J Korean Med Sci 2001; 16: 309-12
ISSN 1011-8934

The Value of Cystoscopy as an Initial Diagnostic Modality for Asymptomatic Microscopic Hematuria

For the patients who visit outpatient clinics due to asymptomatic microscopic hematuria, cystoscopy has been looked upon as rather invasive compared to other diagnostic methods. We tried to elucidate the actual diagnostic value of cystoscopy in the initial evaluation of asymptomatic microscopic hematuria. We reviewed the results of cystoscopic examinations in 213 patients who visited our hospital due to asymptomatic microscopic hematuria. No definite lesion that could explain the microscopic hematuria was detected by means of IVP, urine cytology, and other nephrologic evaluations for all the patients. Among the abnormal cystoscopic findings in 55 patients, the lesions suspected to be directly related to microscopic hematuria were classified as 'significant lesions' (31 patients, 17.6%) which include entities such as bladder cancer (1.31%). 27 of 31 patients with significant lesions (85.2%) were over 50 yr old, and furthermore, 3 patients who were diagnosed as bladder tumor by cystoscopy were over 60 yr. Cystoscopy should be utilized as initial diagnostic modality in older patients with asymptomatic microscopic hematuria to rule out any possibility of bladder cancer occurrence. Further studies are needed to justify implementation of cystoscopy as an initial diagnostic modality in younger patients with asymptomatic microscopic hematuria.

Key Words : *Cystoscopy; Hematuria*

Sung Kyu Hong, Curie Ahn*, Hyeon Hoe Kim

Department of Urology and Internal Medicine*, Seoul National University Hospital, Seoul, Korea

Received : 5 December 2000
Accepted : 7 February 2001

Address for correspondence
Hyeon Hoe Kim
Department of Urology, Seoul National University Hospital, 28 Yongon-dong, Chongno-gu, Seoul 110-744, Korea
Tel : +82.2-760-2425, Fax : +82.2-742-4665
E-mail : hhkim@snu.ac.kr

INTRODUCTION

Cystoscopy is one of the initial diagnostic modalities in the management of microscopic hematuria along with intravenous pyelography, ultrasonography and urine cytology. But, for the patients who visit outpatient clinics, cystoscopy has been looked upon as rather invasive compared to other diagnostic methods. In addition, some clinicians have argued that cystoscopy may be costly and needless as an initial diagnostic tool for asymptomatic microscopic hematuria (AMH).

To date, the significance of the association of AMH and bladder cancer is yet to be determined, and there is no agreement on which adult patient with AMH should undergo more extensive workups. Moreover, there is insignificant evidence to support a relation between the severity of microscopic hematuria and the extent of underlying lesion.

Consequently, questions have been raised about the effectiveness of cystoscopy in the management of AMH. The controversy regarding the implementation of cystoscopy as an initial diagnostic modality for AMH still remains. However, not many have evaluated the clinical usefulness of cystoscopy for AMH exclusively, even though many studies have been performed on the clinical implications of the microscopic hematuria. An approach of careful selection is necessary to be able to better utilize available modalities and increase the diagnostic yield, giving priority to the detection of underlying urological malignancy. We tried to elucidate the actual diagnostic value of cystoscopy as an initial diagnostic modality for AMH.

MATERIALS AND METHODS

From the patients who had visited our hospital due to AMH from March 1994 to November 1998, a total of 213 patients (79 male, 134 female) were selected retrospectively. Average patient age was 49.7 yr. All 213 patients had at least two consecutive demonstrations of hematuria (RBC>1-4/HPF) in microscopic examinations. And, all of 213 patients had no positive findings detected by means of the physical examination (including digital rectal examination), intravenous pyelography (IVP), urine cytology, and other nephrologic evaluations that could

Table 1. Classification of abnormal cystoscopic findings discovered in 55 of the 213 patients with asymptomatic microscopic hematuria

Significant lesions	No. patients (%)	Insignificant lesions	No. patients (%)
Bladder cancer	3 (1.31)	Benign prostatic hyperplasia	16 (6.57)
Chronic nonspecific inflammation	21 (12.5)	Mild trabeculation	6 (1.97)
Mild hyperemia	4 (1.97)	Ureterocele	1 (0.65)
Bladder stone	2 (1.31)	Diverticulum	1 (0.65)
Telangiectasia	1 (0.65)		
Total No.	31 (17.6)	Total No.	24 (9.84)

explain the microscopic hematuria. The nephrologic evaluations included urine culture, coagulation battery, immunoglobulin tests (including IgA), complements (C3/C4), urine acid-fast bacilli staining, and renal ultrasonography. No patient with symptomatic microscopic hematuria was included. All of 213 patients had no history of gross hematuria or of diseases (i.e., bladder tumor) that are known to cause hematuria. With no positive finding observed in other diagnostic measures, all 213 patients subsequently had undergone cystoscopic examinations, and we reviewed their results.

