SCNS. 12. Effects of trimetazidine on pilocarpine-induced convulsions in mice: behavioral changes and glutamatergic system modulation

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Introduction: Epilepsy is one of the most common and serious neurological conditions, affecting more than 50 million people worldwide. The current clinically available antiepileptic drugs are associated with a variety of side-effects and chronic toxicity. Adverse effects associated with these agents are the main limitation for their long-term use. Therefore, the development of new antiepileptic agent with improved efficacy and minimal adverse effects is very important. Trimetazidine (TMZ) is a lipophilic piperazine derivative, a drug of interest in ischemic diseases. It has demonstrated anti-oxidant, anti-inflammatory, antinociceptive and gastroprotective properties in various experimental animal models. The aim of this study was to investigate the antioxidant effect of trimetazidine on pilocarpine-induced seizures in mice. **Methods:** Male Swiss mice, 25-30g received TMZ (5, 10 and 20 mg/kg, i.p.), fenobarbital (FEN 10 and 30 mg/Kg, i.p.), association (TMZ 5 + FEN 10 mg/kg, i.p.) or saline - NaCl 0,9%, i.p. during seven days. 60 minutes after the last injection, pilocarpine (P320 mg/Kg, s.c.) was administered and behavioral tests were performed. After behavioral tests, animals were euthanized and cerebral areas were removed for neurochemical analysis. **Results:** Our results showed that TMZ administration reduced the number of deaths at all doses tested, but the highest dose (20 mg / kg) showed better effect, increased the latency of seizures in 41% (11.76 ± 0.75) compared to control (8.36 ± 0.41) led to absence seizures in 10% of animals and reduced the occurrence of status epilepticus. We observed an increase (168%) in glutamate levels in the hippocampus of animals that received pilocarpine and this effect was reversed with TMZ pretreatment at the higher dose. **Conclusion:** The results of this study suggest that trimetazidine presented anticonvulsant activity in the model of pilocarpine-induced seizures in mice, possibly due to its modulatory action on glutamatergic system.

Keywords: trimetazidine; seizure; glutamate

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