우리나라 선천성 염소 설사 환아에 대한 임상-유전학적 고찰

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Clinico-genetic Study of Congenital Chloridorrhea in Korean Children

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Congenital chloridorrhea (CC), a hereditary disease caused by mutations in the SLC26A3 gene, is clinically characterized by persistent secretory diarrhea resulting in polyhydramnios and premature delivery prenatally as well as dehydration, hypoelectrolytemia, abdominal distention, and failure to thrive immediately after birth. The SLC26A3 gene is a member of the SLC26 sulfate permease/anion transporter family and it is expressed mainly in the apical brush border of intestinal epithelium. In this report, we analyzed the clinico-genetic features of children with genetically confirmed CC. Total 8 unrelated children (5 boys and 3 girls) were recruited. The median age at the clinical or genetic diagnosis was 7.5 months (1-51 months). One patient had an affected sibling. All patients had a prenatal history of polyhydramnios and abdominal distention with/without intestinal pseudo-obstruction, and five patients were born prematurely. Of note, five patients were initially diagnosed as Bartter syndrome (BS) because the history of chronic watery diarrhea was neglected. Blood chemistry in most cases, similarly to BS, showed hyponatremia, hypokalemia, hypochloremic metabolic alkalosis, and hyperreninemic hyperaldosteronism. In addition, stool chloride concentration was >90 mEq/L in (101-166 mEq/L). The genetic study revealed 3 different abnormal splicing mutations (c.1312-2 A>T in intron 11, c.1407+3 A>C in intron 12, and c.2063-1 G>T in intron 18) and 3 different missense mutations (p.Pro(CCG)131Leu(CTG) in exon 5, p.Ser(AGT)134Asn (AAT) in exon 5, and p.Cys(TGC)343Phe(TTC) in exon 9) in the SLC26A3 gene. Of these mutations, c.1312-2 A>T was detected in all patients (3 homozygotes and 5 heterozygotes) and in 11 (69%) alleles, suggesting a founder effect. During the follow-up (median 11.5 months, 2-96 months), no patient developed renal dysfunction. In conclusion, a careful differentiation of CC from BS by careful history taking and urine/stool electrolytes measurement is recommended, and a common mutation (c.1312-2 A>T) should be screened first in the genetic study of SLC26A3 in Korean children with CC.

Key Words : 선천성 염소 설사, Bartter 증후군, SLC26A3
Congenital chloridorrhea, Bartter syndrome, SLC26A3