

ORIGINALS

Is Urinary Cholesterol Determination a Possible Screening Test for Urological Carcinomas?

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Summary. It has been suggested that the determination of urinary cholesterol may be of possible value in the diagnosis of urogenital carcinomas, especially of the prostate, kidney and bladder, but it has not proven whether this method could be used as a screening test in large numbers of patients. 430 males and 545 females over 50 years old were selected for the study. Total urinary cholesterol values exceeding the upper 3 SD limit of 5.1 mg/24 h (regarded as positive results) were present in 13 males (3%) and 9 females (1.6%). Besides benign diseases of the kidney and the urogenital tract, 2 carcinomas of the bladder and 1 carcinoma of the kidney were detected in the male group with elevated urinary cholesterol excretion. In view of the expensive methodology and most importantly because of the low prevalence of urological carcinomas in unselected populations this method cannot be recommended as a primary screening test. This does not exclude the possibility that urinary total cholesterol determinations could be successfully applied in preselected populations with an increased prevalence of urological carcinomas.

Key words: Urinary cholesterol, Screening test, Urological carcinoma, Predictive value.

INTRODUCTION

It has been suggested that the determination of urinary cholesterol may be of possible value in the diagnosis of urogenital carcinomas, especially of the prostate, kidney and bladder (1-14). Even for early clinical stages of these diseases (T1N0M0 - T2N0M0) the diagnostic sensitivity of urinary total cholesterol was considerable

(6, 11, 12, 13). In these studies positive values of 52% for prostatic carcinoma, 56% for renal carcinoma and 64% for carcinoma of the bladder were reported. In advanced clinical stages of these cancers a further increment of the diagnostic sensitivity of the urinary cholesterol method was observed based on the upper 2 SD limit of 3.0 mg/24 h as the cut-off point.

Diagnostic specificity of urinary cholesterol determinations for these malignancies is reduced by the fact that elevated values have been observed in diseases of the kidney and in urinary tract obstruction, especially patients with prostatic adenoma and residual urine (11, 12, 13).

However, even in view of these findings, it seemed to be necessary to investigate whether urinary cholesterol determination could be used as a primary screening test for these carcinomas in large numbers of patients.

MATERIALS AND METHODS

In a period of 3 years we investigated 430 male and 545 female patients (age range male 50 - 83 years, median 62.2; age range female 50 - 84 years, median 59.8).

They were admitted to the department of medicine because of various internal diseases.

The 975 patients consisted of 215 with endocrine and metabolic disorders, 254 with cardiovascular, 312 with gastrointestinal, 108 with respiratory and 86 with haemopoietic disorders. On the date of the urine analysis there was no evidence of neoplasias or disease of the kidney or urinary tract based on the case history, physical examination and laboratory findings. Further specific investigations were done in patients with elevated urinary cholesterol values, including second rectal examination, urography, cystoscopy and renal ultrasonography in most cases.

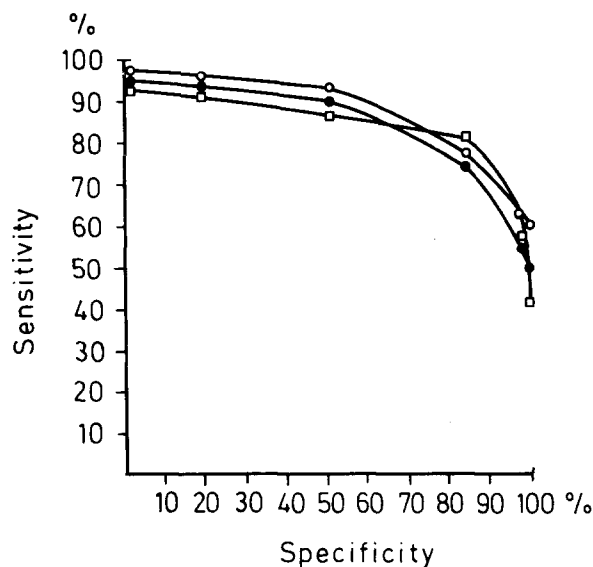


Fig. 1. Correlation of sensitivity and specificity of total urinary cholesterol in T1N0M0 - T2N0M0 stages of prostatic ●, bladder ○ and renal ■ carcinomas

