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ORIGINAL ARTICLE

Treatment of Bartter syndrome. Unsolved issue☆,☆☆

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KEYWORDS
Bartter syndrome;
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Proteinuria

Abstract
Objective: To describe the results of a long-term follow-up of Bartter syndrome patients treated with different drugs.
Method: Patients were diagnosed according to clinical and laboratory data. Treatment protocol was potassium supplementation, sodium, spironolactone, and non-steroidal anti-inflammatory drug. Patients who developed proteinuria were converted to angiotensin conversion enzyme inhibitor. The variables evaluated for each drug were Z-score for weight and stature, proteinuria, creatinine clearance, gastrointestinal complaints, amount of potassium supplementation, serum potassium and bicarbonate levels, and findings of upper digestive endoscopy.
Results: 20 patients were included. Follow-up was 10.1 ± 5.2 years. 17 patients received indomethacin for 5.9 ± 5.3 years; 19 received celecoxib, median of 35 months; and five received enalapril, median of 23 months. During indomethacin, a statistically significant increase was observed in the Z-score for stature and weight, without a change in the creatinine clearance. Seven of 17 patients had gastrointestinal symptoms, and upper digestive endoscopy evidenced gastritis in three patients and gastric ulcer in four patients. During celecoxib use, a significant increase was detected in the Z-score for stature and weight and a reduction of hyperfiltration; seven patients presented gastrointestinal symptoms, and upper digestive endoscopy evidenced mild gastritis in three. During enalapril use, no significant changes were observed in the Z-score for stature, weight and creatinine clearance. The conversion to enalapril resulted in a significant reduction in proteinuria.

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Conclusion: The authors suggest starting the treatment with celecoxib, and replacing by ACEi if necessary, monitoring the renal function. The safety and efficacy of celecoxib need to be assessed in larger controlled studies.

PALAVRAS-CHAVE
Síndrome de Bartter;
Medicamento anti-inflamatório não esteroide;
Enalapril;
Proteinúria

Tratamento da síndrome de Bartter. Problema não resolvido

Resumo
Objetivo: Descrever os resultados de um acompanhamento de longo prazo de pacientes com síndrome de Bartter tratados com diferentes medicamentos.
Método: Pacientes diagnosticados segundo os dados clínicos e laboratoriais. Protocolo de tratamento: suplementação de potássio, sódio, espironolactona e medicamento anti-inflamatório não esteroidal. Os pacientes que desenvolveram proteinúria foram submetidos a inibidor da enzima de conversão da angiotensina. As variáveis avaliadas durante o uso de cada medicamento foram: escore Z para peso e estatura, proteinúria, depuração da creatinina, queixas gastrointestinais, quantidade da suplementação de potássio, níveis séricos de potássio e bicarbonato e achados da endoscopia digestiva alta.
Resultados: Foram incluídos 20 pacientes. O acompanhamento foi de 10,1±5,2 anos. No total, 17 pacientes receberam indometacina por 5,9±5,3 anos, 19 receberam celecoxib por aproximadamente 35 meses e cinco receberam enalapril por aproximadamente 23 meses. Durante o uso de indometacina, observamos um aumento estatístico significativo no escore Z para estatura e peso, sem alteração na depuração da creatinina. 7/17 pacientes apresentaram sintomas gastrointestinais, e a endoscopia digestiva alta mostrou gastrite em três pacientes e úlcera gástrica em quatro. Durante o uso de celecoxib, detectamos um aumento significativo no escore Z para estatura e peso e uma redução da hiperfiltração; sete pacientes apresentaram sintomas gastrointestinais e a endoscopia digestiva alta mostrou gastrite leve em três pacientes. Durante o uso de enalapril, não observamos alterações significativas no escore Z para estatura, peso e depuração da creatinina. A mudança da medicação para enalapril resultou em uma redução significativa na proteinúria.
Conclusão: Sugerimos iniciar o tratamento com celecoxib e, caso necessário, substituí-lo por ACEi, monitorando a função renal. A segurança e a eficácia do celecoxib precisam ser comprovadas com grandes estudos controlados.

Introduction

Bartter syndrome (BS) encompasses a group of rare genetic, autosomal recessive, renal tubular diseases characterized by urinary loss of sodium, potassium, and chloride; hypokalemic metabolic alkalosis; high plasma levels of renin and aldosterone; and high levels of prostaglandins (PGs) in blood and urine as a secondary phenomenon. Clinically patients present polyuria, polydipsia, failure to thrive, life-threatening episodes of dehydration, episodes of fever, and normal or low blood pressure. Frequently, pediatricians are the first professionals to attend to these patients and it is therefore important to be aware of this condition, since prognosis is better with earlier diagnosis and treatment. There are different types of BS, and clinical and laboratorial variability depends on the affected tubular carrier.[1,2] According to the affected region, some differences can be observed in the management of the disease, for instance, type II BS is associated with very mild hypokalemia, whereas in type IV BS, treatment with indomethacin is much less effective.[3]

The present study aimed to describe the results of a long-term follow-up of BS patients treated with different drugs.

Patients and methods

This retrospective study, based on a prospective protocol, enrolled patients with clinical and laboratorial diagnosis of BS from 1993 until 2012, and adherent to the treatment, which was evaluated by adherence to scheduled clinic appointments and serum bicarbonate and potassium levels. Genetic analysis is not available in this service.

Treatment protocol

The protocol was initially based on electrolytes supplementation (potassium and, in some cases, sodium), spironolactone, and the non-selective non-steroidal anti-inflammatory drug (nsNSAID), indomethacin. However, during the period of indomethacin treatment (1993 to 2003), six of 12 (50%) patients presented significant gastrointestinal