAo by retrograde insertion of an intraluminal suture coated with poly-L-lysine. At 24 h from MCAo onset, 46 rats were randomized into 4 treatment groups in a double-blinded manner: hCG+EPO (3 IM doses hCG at 300 IU/kg over 5 days, followed by 3 IV doses EPOGEN at 1440 IU/kg over 3 days), hCG+saline in same schedule, saline+EPO in same schedule, or neither drug (saline+saline). Primary endpoint was Composite Neurological Score (0–12 points, 0=normal), measured 60 min into occlusion, then at 1h post-infarct, 24 h post-infarct, and a total of 11 times until 12 weeks post-infarct. RESULTS: Body and cranial temperature showed no significant group differences between groups. The Composite Neurological Score was different over time across treatment groups ($p<0.056$, repeated measures ANOVA time X treatment group). Pairwise testing of groups found that the hCG+EPO group had significantly lower scores at 8/10 post-stroke time points as compared to saline+saline. The hCG+EPO group scores were lower than scores in the single-drug (hCG+saline and saline+EPO) groups in all but one instance but significantly so at only 2 time points. The 2 single-drug treatment arms did not significantly differ at any time point. Infarct volume (estimated at Bregma -0.92) in the hCG+EPO group (25 +/- 18 % of non-stroke hemisphere, mean +/- SD) was reduced as compared to saline+saline (46 +/- 27%, $p < 0.04$), saline+EPO (45 +/- 27%, $p < 0.06$), and hCG+saline (47 +/- 25%, $p < 0.04$) groups. CONCLUSION: The current therapeutic strategy improved behavioral outcome and preserved brain tissue with a time window of 24 hours after stroke onset. Extensive human experience exists for both hCG and EPO, suggesting high potential for translation into studies of acute human stroke.