Table 1

Diseases	Males	Females
Carcinoma of the kidney	1	-
Carcinoma of the bladder	2	-
Carcinoma of the prostate	-	-
Adenoma of the kidney	1	1
Adenoma of the prostate	2	-
II-III		
Renal cyst	1	1
Urolithiasis	1	1
Other diseases of the kidney	1	3
Unexplained	5	3

Total urinary cholesterol was analyzed in 2 ml aliquots of 24 h urines with a gas-liquid chromatographic assay using 4-androstendione as internal standard and peak-height ratio technique for quantitation. This method has been described in detail previously (11).

The upper 3 SD value of 5.1 mg/24 h of total urinary cholesterol was used as the upper limit of the normal range to avoid a high rate of positive test results. When this value is adopted the specificity of the method should be about 99%, a level which is absolutely necessary in screening studies in view of the low prevalence of urological cancers. Diagnostic sensitivity decreases little using this cut-off point in comparison to the common upper 2 SD value of 3.0 mg/24 h total urinary cholesterol. A correlation between diagnostic sensitivity and diagnostic specificity for urinary total cholesterol and prostatic, bladder and renal

cancers in T1N0M0 - T2N0M0 stages is illustrated in Fig. 1.

Total urinary cholesterol values exceeding 5.1 mg/24 h were found in 13 male (3.0%) and 9 female (1.6%) patients. In the male group 2 carcinomas of the bladder (T1N0M0 and T2N0M0) and 1 carcinoma of the kidney (T2N0M0) were detected after further investigations, as well as benign diseases of the kidney and the urogenital tract (Table 1). No urological malignancies were diagnosed in female patients with urinary cholesterol hyperexcretion (Table 1).

DISCUSSION

Hyperexcretion of urinary cholesterol in association with urological malignancies has been observed in several studies (1-14) and was suggested to be of possible value in the diagnosis of these diseases (1, 2, 3, 4, 5, 6, 10, 11, 12). In this study positive test results have been obtained in 13 out of 430 male patients and in 9 out of 545 female patients. After further investigations 2 carcinomas of the bladder and 1 carcinoma of the kidney were diagnosed in the male group while in female patients no malignancies could be detected. In most cases other non-malignant diseases of the kidney or the urological tract seemed to be responsible for the measured increments of urinary cholesterol. 8 patients with unexplained urinary cholesterol hyperexcretion deserve follow-up studies, since the presence of occult carcinomas could not be excluded with absolute certainty.

In the population investigated the predictive value of a positive urinary cholesterol test result and the presence of urological neoplasms was 0.23 in the male and 0.0 in the female group.

The high predictive value in the male group was obviously due to patient selection since comparable results could not be expected in testing unselected populations, as in cancer screening projects. The predictive value of 0.0 in the female patients was most probably caused by the low prevalence of urological neoplasms in females.

Discussing the clinical value of the urinary cholesterol method as a primary screening test for urological carcinomas one has to regard the expensive methodology, including the use of 24 h urine collections and most importantly the low prevalence (male 1:500 - 1:1000; female 1:2000 - 1:2500) of these diseases in unselected populations.

Even using a possible colorimetric determination of urinary cholesterol after extraction with organic solvents and the use of morning urine samples, this method cannot be recommended as a primary screening test for urological carcinomas.

This does not necessarily exclude the possibility that the urinary cholesterol method could be successfully applied in preselected populations with an increased prevalence of urological carcinomas which have been revealed in cancer screening programs by a positive test for microscopic haematuria. However, it has to be pointed out that the presence of occult blood in the urine does not lead to a significant increase in urinary cholesterol excretion, which could be found only in patients with macroscopic haematuria.

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