

Haematuria in the Diagnosis of Urinary Calculi

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Abstract

The aims of this study were to compare the sensitivity of urine dipstix (Combur 9 test) versus urine microscopy in detecting haematuria and to determine the proportion of patients with renal or ureteric colic due to urinary calculi who have haematuria.

This is a prospective study of 122 patients presenting to an emergency department in a tertiary teaching hospital with symptoms suggestive of renal or ureteric colic. The same urine specimen tested using dipstix was sent for urine microscopic examination for haematuria, after which a plain radiograph of the kidneys, ureter and bladder was done. An early intravenous urogram was done (delay of an average of 4 days). Telephone interviews were done to determine whether any calculi had been passed. Urine dipstix detected haematuria in 95.4% [95% confidence intervals (CI) 87.1% to 100.0%] of patients with urinary calculi, whilst urine microscopy detected haematuria in 70.8% (95% CI 58.2% to 92.6%). This study showed that urine Combur 9 is more sensitive than urine microscopy in detecting haematuria. The combined use of urine Combur 9 and microscopy does not increase the sensitivity of detecting haematuria. In the absence of haematuria on urine Combur 9 for suspected ureteric colic, alternative diagnoses should be considered.

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Introduction

Patients with renal or ureteric colic are commonly seen at our Emergency Department. We routinely check their urine for haematuria using the Combur 9 test (Boehringer Mannheim, Germany) alone without doing urine microscopy unless the patient shows pyuria on the Combur 9 test. Over the years, our observation has been that virtually all of these patients have haematuria in some degree shown on the Combur 9 test. We have observed that even if the initial urine Combur 9 test was negative for haematuria, a repeat test done about an hour later would always be positive for haematuria. To our knowledge, there are many emergency physicians and urologists who still rely on urine microscopy to detect haematuria in patients suspected of having urinary calculi.

There was no reliable information in the literature correlating haematuria and urinary calculi. This observation was confirmed by Press and Smith¹ who were unable to find any studies supporting a 10% incidence of negative haematuria in patients with acute urinary lithiasis as suggested by Drach.² We had decided to carry out

a study to document the proportion of patient with urinary calculi who have haematuria shown on urine Combur 9, urinary microscopic analysis or both and to find out how detection of haematuria using urine Combur 9 compares with urine microscopy.

Materials and Methods

This is a prospective study of 141 non-consecutive patients presenting to our Emergency Department between 21 July 1994 and 1 February 1995. Prior approval was obtained from the Medical Affairs Department of our hospital. Patients were entered into the study if they had classical presentation of loin or loin to groin pain, consistent with a clinical diagnosis of renal or ureteric colic.

All patients after history and physical examination were asked to produce a sample of urine for Combur 9 testing by the Emergency Department doctors or nurses. Combur 9 test manufactured by Boehringer Mannheim is a nine-patch test strip. Among the 9, 1 is for detection of blood. Haemoglobin and myoglobin catalyze the oxidation of the indicator contained on the test paper by

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an organic hydroperoxide. Scattered or compacted green dots on the test patch are indicative of intact erythrocytes [practical sensitivity limit 5 red blood cells (RBCs)/ml]. Haemoglobin, haemolysed erythrocytes and myoglobin are indicated by a uniform green coloration of the test patch. The practical sensitivity limit for haemoglobin corresponds to 10 RBCs/ml. Ascorbic acid does not interfere with the test because it contains iodate.

The same urine specimen tested by Combur 9 was then sent to the laboratory for microscopic examination using the Microtitre Plate Sedimentation Method. 300 μ l of well-mixed (unspun) urine was transferred into a flat bottom microtitre plate well and left standing for 20 to 30 minutes to allow the sediment to settle before examination with a microscope. Our laboratory facilities are accredited by the College of American Pathologists (Lab No. 30107-01). Whenever necessary, patients were given pain relief, mainly by an intramuscular injection of a non-steroidal anti-inflammatory drug.