Also, we classified the patients into 2 groups (significant/insignificant lesion groups) according to the cystoscopic findings. The lesions that could explain hematuria were designated as "significant lesions", and the others as "insignificant lesions".

RESULTS

Abnormal cystoscopic findings were discovered in 55 (27.6%) of the 213 patients who underwent initial cystoscopic examinations. The lesions that are suspected to be directly related to microscopic hematuria were classified as "the significant lesions" (31 patients, 17.6%); biopsy-proven bladder cancer in 3 patients (1.31%), biopsy-confirmed chronic nonspecific inflammation in 21 (12.5%), mild hyperemia in 4 (1.97%), bladder stone in 2 (1.31%), and telangiectasia in 1 (0.65%) (Table 1). 27 of the 31 patients with significant lesions (85.2%) were over 50 yr old, and furthermore, 3 patients who were diagnosed with bladder tumor by cystoscopy were over 60 yr (Table 2). All 3 patients with bladder cancer had no other abnormal findings in other workups, and the diagnosis of transitional cell carcinoma was confirmed from the biopsy. And, all bladder cancers diagnosed by cystoscopy were under 0.5 cm in diameter and confined to mucosa. The lesions that were assessed as not directly related with microscopic hematuria (the insignificant lesions) were benign prostatic hyperplasia (16 patients, 6.57%), mild trabeculation (6 patients, 1.97%), small ureterocele and diverticulum (1 patient, 0.65%).

Table 2. Age distribution of the 'significant lesion' group

Age (yr)	No. patients
31-40	1
41-50	3
51-60	13
61-70	13
71-80	1
Total	31

No complications from the cystoscopic examination was reported in any of the patients.

DISCUSSION

Without any doubt, the most important cause of microscopic hematuria is the tumor of the urinary tract. Accordingly, most of the studies on AMH had been geared toward diagnosing genitourinary tumors. Carson et al. (1) reported that 22 cases (11%) of bladder cancer were discovered among 200 patients who initially presented with AMH, and also Howard and Golin (2) reported that 16 patients (6.5%) were diagnosed with bladder cancer among 246 patients with AMH. And Murakami et al. (3) reported that among the 1,000 patients who presented with AMH, eventually about 30 patients were diagnosed with tumors of urinary tract (including bladder cancer, renal cell carcinoma, prostate cancer, renal pelvis tumor) in their study. Also, in the study by Mohr et al. (4), after 3-yr follow up of 353 patients who initially presented with AMH, 1 patient was diagnosed with bladder cancer. Overall, previous studies have shown patients with AMH to have incidences of malignancy ranging from 2 to 22% (5, 6).

Unfortunately, however, these aforementioned reports could not specify sole diagnostic value of the cystoscopy, and their results stemmed from assessments of the positive findings from various diagnostic modalities such as IVP, cytology, and ultrasonography. In addition, the percentages of malignancies detected exclusively by the cystoscopy are not assessed in these reports. However, the fact that tumors of urinary tract can present initially as only AMH should not be ignored, and without doubt, the clinical implication of tumors of the urinary tract compared with the benign diseases is of much greater importance. In present study, we tried to unveil the ex-

clusive diagnostic value of cystoscopy for AMH. And among 213 patients with AMH who had no positive finding in other diagnostic measures, 3 patients were diagnosed with bladder cancer through initial cystoscopy alone. Therefore, in these 3 AMH patients with negative findings in all the other diagnostic measures, the cystoscopy proved to be critical.

