Eplerenone in the treatment of Gitelman's syndrome

A study of Gitelman's syndrome in which the subject was intolerant of several medications, but responded well to eplerenone is presented.

A 21-year-old woman who presented with lethargy was found to have a serum potassium of 2.6 mmol/L (normal 3.5–5 mmol/L). There was no significant medical or family history and she denied intake of any medications, laxatives, purgatives or diuretics. Physical examination was unremarkable with normal blood pressure. Serum magnesium was 0.6 mmol/L (normal 0.7–1.1 mmol/L), serum aldosterone was 530 pmol/L (normal 110–860 pmol/L), plasma renin activity was 204 mU/L (normal 2–45 mU/L) and 24-h urine calcium was less than 0.2 mmol (normal up to 7.5 mmol). Urine diuretic screen was negative, DNA sequence analysis confirmed the diagnosis of Gitelman's syndrome with pathogenic mutations 2186G>T (G729V) in exon 18 and 2872A>T (R958W) in exon 25 in the *SLC12A3* gene.

The patient was intolerant of spironolactone, amiloride, non-steroidal anti-inflammatory drugs and several forms of oral potassium supplements because of nausea, vomiting and diarrhoea. Upper and lower gastrointestinal endoscopies were normal. She was subsequently commenced on eplerenone 50 mg b.i.d. with normalization of her serum potassium within 1 week, resolution of lethargy and without adverse effects. Nine months after starting eplerenone the patient is asymptomatic with serum potassium 3.8 mmol/L and serum magnesium 0.9 mmol/L.

Gitelman's syndrome is an autosomal recessive disorder caused by mutations affecting the NaCl cotransporter *NCCT* located in the apical membrane of the distal convoluted tubule. Many cases of Gitelman's syndrome are compound heterozygotes. Mutant alleles are quite frequent in the general population, the estimated prevalence of heterozygotes being as high as 1%. The characteristic biochemical features of Gitelman's syndrome are hypokalaemia, mild volume contraction, hypocalciuria and magnesium wasting. Treatment is with combinations of non-steroidal anti-inflammatory drugs, potassium-sparing diuretics and potassium supplements. Hypotension may limit the use of angiotensin-converting enzyme inhibitors. One study found that spironolactone was more effective than amiloride in correcting hypokalaemia with Gitelman's syndrome.[1]

Eplerenone is a selective aldosterone blocker, with significantly lower affinity for androgen, progesterone and glucocorticoid receptors than spironolactone and thus is not associated with anti-androgenic side-effects, such as gynecomastia, impotence and menstrual irregularities. One 8-week study found equivalent frequencies of adverse effects with spironolactone and eplerenone therapy in individuals with hypertension.[2] Discontinuation rates, due to adverse effects was 8% with spironolactone in the Randomized Aldactone Evaluation study compared with 4% with eplerenone in the Eplerenone Postacute Myocardial Infarction Heart Failure Efficacy and Survival study.[3,4] Eplerenone is significantly more expensive than spironolactone and is currently only approved in Australia for treatment where heart failure with ejection fraction of less than 40% occurs within 14 days of acute myocardial infarction. In the USA it is also approved for treatment of hypertension.

In conclusion, a study of Gitelman's syndrome in which the patient was intolerant of multiple agents but responded well to eplerenone is presented. Eplenerone may be useful in conditions associated with hypokalaemia, such as Barrter's syndrome and primary aldosteronism, where the patient is intolerant of other potassium-sparing diuretics.

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