Plain radiographs of the kidneys, ureters and bladder (KUB) were done at the Emergency Department during that attendance. A data form was filled in by the emergency physician. An early intravenous urogram (IVU) appointment was made at the Department of Diagnostic Imaging. The patients were also given a referral letter to the urology specialist clinic for a follow-up after the IVUs were done. In patients who did not turn up for IVUs or whose initial KUBs suggested a radioopaque calculi but the IVUs done were reported as negative, telephone interviews were done at least 6 months later to find out whether any calculi had been passed.

Haematuria was considered present if either of the following was detected:

- 1) Urine Microscopy:
 - In males, if there were more than 5 RBCs/high powered field (hpf).
 - In females, if more than 10 RBCs/hpf.
- 2) Urine Combur 9:
 - Detection of 1+, or more of intact red blood cells or haemoglobin.

Urinary calculi was considered to be present if IVU confirmed the presence of urinary calculi or if urinary calculi were passed by the patient.

Results

Out of the 141 patients who fulfilled the inclusion criteria, only 122 had complete urine microscopy and Combur 9 results (Fig. 1). Hence only 122 patients could be analysed and compared.

There was lapse of an average of 4 days between the KUBs and IVUs. Those patients who did not turn up for their IVU appointments and who were not contactable by telephone had to be excluded. Out of 4 patients whose initial KUBs suggested urinary calculi but the eventual

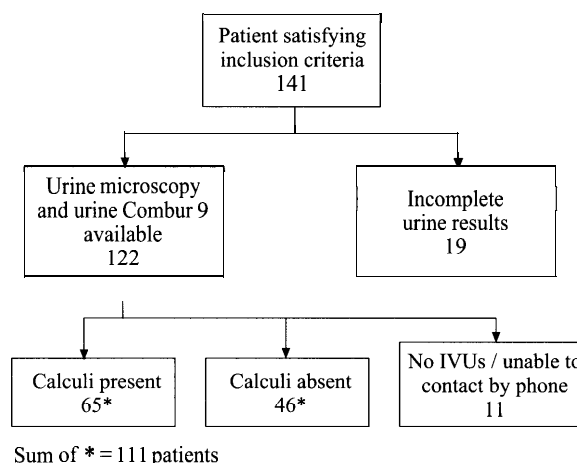


Fig. 1. How patients were recruited

TABLE I: URINE COMBUR 9 VERSUS URINE MICROSCOPY IN DETECTING HAEMATURIA WHEN POSITIVE HAEMATURIA IS DEFINED AS 1+ AND ABOVE

Urine Combur 9	Urine Microscopy		Total
	Positive	Negative	
Positive ($\geq 1+$)	77	37	114
Negative (0)	0	8	8
Total	77	45	122

Sensitivity = 100% (95% CI 95.3% to 100.0%)

Specificity = 17.8% (95% CI 8.0% to 28.4%)

IVUs done revealed no calculi, 2 could not be contacted by telephone to find out whether calculi were passed. These 2 patients were considered to have no calculi. Sixty-five had urinary calculi present while 46 had no urinary calculi. Hence, only 111 patients could be analysed for the sensitivity and specificity of urine Combur 9 testing versus urine microscopy in detecting haematuria in urinary calculi.

Patient's Profile

There were 114 men and 27 women giving a ratio of 4.2:1. Their ages ranged from 17 to 70 years with a mean of 39.7 years. There were 95 (67.4%) Chinese, 30 (21.3%) Malays, 11 (7.8%) Indians and 5 (3.5%) Others.

Urine Combur 9 versus Urine Microscopy in Detecting Haematuria

Only 122 patients had complete urine microscopy and Combur 9 results. One hundred and fourteen (93.4%) had haematuria $\geq 1+$ on urine Combur 9; of whom only 77 (63.1%) had positive urine microscopy (Table I). All 8 with negative urine Combur 9 had negative urine microscopy. No patients had haematuria detected on microscopy but not on urine Combur 9.

