Unexplained sudden death in Rett syndrome: protective effect of ω-3 PUFAs

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Rett syndrome (RTT) is the second commonest cause of severe intellectual disability in females. RTT is caused by mutations in the methyl-CpG binding protein 2 (*MECP2*) gene. In RTT a 300- folds increased risk of sudden death has been reported. This fatal event is to be considered as unexplained as its causes are unknown, although a cardiac event has been previously postulated. In the present study, a protective effect of ω-3 fatty acids against the phenomenon of the unexplained sudden death in Rett syndrome was tested.

A cohort of patients on a regular clinical and biochemical follow-up (n=214) were examined. A supplementation with ω-3 fatty acids at high dosage (250 ± 45 mg/kg b.w./day) was proposed and the number of sudden death during 5-years were recorded. Fatty acids profile in erythrocytes, fatty acid oxidation end products (F_2-isoprostanes, F_2-dihomo-isoprostanes, and F_4-neuroprostanes), and a pro-oxidizing agent (non-protein-bound iron) were measured.

A significantly lower risk of sudden death was observed for the ω-3 fatty acids-supplemented population (O.R.: 0□019; 95% CI 0□004 to 0□090, $P < 0□001$).The reduced risk of sudden death in the ω-3 fatty acids-supplemented group was found to be associated with increased docosahexaenoic acid, eicosapentaenoic acid blood levels and ω-3 index, as well as decreased levels of non-protein-bound iron and isoprostanes.

Our data indicate that a continued supplementation with ω-3 PUFAs at high dosage in RTT patients is safe and potentially life saving. In addition, plasma levels of F_4-NeuroPs appear to be significant predictors for sudden death in RTT patients.

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