The 10,000 Fold Effect of Retrograde Neurotransmission, a New Concept for Stroke Revival: Use of Intracarotid Sodium Nitroprusside

Authors : Vinod Kumar

Abstract : Background: Tissue Plasminogen Activator (tPA) showed a level 1 benefit in acute stroke (within 3-6 hrs). Intracarotid sodium nitroprusside (ICSNP) has been studied in this context with a wide treatment window, fast recovery and affordability. This work proposes two mechanisms for acute cases and one mechanism for chronic cases, which are interrelated, for physiological recovery. a)Retrograde Neurotransmission (acute cases): 1)Normal excitatory impulse: at the synaptic level, glutamate activates NMDA receptors, with nitric oxide synthetase (NOS) on the postsynaptic membrane, for further propagation by the calcium-calmodulin complex. Nitric oxide (NO, produced by NOS) travels backward across the chemical synapse and binds the axon-terminal NO receptor/sGC of a presynaptic neuron, regulating anterograde neurotransmission (ANT) via retrograde neurotransmission (RNT). Heme is the ligand-binding site of the NO receptor/sGC. Heme exhibits > 10,000-fold higher affinity for NO than for oxygen (the 10,000-fold effect) and is completed in 20 msec. 2)Pathological conditions: normal synaptic activity, including both ANT and RNT, is absent. A NO donor (SNP) releases NO from NOS in the postsynaptic region. NO travels backward across a chemical synapse to bind to the heme of a NO receptor in the axon terminal of a presynaptic neuron, generating an impulse, as under normal conditions. b)Vasospasm: (acute cases) Perforators show vasospastic activity. NO vasodilates the perforators via the NO-cAMP pathway. c)Long-Term Potentıaıon (LTP): (chronic cases) The NO–cGMP-pathway plays a role in LTP at many synapses throughout the CNS and at the neuromuscular junction. LTP has been reviewed both generally and with respect to brain regions specific for memory/learning. Aims/Study Des'gn: The principles of "generation of impulses from the presynaptic region to the postsynaptic region by very potent RNT (10,000-fold effect)" and "vasodilation of arteriolar perforators" are the basis of the authors' hypothesis to treat stroke cases. Case-control prospective study. Mater'als And Methods: The experimental population included 82 stroke patients (10 patients were given control treatments without superfusion or with 5% dextrose superfusion, and 72 patients comprised the ICSNP group). The mean time for superfusion was 9.5 days post-stroke. Pre- and post-ICSNP status was monitored by NIHSS, MRI and TCD. Results: After 90 seconds in the ICSNP group, the mean change in the NIHSS score was a decrease of 1.44 points, or 6.55%; after 2 h, there was a decrease of 1.16 points; after 24 h, there was an increase of 0.66 points, 2.25%, compared to the control-group increase of 0.7 points, or 3.53%; at 7 days, there was an 8.61-point decrease, 44.58%, compared to the control-group increase of 2.55 points, or 22.37%; at 2 months in ICSNP, there was a 6.94-points decrease, 62.80%, compared to the control-group decrease of 2.77 points, or 8.78%. TCD was documented and improvements were noted. Conclusions: ICSNP is a swift-acting drug in the treatment of stroke, acting within 90 seconds on day 9.5 post-stroke with a small decrease after 24 hours. The drug recovers from this decrease quickly.

Keywords : brain infarcts, intracarotid sodium nitroprusside, perforators, vasodilatıons, retrograde transmission, the 10,000-fold effect
Conference Title : ICSCRM 2015 : International Conference on Stem Cells and Regenerative Medicine
Conference Location : Bangkok, Thailand
Conference Dates : December 17-18, 2015