Hence, urine Combur 9 has 100% sensitivity when positive haematuria is defined as 1+ and above. Refer-

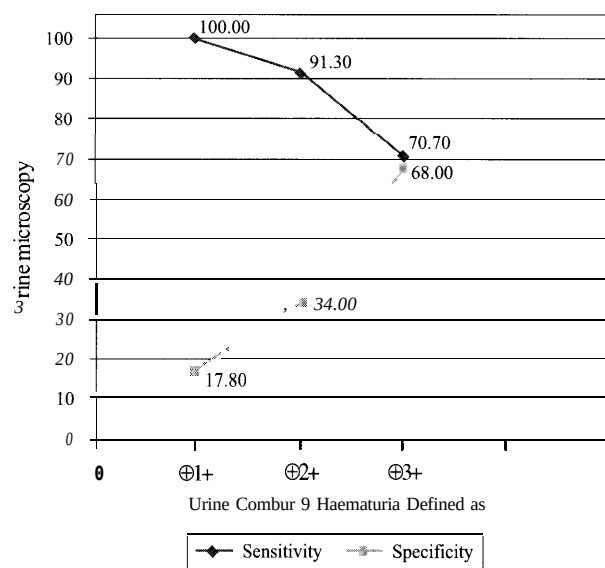


Fig 2. Urine Combur 9 versus urine microscopy in detecting haematuria when positive haematuria on urine Combur 9 is defined differently.

ring to Figure 2, as the definition of haematuria on urine Combur 9 becomes more stringent, as expected, the sensitivity decreases while the specificity increases.

Haematuria as an indicator of urinary calculi using urine Combur 9, urine microscopy or both (positive haematuria on Combur 9 test is defined as $\geq 1+$)

There were 65 patients out of 111 patients who had urinary stones (Fig. 1). Urine Combur 9 test picked up haematuria in 62 of these patients giving it a sensitivity of 95.4% (Table III). Urine microscopy however detected haematuria in only 46 (70.8%) patients (Table II). Urine microscopy did not improve on urine Combur 9 in the sensitivity of detecting haematuria, as all urine microscopy positive haematuria were also detected on urine Combur 9 (Table IV).

Sensitivity and specificity of detecting urinary calculi if positive haematuria on Combur 9 test is defined differently

Table V shows the different sensitivities and specificities of detecting haematuria with stricter definition of haematuria on Combur 9 test. It can be seen that even with the strictest definition of 3+ on Combur 9 testing, the specificity was only 36.9%.

Prevalence of asymptomatic haematuria using Combur 9 test

To find out the prevalence of asymptomatic haematuria on Combur 9 test, a control group of 15 males (average age 29.7 years) and 15 females (average age 29.9 years) had their urine tested with Combur 9 test. Four of the females had RBCs of 1+ on Combur 9 test. All 4 had no haematuria on urine microscopy (range 0 to 1 RBCs/hpf).

TABLE II: HAEMATURIA IN URINARY CALCULI USING URINE MICROSCOPY ALONE

Urine Microscopy	Urinary Calculi		Total
	Present	Absent	
Positive	46	23	69
Negative	19	23	42
Total	65	46	111

Sensitivity = 70.8% (95% CI 58.2% to 92.6%)

Specificity = 50.0% (95% CI 35.0% to 65.1%)

Negative haematuria = 29.2%

TABLE III: HAEMATURIA IN URINARY CALCULI USING URINE COMBUR 9 ALONE

Urine Combur 9	Urinary Calculi		Total
	Present	Absent	
Positive	62	42	104
Negative	3	4	7
Total	65	46	111

Sensitivity = 95.4% (95% CI 87.1% to 100.0%)

Specificity = 8.7% (95% CI 2.4% to 17.4%)

Negative haematuria = 4.6%

TABLE IV: COMPARISON BETWEEN URINE COMBUR 9, URINE MICROSCOPY OR BOTH IN DETECTING HAEMATURIA IN URINARY CALCULI (POSITIVE HAEMATURIA ON URINE COMBUR 9 IS DEFINED AS $\geq 1+$)

