KChIP1 regulation of Kv 4.3 potassium channels and GABAergic transmission in primary hippocampal cells.

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INTRODUCTION

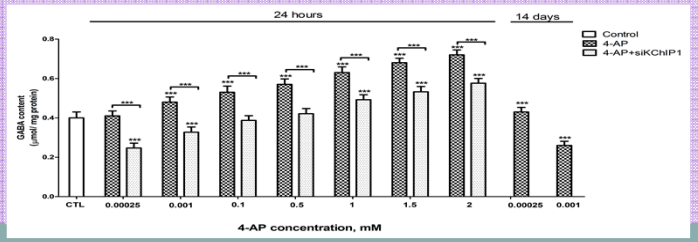
4-Aminopyridine (4-AP) is a potassium channel blocker used for the treatment of neuromuscular disorders. Otherwise, it has been described to produce a large number of adverse effects among them cell death mediated mainly by blockage of K+ channels. Specifically, 4-AP has been reported to produce cell death in central nervous system on hippocampal cells. On the other hand, Kv channel interacting protein 1 (KChIP1) is a neuronal calcium sensor protein that is predominantly expressed at GABAergic synapses and it has been related with modulation of K+ channels, GABAergic transmission and cell death. According to this, KChIP1 could modulate K+ channels and GABAergic transmission, which mediate the toxic effects induced by 4-AP.

METHODS

We evaluated, in wild type and KChIP1 silenced (siKChIP1) primary hippocampal neurons, the effect of 4-AP (0.25 mM to 2 mM) after 24 h and after 14 days 4-AP alone exposure on KChIP1 and Kv 4.3 potassium channels gene expression and GABAergic transmission.

RESULTS

We observed that 4-AP modulates KChIP1 which regulates Kv 4.3 channels expression and GABAergic transmission. Our study suggests that KChIP1 is a key gene that may have a protective effect up to certain concentration after short-term 4-AP treatment, but this protection would be erased after long term exposure, due to KChIP1 down-regulation predisposing cell to 4-AP induced damages.



CONCLUSIONS

These data might help to explain protective and toxic effects observed after overdose and long term exposure.