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Short Communication

Treatment of Deficiency of Hypoxanthine-Guanine Phosphoribosyltransferase (HPRT) with Allopurinol

William L. Nyhan[1]* and Gary Eddey[2]

[1]*Department of Pediatrics, University of California, USA*
[2]*Department of Pediatrics, Rutgers New Jersey Medical School, USA*

Abstract

Lesch-Nyhan-Nyhan disease is (LND) an X-linked recessive disorder of the purine salvage pathway characterized by hyperuricemia. Untreated patients develop gout and uric acid nephrolithiasis. The disease also characterized by cognitive impairment, dystonia and dramatic behavioral manifestations, including the hallmark of features of severe, involuntary and wide ranging self-injurious behaviors, most characteristically biting, leading to loss of tissue about the lips and fingers.

***Corresponding author**
William L. Nyhan, Department of Pediatrics, University of California, San Diego, 9500 Gilman Dr./La Jolla/ CA/92093-0830, USA, Tel: 619-543-3580; Email: wnyhan@ucsd.edu

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INTRODUCTION

The safety and efficacy of treatment with allopurinol in patients with deficiency of activity of HPRT has been established as summarized by Torres, Prior, and Puig [1], 2007. They reported experience with 19 patients. Allopurinol dosage ranged from 3.7-9.7mg/kg of body weight (mean 6.4). There were no adverse events. Patients experienced 47% mean reduction in serum urate concentration and a 74% reduction in reduction in reduction in the ratio of urate to creatinine in urine. Mean increase in hypoxanthine and xanthine excretion was 5.4 and 9.5-fold.

In our experience total purine excretion does not change; uric acid becomes minimal, and amounts of hypoxanthine and xanthine vary with doses. We aim by dosage modification to achieve maximal levels of hypoxanthine, which is soluble and minimal levels of xanthine which like uric acid may lead to calculi. Patients were treated with allopurinol in doses up to 1200mg per day.

METHODS

Morning samples were collected in most Lesch-Nyhan patients, while in those with more tractable behavior, 24-hour samples were collected. All samples were kept at 10°. Excretion of uric acid, hypoxanthine and xanthine was quantified.

RESULTS

Doses of allopurinol range from 800 to 1200mg/24 hr. Concentrations of uric acid in the blood decreased to 1.2 mg/dl or below. There was no evidence of calculi, and there were no urinary tract infections.

DISCUSSION

HPRT1 gene is located on the long arm of the X chromosome, and over 600 different mutations have been identified. The disease occurs largely in males but there have been documented cases of the disease in females [2], a consequence of nonrandom inactivation of the paternal X chromosome. In others, especially twins, it reflects a skewed pattern in which there is preferential inactivation of one X in the affected twin and the other in her normal twin [3].

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