Thus, the question should be raised. "Is the cystoscopy necessary as an initial diagnostic procedure in every patient with AMH?" Even with the introduction of flexible instruments, the cystoscopy is relatively invasive compared with other modalities, and in reality, some doctors are reluctant to recommend it to every patient with microscopic hematuria. Many have doubted the efficacy of the cystoscopy in the investigation of AMH. The matter of cost-effectiveness is a much debated issue of major implication as is with other diagnostic modalities. If all patients with AMH were to have cystoscopic examination, then there would be a large number of new referrals to urologists, and subsequently, there also would be a considerable increase in the number of cystoscopic examinations with negative findings, which may be observed as being useless. From their 10-yr prospective study of 177 patients who first presented with AMH, Bard (7) reported that not a single case of genitourinary tumor had been detected, and claimed the cystoscopy to be unnecessary considering its relative invasiveness. Also, Jones et al. (8) stated that the cystoscopy proved to be of little value as an initial diagnostic modality for the microscopic hematuria, sighting the fact that the cystoscopy was useful in reaching diagnosis in only 3 of 100 patients enrolled in their study. And, Defelippo et al. (9) reported that bladder tumor was detected in 72% of patients with bladder tumor preoperatively by means of IVP, and raised the question about the actual value of cystoscopy. In the present study, only 3 of the 213 patients with negative findings in all the other diagnostic modalities were diagnosed with bladder cancer via initial cystoscopy. And the cystoscopic findings we classified as "the significant lesions" due to their possible relationship with microscopic hematuria may actually be clinically insignificant with the exception of bladder cancer. Therefore, disregarding the clinical importance of cancer detection, these results may give the impression of cystoscopy as being unnecessary component of the initial evaluation of AMH.

However, with a lingering possibility of malignancy, many conservative doctors still consider cystoscopy to be an important diagnostic tool in the evaluation of AMH. Green et al. (10) claimed that the cystoscopy should be performed in all of the patients who presented with microscopic hematuria without any discrimination according to the age of the patients, and Howard et al. (2) also made similar proposal. Also, Itzchak et al. (11) stated that bladder tumors under diameters of 0.5 cm is difficult to detect with ultrasonography and stressed the necessity of the cystoscopy. In addition, Hattori et al. (12) noted in their study of bladder tumor patients that cystoscopy is much superior to IVP and cytology as diagnostic modality for bladder tumor. Also, Murakami et al. (3) claimed that even though urine cytology is less invasive and can be repeated without any risk of complications, due to its low detection rate for low stage and low grade bladder tumors, the cystoscopy (detection rate: 90%) is a vital part of the surveillance for bladder tumor. Reviewing previous literatures, even though the reports discussing actual exclusive value of cystoscopy in the initial evaluation of AMH are scarce, it is evident that the usefulness of cystoscopy in the diagnosis of bladder cancer is unmatched compared with other modalities. And considering aforementioned incidences of malignancies, mostly being bladder cancer, reported in patients with AMH, the relative importance of cystoscopy should not easily be discounted in the evaluation of AMH. In the analysis of present series, a simple numerical comparison of 3 patients diagnosed with bladder tumor and the other patients are not justified. And, the fact that malignancy which otherwise could have been missed was detected via cystoscopy should not be disregarded. An argument could be made that small, low-stage bladder cancer not detected by initial IVP, urine cytology, and ultrasonography may not pose immediate problem. However, one of the rationales for investigating patients with microscopic hematuria is that malignancy may be diagnosed at an early stage, and the implementation of cystoscopy as an initial diagnostic procedure is advocated in this regard. In our series, bladder cancers in all 3 patients were detected in early stage with the cancer still confined to mucosa. Whelan et al. (13) have shown a trend suggesting that earlier treatment of bladder cancer may result in a lower risk of progression of disease even though this remains to be verified by larger studies.

With the controversy still surrounding clinical value of cystoscopy as an initial diagnostic modality for AMH, many efforts have been made to establish a new diagnostic protocol for AMH. Despite the efforts made, it was impossible to discriminate so called "high risk group" among the patients with AMH. Although many protocols have been reported, no general guidelines have been set in concerning the appropriate age of patients to perform cystoscopy in the surveillance of bladder cancer. Many institutions have their own guidelines concerning the choices of initial diagnostic procedures for AMH. With the concept of minimal invasiveness and cost-cutting sweeping through the whole medical fields, many institutions have already abandoned cystoscopy as

