649

REPETITIVE ADMINISTRATION OF LEVETIRACETAM DOES NOT REDUCE HYPOXIC-ISCHAEMIC BRAIN INJURY IN NEWBORN MICE

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Background: Perinatal asphyxia remains an important cause of brain injury in full term infants. Induced hypothermia has shown substantial benefit to asphyxiated newborns. Seizures are a common feature of hypoxic-ischaemic encephalopathy (HIE) and have been shown to exacerbate brain injury in HIE. Anticonvulsive treatment is a matter of debate. Studies have shown a high frequency of off-label drug therapy in neonates, particular for levetiracetam (LEV).

Aim: To evaluate the effect of LEV treatment in an established animal model of hypoxic-ischaemic (HI) brain injury in newborn mice.

Methods: On postnatal day nine (P9) mice pubs were randomly assigned firstly to sham operation or HI, secondly to the two treatment groups: i) LEV (50mg/kg body weight) ii) vehicle, both starting 1h after injury and administered repetitively every 12hrs. Primary analysis on P12 assessed the extent of brain injury and number of cells positively stained for activated caspase-3.

Results: LEV treatment showed no significant effect on brain injury in cortical grey and white matter ($p=0.63$), hippocampus ($p=0.82$), thalamus ($p=1.0$) and striatum ($p=0.21$), ($n=8$-15, vs. control). Immunohistochemistry showed a trend towards an increase of cells positively stained for activated caspase-3 in the thalamus (LEV group), but did not reach statistic significance ($p=0.14$, $n=4$-5, vs. control).

Conclusion: The preliminary results of this study show no effect of LEV in an animal model of HIE. The increase in positively stained cells for activated caspase-3 needs to be further investigated, as well as a more detailed analysis of the underlying mechanisms exerted by this new substance.