	Haematuria Using:		
	Urine Combur 9 (%)	Urine Microscopy (%)	Both (%)
Sensitivity	95.4	70.8	95.4
Specificity	8.7	50.0	8.7

TABLE V: SENSITIVITY AND SPECIFICITY OF DETECTING URINARY CALCULI IF POSITIVE HAEMATURIA ON COMBUR 9 TEST IS DEFINED DIFFERENTLY

Urine Combur 9 Haematuria Defined as	Sensitivity (%)	Specificity (%)	False Positive Rate (1 - Specificity)
⊕1+	62/65 (95.4)	4/46 (8.7)	91.3
⊕2+	56/65 (86.1)	11/46 (23.9)	76.1
3+	45/65 (69.2)	17/46 (36.9)	63.1

Two of the males had RBCs on Combur 9 test. One of the males had 2+ haematuria. This correlated with a urine microscopy of 4 RBCs/hpf. Another had haematuria of 3+ on 2 separate occasions. The first occasion corresponded to a microscopic examination of 5 RBCs/hpf while the second to 4 RBCs/hpf.

Discussion

The patient profile in this study is comparable to other studies with a male to female ratio of 4.2:1 and a mean age of 39.7 years.^{3,4} The racial distribution reflects quite closely to that of the total population of Singapore.

What constitutes significant haematuria is a matter of debate in the literature because the normal excretion of erythrocytes in the urine is difficult to ascertain. There have been varying definitions of significant haematuria. Press and Smith from New Hyde Park defined significant haematuria as greater than 0 to 1 RBCs/hpf. In their paper, they quoted 2 others studies by Mariani et al and Elton et al defining significant haematuria as >3 RBCs/hpf. Chia et al⁴ defined significant haematuria as >5 RBCs/hpf in males and >10 RBCs/hpf in females. We have chosen to use Chia et al's definition of significant haematuria as we believe this is probably the most widely accepted definition amongst urologists.

There are a number of dipstix tests available in the market. Among the unique features of Boehringer Mannheim's combur test strips include the following:

- The absorbent paper prevents smudging of the colour test pads.
- The comparison colours printed on the vial do not require user to rotate vial for easy reading of the test results.
- The test strips are contained in an aluminium or plastic vial closed with a desiccant stopper which protects against humidity and light instead of having the desiccant in the vial which may be lost in the process of handling.

Urine Combur 9 is more sensitive than urine microscopy in detecting haematuria. This may be due to various reasons. Haemolysis may be a factor.⁵ In one study by Adams et al⁶ on haematuria, they found evidence of haemolysed blood in 90% of urine. Only 10% of the urine specimens contained intact erythrocytes without evidence of haemolysis. Since the extent of haemolysis may vary widely from one urine specimen to another, microscopic enumeration of erythrocytes cannot give a reliable indication of the total amount of bleeding.

Defining haematuria on Combur 9 test as 1+ and above may seem to create a high false positive rate (Table V). However, among the 13 patients in the study with RBCs 1+ on Combur 9 test, 5 had urinary calculi (4 with haematuria on urine microscopy while 1 did not). Since making a stricter definition of haematuria on Combur 9 test may increase the specificity but risk misdiagnosing a significant percentage of patients with calculi, it would be more prudent to use a practical definition of haematuria as 1+ and above on Combur 9 test. Referring to Table V, using the strictest definition of haematuria of 3+, the sensitivity would then almost equal that using

urine microscopy (69.2% versus 70.8%). However, the specificity does not reach the level using urine microscopy (36.9% versus 50.0%). Urine microscopy costs 5 times more than urine Combur 9 test (S\$10 versus S\$2). In addition to this, Combur 9 test is so much more convenient and the result is obtained faster compared to urine microscopy.

