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Excretion of Urinary Tamm-Horsfall Glycoprotein in Girls with Recurrent Urinary Tract Infections

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Summary. Tamm-Horsfall glycoprotein (THG) might constitute a bacteria-fixing mucus which contributes to the non-immunological anti-infectious mechanisms of the lower urinary tract. To evaluate the role of THG in girls with idiopathic recurrent lower urinary tract infections, the THG excretion and concentration in 24-h urine were measured by a radial immunodiffusion method in 16 patients with a median age of 9 years and in 14 healthy age-matched girls. The results showed no significant differences in the THG excretion or concentration between the patients and the controls. Transiently decreased THG excretion rates as well as functional changes in the ability and/or capacity to trap bacteria, however, may leave girls periodically prone to colonization of the bladder. Thus, further studies are warranted to evaluate the importance of THG in the bladder defence mechanism.

Key words: Tamm-Horsfall glycoprotein, Urinary excretion, Recurrent urinary tract infections, Girls.

Introduction

Recurrent urinary tract infection (UTI) frequently occurs in otherwise healthy girls [5, 12]. Despite numerous studies, the causes for the varying susceptibility to UTI in girls without urinary tract malformations remain obscure.

In 1980 Ørskov et al. [13, 14] reported that *E. coli* with type 1 fimbriae are trapped by Tamm-Horsfall glycoprotein (uromucoid) found in abundance in normal urine. They suggested that Tamm-Horsfall gylcoprotein (THG) constitutes an important non-immunological anti-infectious mechanism in the bladder.

No previous studies have been performed to compare the excretion of THG in girls suffering from recurrent UTI and healthy subjects.

The present study was undertaken to compare the urinary excretion and concentration of THG in girls suffering from recurrent UTI and age-matched controls.

Materials and Methods

The sutdy group comprised 16 otherwise healthy girls between 5 and 17 years (median 9 years) with uncomplicated recurrent lower UTI. All patients had experienced at least two symptomatic episodes of UTI with positive urinary cultures ($> 10^5$ colonies/ml urine of the same organism) within the last year. All patients had been free from UTI during the preceding three months. In each girl structural abnormalities of the urinary tract had been excluded by normal intravenous pyelograms and normal voiding cystourethrograms. No radiological signs of kidney damage were noted in the patients.

The control group comprised 14 girls between 6 and 14 years (median 10 years) who, based on history and urinary culture, were hitherto free from UTI.

For the determination of urinary THG, a 24-h urine sample was collected in each girl. THG was determined immunologically according to Bichler [1]. The antibody used was obtained from Behringswerke AG, Marburg, FRG. The standard was produced by isolating THG according to Tamm and Horsfall [11]. After three precipitations the protein concentration was determined according to Lowry et al. [1]. No further attempts have been made to purify the THG.

The Mann-Whitney rank test was used for statistical analysis. Probabilities < 0.05 were considered significant.

Results

In the preceding year the 16 girls in the study group hat 39 bacteriologically proven urinary tract infections. On 31 occasions (79%) the organism was *E. coli*, while in the remaining cases other enterobacteriae were isolated.

In the UTI group the concentration of THG ranged from 11 to 313 mg/l (median 80 mg/l), while in the control group the concentration varied between 44 and 2,200 mg/l (median 80 mg/l). The 24-h THG excretion ranged from 7.9 to 172.2 mg (median 69.0 mg) in the UTI group versus 18.0 to 2,750.0 mg (median 63.2 mg) in the control group. No significant difference was found in THG urinary concentration nor in excretion among the patient and control groups ($p > 0.05$).

Discussion

The natural defence mechanisms of the bladder against urinary tract infections are complex and as yet incompletely understood. The adherence of the bacteria to the mucosal epithelial cells of the bladder is considered a prerequisite for the development of urinary tract infections [8]. This process, however, may be influenced by the biological fluid bathing both cell types [8].

Although isolated and described in 1950 by Tamm and Horsfall [10] the biological functions of THG are only partly understood. THG is known to inhibit viral hemagglutination [10, 11] and is suggested to promote clacium phosphate crystal formation which may lead to stone formation in the urinary tract [2].

THG is produced in the distal renal tubule [9] and is the most abundant protein of renal origin in normal urine [7]. Its carbohydrate chain contains mannose residues which may compete with epithelial surface receptors for bacteria type 1 fimbriae or other bacterial surface lectins. Consequently, the THG in the urine may prevent bacteria from becoming attached to the bladder wall. This would enhance the bacterial washout effect, constituting an efficient antibacterial defence mechanism against bacterial colonization of the bladder. Therefore it may be hypothesized that decreased, absent or altered THG in the urine would leave some girls more prone to UTI.

The present study showed neither a decreased output nor a lowered urinary concentration of THG in the girls with recurrent UTI. Accordingly, the hypothesis that a reduced output of THG may influence the pathogenesis of UTI in young girls may be wrong. However, as diurnal and day to day variations in THG excretion have been observed [3, 7] indicating that transiently low excretion rates may leave the girls susceptible to bacterial colonization of the bladder. Such variations in the excretion rate of THG may have been overlooked in the present study. Furthermore, functional heterogeneity of THG due to changes in the composition of the urine (pH, osomolality ect.) or genetic polymorphism may influence the ability and/or capacity of THG to trap bacteria. Thus, despite a normal THG excretion rate the ability and/or capacity to trap bacteria may be decreased. This concept is supported by a recent report which shows that THG from different individuals exhibit considerable heterogeneity of the electrophoretic patterns and lectin binding profiles [4].

Therefore, it is concluded that further studies of excretion rates and the heterogeneity of the glycopart of THG in patients with recurrent UTI are warranted to gain more insight into the importance of THG in the bladder defence mechanism against urinary tract infections.

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