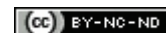


C-Reactive Protein as a Predictor for Early Intervention in Patients with Ureteric Calculus- A Prospective Study

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ABSTRACT

Introduction: Inflammation of ureteric wall may impede the passage of calculus which reduces the chances of spontaneous expulsion. C-Reactive Protein (CRP) being an acute phase reactant elevates in almost all inflammatory conditions.

Aim: To determine whether CRP levels can predict the need for early intervention in symptomatic ureteric calculus.

Materials and Methods: The sample was estimated to be 140 patients over the age of 18 years during the study duration of six months. Ureteric calculus measuring 5-10 mm were subjected to Medical Expulsion Therapy (MET) (Silodosin 8 mg at night). CRP levels were estimated on day 1 and day 7 from the presentation. CRP less than 6 mg/L was considered normal, represented as 'negative' in the present study; more than or equal to 6 mg/L was taken as 'positive'. Patients who demonstrated rising/

elevated CRP were considered for early endoscopic/surgical intervention. Data was analysed by Statistical Package for the Social Sciences (SPSS) v19.00.

Results: Out of the 140 patients, 56 patients had positive CRP on day 7, of which only nine patients had expelled the stone at the end of two weeks (16.07%). Out of 84 negative CRP group patients, 56 showed evidence of spontaneous calculus expulsion within one week and 18 patients at the end of two weeks and 10 patients did not demonstrate spontaneous expulsion at the end of two weeks and required intervention. The present study showed a statistically significant correlation between the positive CRP levels and the rates of spontaneous expulsion of ureteric calculus ($p=0.0001$).

Conclusion: CRP can be used as a predictor for an early intervention of symptomatic ureteric calculus.

Keywords: Inflammation, Ureteric coli, Urolithiasis

INTRODUCTION

Ureteric colic is one of the most common causes of acute abdomen presenting to the emergency department, representing about 20% of all cases of urolithiasis [1]. It is, however, observed that calculi measuring <7 mm, especially those located in the distal ureter, can get spontaneously extruded with MET [2]. The calculus within the lumen of the ureter causes an inflammatory reaction, which combined with the distension of the renal capsule, is the possible explanation for the intense pain associated with this condition. Ureteric calculus measuring <5 mm in its maximum diameter can be missed on both X-ray or USG abdomen and pelvis [2]. Inflammation of the ureteric wall may also impede the passage of the calculus within, hence reducing the chance of spontaneous extrusion. Plasma CRP is a non-specific, acute phase reactant protein, and is found to elevate in almost all inflammatory conditions [3]. Hence, it is postulated that CRP can be elevated in ureteric inflammatory disorder secondary to the luminal inflammation and occlusion. The estimation of CRP has the added advantage of being quick, inexpensive and non-invasive, and also is easily available in all medical centers. Hence, the aim of this study was to determine whether CRP levels can predict the need for early intervention in symptomatic ureteric calculus.

MATERIALS AND METHODS

This was a prospective, single-institution study. The study sample was estimated to be 140 patients over the age of 18 years, males and females who presented to the emergency department or Outpatient Department with symptomatic ureteric calculus measuring 5-10 mm between March 2018 to December 2018. Approval to conduct the study was sought from the Institutional Ethics Committee (IEC 2018/32/2). Those patients with active urinary tract infection, moderate to severe hydronephrosis, multiple calculi, malignancy or impaired renal function were excluded from the study. After obtaining a written and informed consent, patients were subjected to clinical examination with biochemical and radiological evaluation. Calculus size was measured using Non-contrast CT scan of abdomen and

pelvis. All these patients were then subjected to MET (Silodosin 8 mg at night). CRP levels were estimated on day 1 and day 7 from the presentation. CRP less than or equal to 6 mg/L was considered normal, represented as 'negative' in this study; more than 6 mg/L was taken as 'positive'. Patients who demonstrated rising/elevated CRP were considered for early endoscopic/surgical intervention. Those patients with normal or demonstrating down trend of CRP on Day 7 are followed-up for two weeks. If the ureteric calculus has not been expelled after two weeks, then patients were subjected for endoscopic/surgical intervention.

Sample Size Estimation

Sample size was estimated by using the proportion of spontaneous expulsion of the calculus in patients with negative CRP which was 90.9% from the study by Park CH et al., [4] using the formula:

$$Z_{(1-\alpha/2)}^2 p(1-p)/d^2. p=90.9 \text{ or } 0.909, q=9.1 \text{ or } 0.091, d=5\% \text{ or } 0.05$$

Using the above values at 95% confidence level a sample size of 127 subjects with symptomatic ureteric calculus were included in the study. Considering 10% non-response a sample size of $127+13 \approx 140$ subjects were included in the study.