The IVU is generally considered as the "gold standard" diagnostic test for urinary calculi.^{1,7,8} However in our study, IVU could not be done on the same day due to logistic problem.

There was a delay of an average of 4 days between the KUB and IVU. A stone may have passed out between the time the KUB and the IVU were done. To circumvent this problem, whenever possible, we tried to do a telephone interview to find out whether any stone was passed in cases where the IVUs done revealed no calculi. Passage of a stone or positive IVU as a criterion for the presence of ureteral stone was also used in a study by Elton et al.⁸

As we can see from Tables II and III, the sensitivity of detecting urinary calculi using urine microscopy alone and urine Combur 9 alone was 70.8% and 95.4%, respectively. A combination of urine microscopy and urine Combur 9 did not increase the sensitivity of detecting haematuria at all (Table IV). This contrasts with Press and Smith's study¹ where the sensitivity of using microscopy alone as an indicator of acute urinary lithiasis was 85.5% while a combination of urine microscopy and dipstick was 94.5%. The dipstix used in this study was that manufactured by Ames Division, Miles Laboratories, Elkhart, Ind.

The prevalence of negative haematuria using urine microscopy alone was 29.2% compared to 4.6% when urine Combur 9 was used alone or in combination with urine microscopy. This contrasts with Press and Smiths study¹ on the incidence of negative haematuria in acute urinary lithiasis where they found a 14.5% incidence of negative haematuria using urine microscopy alone in contrast to 5.5% when a combination of urine microscopy and dipstick was used. Elton et al⁸ found that a patient presenting to their emergency department with acute flank pain and haematuria (defined as >3 RBCs/hpf) has a 90% probability of a ureteral stone. However, they did not use haematuria on urine dipstix in their clinical prediction rule for the diagnosis of ureteral calculi.

Conclusion

Our study showed that urine Combur 9 is more sensitive than urine microscopy in detecting haematuria in urinary calculi (95.4% versus 70.8%). There was no increased sensitivity in using a combination of urine microscopy and urine Combur 9 in detecting haematuria. Hence, in the emergency department setting, it is sufficient to use urine Combur 9 alone to detect haematuria.

The prevalence of haematuria in urinary calculi using urine Combur 9 alone was 95.4%. Thus, when there is no haematuria detected using urine Combur 9 in a patient with isolated right or left iliac fossa pain, alternative diagnoses to ureteric colic should be considered.

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REFERENCES

1. Press S M, Smith A D. Incidence of negative haematuria in patients with acute urinary lithiasis, presenting to the emergency room with flank pain. *Urology* 1995; 45:753-7.
2. Drach G W. Urinary lithiasis: Aetiology, diagnosis and medical management. In: Walsh P C, Retik A B, Stamey T A, Vanghan E D Jr, editors. *Campbell's Urology*. 6th ed. Vol. 3. Philadelphia: WB Saunders, 1992:2085-116.
3. Weiss A, Price R, Sage M, Barratt L. The intravenous pyelogram in renal colic. *Australas Radio* 1988; 32:429-33.
4. Chia S J, Lau W, Tan P K, Consigliere D, Li M K, Low C H. Ureteric colic: Value of initial investigations and outcome. *Ann Acad Med Singapore* 1995; 24:366-9.
5. Arm J I, Peile E B, Rainford D J, Strike P W, Tettmar R E. Significance of dipstick haematuria. I. Correlation with microscopy of the urine. *Br J Urol* 1986; 58:211-7.
6. Adams E C, Fetter M C, Free H M, Free A H. Haemolysis in haematuria. *J Urol* 1962; 88:427-30.
7. Mutgi A, Williams J W, Nettleman M. Utility of the plain abdominal roentgenogram. *Arch Intern Med* 1991; 151:1589-92.
8. Elton T J, Roth C S, Berquist T H, Silverstein M D. A clinical prediction rule for the diagnosis of ureteral calculi in emergency departments. *J Gen Intern Med* 1993; 8:57-62.