

Behavioral parameters evaluation after homeopathic *Zincum metallicum* treatment: a transgenerational study in mice

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Zincum metallicum (ZM) is a homeopathic medicine whose material medica is defined by diverse behavioral and mental symptoms, including depression. Moreover, as a microelement, zinc itself is involved in several functions of Central Nervous System, including development and cell maturity during the intra-uterus life. Herein, the putative transgenerational effects of different homeopathic potencies of ZM upon behavioral parameters in P and F1 generations were evaluated. Since mice and the tail suspension test (TST) are references for evaluating antidepressant agent activity, the TST together with the open field test (OPT) and the elevated plus maze test (EPM) were used to analyze offspring behavioral parameters. All animal procedures were in agreement with the Brazilian ethical research practices and were approved by the institutional ethical committee (CEUA-UNIP) under the protocol 156/2013. Four groups of seven females Balb/C mice were exposed to 0,1mL of ZM 5cH, 30cH, 200cH and lactose 5cH, diluted in 250mL of drinking water, during pregnancy and post partum period, in a total of 31 days. The flasks were coded before the remedies administration and all experimental procedures, including statistical analysis were done in blind. The parents were previously distributed in a Completely Randomized Design for the mates, according to the TST previous results. Mothers were re-evaluated for TST after weaning and mice of F1 generation were evaluated for TST, EPM and OPT when they reached two months old. According to the time of immobilization in TST, animals were classified as healthy (h), intermediate (i) and depressed (d) (< 116; 117-180 and >180 seconds of immobilization, respectively). No significant changes were seen among the groups regarding to the number of newborns, sex proportions, TST, OPT and EPM behavioral parameters, besides the fact that the treatment with ZM 200cH was associated to the majority of healthy F1 mice (male: n=8: 7h+1i+0d; female: n=8: 8h+0i+0d), in relation to the number of delivery per group (Fisher test, $p \leq 0.01$). Treatment with ZM 5cH, instead, produced reduced number of pups with no male mouse among F1 generation. We conclude that the treatment of pregnant females with ZM 200cH produced the best results in F1 generation regarding reproduction and behavioral parameters and the treatment with ZM 5cH reduced births in relation to control. The involved mechanisms have to be elucidated in the next steps of the study.

Keywords: UHD, Depression-anxiety behavior, transgenerational mice.



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