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Effect of cyclic, low dose pyrimethamine treatment in patients with late onset Tay-Sachs disease: An open label, extended pilot study

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Late onset Tay-Sachs disease (LOTS) is a rare neurodegenerative lysosomal storage disease which results from mutations in the gene encoding the α -subunit (HEXA) of beta-hexosaminidase enzyme (HexA). At present, no effective treatment exists for LOTS. Pyrimethamine (PMT) was previously shown to act as a HexA chaperone in human fibroblasts *in vitro* carrying some (e.g., aG269S), but not all LOTS-related mutations. The present study assessed the effect of cyclic, low dose and long term pyrimethamine treatment on HexA in subjects with LOTS. In an open label trial in 4 LOTS patients, PMT was initiated at an average daily dose of similar to 2.7 mg and administered cyclically guided blood lymphocyte HexA activity for a mean duration of 82.8 (+/- 22.5; SD) weeks. HexA activity rose in all subjects, with a mean peak increase of 2.24 folds (+/- 0.52; SD) over baseline activity was observed. The mean treatment time required to attain this peak was of 15.7 (+/- 4.8; SD) weeks. Following increase in activity, HexA gradually declined with the continued use of PMT, which was then stopped, resulting in the return of HexA activity to baseline. A second cycle of PMT treatment was then initiated, resulting again in an increase in HexA activity. Three of the patients experienced a measurable neuropsychiatric deterioration whereas one subject remained entirely stable. We conclude that cyclic low dose of PMT can increase HexA activity in LOTS patients. However, the observed increase is repeatedly transient and not associated with discernible beneficial neurological or psychiatric effects.

Biography

Ruth Navon is currently working in the 1Tel Aviv University, Israel. Ruth Navon international experience includes various programs, contributions and participation in different countries for diverse fields of study. Ruth Navon research interests reflect wide range of publications in various national and international journals.

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