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Pregnenolone - Deficiency in Patients with Fibromyalgia syndrome with and without Small Fiber Pathology - a "Supply Chain Problem"?

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OBJECTIVE

In the present study we evaluated the hypothesis that decreased pregnenolone levels are frequent in patients with fibromyalgia (FMS) and if there is a difference in the results of skin punched diagnosed small fiber neuropathy (SFN) or not.

BACKGROUND

Synthesis of Pregnenolone (PR) is the first and rate-limiting step in steroidogenesis, converting cholesterol to pregnenolone by a single enzyme (CYP11A1) in mitochondria (Illustration) as a precursor to all biological steroid hormones.
PR is also a potential biomarker for mitochondrial function. SFN can explain neuropathic pain symptoms in FMS, estimated in a metaanalysis (Oaklander, 2019) in 49% of FMS patients as a frequent condition.

METHODS

Pregnenolone-sulfate (PR-S) serum levels can be easily tested to evaluate PR-deficiency. Age dependent normal levels range from 27 - 80 ug /l. We studied 44 patients with the clinical diagnosis of FMS, (40 f/4 m) with an average age of 53.8 years. Twenty-two (22) had the skin biopsy confirmed diagnosis of SFN, the other half (22) had negative SFN biopsy results. All PR-S serum levels were compared to a control group.

RESULTS

The average PR-S level in the entire study group of 44 FMS patients was 21.4 ug/l (median 20). No significant difference was found in PR-S levels of SFN positive patients versus patients with normal small fiber density. The average PR-S range in FMS patients was significantly lower compared to a control group of 35 patients, average age 51.2 (29f/6m) with various neurological disorders (migraine/ MS/ low back pain) with a PR-S range of 41.2ug/l, (median 41).

CONCLUSIONS

Our findings suggest a high probability of an association of low PR-S levels and PR deficiency in FMS patients. Acting as a unique and limiting hormone, PR is not only a precursor for all biological steroid hormones and a probable biomarker for mitochondrial dysfunction but in addition could act as an effective neurosteroid to fatigue. This could lead to possible future therapeutic approaches. Further extensive studies are necessary in order to prove the hypothesis that low PR-S levels cause a "supply chain problem", thus also explaining the variety of symptoms in FMS, especially fatigue and post exertion malaise.

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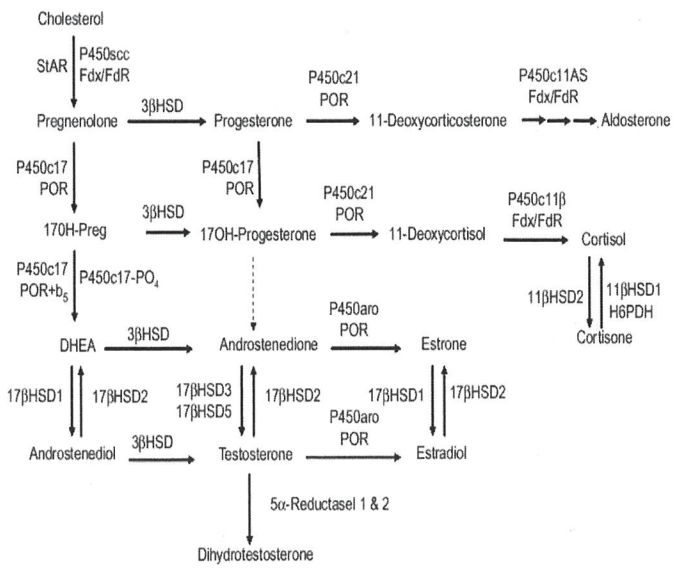
ILLUSTRATION



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