STATISTICAL ANALYSIS

All the demographic data was recorded in a semi-structured proforma and entered in an MS Excel spread sheet and using SPSS software version 19.00. Statistical analysis of the study was conducted using the mean, standard deviation, and Chi-square test. A p-value of <0.05 was considered as statistically significant.

RESULTS

A total of 140 patients were included in the study, of which 106 (75.71%) patients were males. The mean age of the study population was 29.34 years. The mean stone size was 7.23 mm. It was found that 84 out of 140 patients had negative CRP (<6 mg/L) on day 7, while the remaining 56 had positive CRP levels. Of the

negative CRP group patients, 56 showed evidence of spontaneous calculus expulsion within one week and 18 patients at the end of two weeks. This shows an 88.09% calculus expulsion rate in those that had negative CRP levels. It was found that only 10 patients did not demonstrate spontaneous expulsion at the end of 2 weeks and required intervention. The results were comparable between males and females. Of the 140 patients, 56 patients had positive CRP on day 7, of which only nine patients had expelled the stone at the end of two weeks (16.07%). Out of the 56 patients with positive CRP, 32 patients had more than two emergency visits to hospital for pain which required admission (57.14%). It was also observed that the episodes of pain in abdomen and revisit rates were higher in patients with positive CRP levels. This study showed a statistically significant correlation between the positive CRP levels and the rates of spontaneous expulsion of ureteric calculus ($p=0.0001$) [Table/Fig-1].

	CRP positive (>6 mg/dL)	CRP negative (<6 mg/dL)
Stone expelled	9	74
Stone not expelled	47	10
Stone expulsion rates	16.07%	88.09%

[Table/Fig-1]: Correlation of CRP with stone expulsion rates. Chi-square test used. p -value=0.0001 (Highly significant)

DISCUSSION

Urolithiasis is a common cause of acute abdomen presenting to the emergency department. The decision to manage such cases conservatively or not depends on various factors such as stone size, location, renal function, duration of symptoms and associated co-morbidities. According to the American Urological Association guidelines, about 98% of ureteric calculi smaller than 5 mm pass spontaneously with MET [5]. However, some calculi do not respond to MET and require endoscopic intervention for the relief of obstruction. The presence of a calculus within the ureter causes oedema, spasm and inflammation, which is responsible for the luminal occlusion, thereby hindering the spontaneous passage of the calculus. There are several markers of inflammation such as CRP and Erythrocyte Sedimentation Rate (ESR) that are routinely performed in systemic inflammatory conditions. Studies have demonstrated that treatment directed as reducing the inflammatory response in the ureter due to the calculus can aid in spontaneous passage of the calculus [6]. CRP is identified as a one such marker, and hence, has the potential to be utilised a marker of inflammation induced by the ureteric calculus. CRP, moreover, can be used as a predictor of spontaneous passage of ureteric calculus, and aid in planning the further management of such calculi [6,7].

In a study done by Angulo JC et al., it was observed that in patients with low CRP, the chances of spontaneous passage of ureteric calculus was higher [8]. In the present study similar results were found, where 74 of the 84 patients with negative CRP had spontaneous expulsion of the calculus at the end of the two week follow-up period. In another study conducted by Park CH et al.,

in patients with negative CRP, 90.9% patients demonstrated spontaneous expulsion of the calculus, which was similar to the present study [4]. Also, it was noted that in patients with positive CRP, spontaneous expulsion was seen only in 58.8%; in the study, only nine out of the 56 patients with positive CRP has spontaneous expulsion of the calculus. Hence, they concluded that the higher the CRP, lower was the spontaneous passage rate of the calculus, which was similar to the findings in the present study. In a study done by Sagar S and Kaushal S, patients those who had spontaneous expulsion of the calculus had normal CRP levels in comparison to those who did expel the calculus [9]. In a study done by Jain A et al., they noted that patients with negative CRP have a higher rate of spontaneous expulsion of calculus [10].

Limitation(s)

In the present study the sample size was small, however, multi-centric randomised control trials are necessary on a larger population to confirm the utility of CRP as a non-invasive and easily implementable predictor for early intervention in ureteric calculus.

CONCLUSION(S)

The results have shown that patients with negative CRP have a higher rate of spontaneous expulsion of ureteric calculus, showing good response to MET. Hence, CRP can be used as a predictor for early intervention of symptomatic ureteric calculus. Thus, patients with positive CRP levels can be given option to undergo early intervention instead of MET.

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