an initial diagnostic modality for AMH regardless of patients' age. However, since there is still little evidence to fully support this position, and large population-based studies to determine the prevalence of AMH and the efficacy of cystoscopy are scarce, the cystoscopy should not be completely excluded from the list of initial diagnostic modalities for AMH. Hattori et al. (12) reported that the cystoscopy proved significant among the patients with microscopic hematuria who are over the age of 40. Also, Sultana et al. (14) reported that full initial investigation including cystoscopy is justified with older patients with AMH, as malignancy will be detected in a significant proportion of patients with AMH. In their series, the incidence of malignancy was reported to be 5% among the total of 126 AMH patients aged 50 yr or more. But, as with other aforementioned reports, these series have not focused exclusively on the efficacy of cystoscopy alone. In our study, we focused on the efficacy of cystoscopy and tried to evaluate its value as an initial diagnostic modality for AMH by the selection of AMH patients with no positive findings in all the other diagnostic modalities and measures. In our series, all 3 patients with bladder cancer were over 60 yr of age, and the most of the patients (85.2%) with significant lesion discovered in cystoscopic exam were over the age of 50 yr. As previously mentioned, the interpretation of our present results may be complicated, and also findings of any statistical significance may not be observed. However, the significance of this study may lie in the observation of patients with AMH being diagnosed with malignancy in early stage solely via cystoscopy. Also, the fact that patients with AMH who had been diagnosed with bladder cancer were all over the age of 60 yr may give support to justifying initial cystoscopy in the evaluation of older patients with AMH.

We recognize the fact that our present study may be considered preliminary not being a larger-sized study. Also, in cost-conscious medical environment, the emphasis on the incidence of malignancy may not be enough to support the usage of cystoscopy as an initial diagnostic modality for AMH. To date, no randomized, prospective studies have compared the outcomes of patients with AMH undergoing cystoscopy with those of patients undergoing minimal evaluation. Further studies are needed to set a more definite guidelines, but necessity of the cystoscopy as an initial diagnostic modality in older patients with AMH should not be ignored.

In summary, the cystoscopy should be utilized as an initial diagnostic modality in older patients with asymptomatic microscopic hematuria to rule out any possibility of bladder tumor occurrence. Any recommendations regarding specific range of patients' age should be reserved until further studies are completed. Further studies are needed to justify implementation of cystoscopy as an initial diagnostic modality in younger patients with asymptomatic microscopic hematuria. However, we believe that the implementation of cystoscopy as an initial diagnostic modality in older patients with AMH may even prove to be cost-effective in the future considering clinical implication of malignancy. Without having any concrete medical evidence, the cystoscopy should not be easily excluded from choices of initial diagnostic measures in the management of AMH.

REFERECES

1. Carson CC III, Segura JW, Greene LF. *Clinical importance of microhematuria. JAMA 1979; 241: 149-50.*
2. Howard RS, Golin AL. *Long term follow up of asymptomatic microhematuria. J Urol 1991; 145: 335-6.*
3. Murakami S, Igarashi T, Hara S, Shimazaki J. *Strategies for asymptomatic microscopic hematuria: a prospective study of 1034 patients. J Urol 1990; 144: 99-101.*
4. Mohr DN, Offord KP, Owen RA, Melton LJ 3d. *Asymptomatic microhematuria and urologic disease: a population-based study. JAMA 1986; 256: 224-9.*
5. Britton JP, Dowell AC, Whelan P, Harris CM. *A community study of bladder cancer screening by the detection of occult urinary bleeding. J Urol 1992; 148: 788-90.*
6. Ritchie CD, Bevan EA, Collier SJ. *Importance of occult haematuria found at screening. Br Med J 1986; 292: 681-3.*
7. Bard RH. *The significance of asymptomatic microhematuria in women and its economic implications: a ten-year study. Arch Intern Med 1988; 148: 2629-32.*
8. Jones DJ, Langstaff RJ, Holt SD, Morgans BT. *The value of cystourethroscopy in the investigation of microscopic hematuria in adult males under 40 years: a prospective study of 100 patients. Br J Urol 1988; 62: 541-5.*
9. DeFelippo NP, Fortunato RP, Mellins HZ, Ritchie JP. *Intravenous urography: important adjunct for diagnosis of bladder tumours. Br J Urol 1984; 56: 502-5.*
10. Greene LF, O'Shaughnessey JEJ, Hendricks ED. *Study of five hundred patients with asymptomatic microhematuria. JAMA 1956; 161: 610-4.*
11. Itzchak Y, Singer D, Fischelovitch Y. *Ultrasonographic assessment of bladder tumors. I. tumor detection. J Urol 1981; 126: 31-3.*
12. Hattori R, Ohshima S, Ono Y, Miyake K. *The significance of cystoscopy for the diagnosis of urothelial tumors. Int Urol & Nephrol 1993; 25: 135-9.*
13. Whelan P, Britton JP, Dowell AC. *Three-year follow-up of bladder tumours found on screening. Br J Urol 1993; 72: 893-6.*
14. Sultana SR, Goodman CM, Byrne DJ, Baxby K. *Microscopic hematuria: urological investigation using a standard protocol. Br J Urol 1996; 78: 691-6.*