

The Role of Intraprostatic Inflammation in the Acute Urinary Retention

Seyed Alaeddin Asgari¹, Mohaddeseh Mohammadi²

¹ MD, Associated Professor of Urology, Urology Research Center, Guilan University of Medical Sciences, Rasht, Iran.

² MD, Urology Research Center, Guilan University of Medical Sciences, Rasht, Iran.

Correspondence to:

Dr. Mohaddeseh Mohammadi, Urology Research Center, Guilan University of Medical Sciences, Rasht, Iran.
Email: mohaddese_mohammadi@yahoo.com

Date of Submission: Oct 10, 2010

Date of Acceptance: Dec 18, 2010

INTRODUCTION

BPH is one of the most common diseases affecting old aged men and its incidence and prevalence will increase with age.^{1,4} It is reported that an estimated 70% of men aged 61-70 years and 90% of those aged 81-90 have pathological BPH.⁵ The prevalence of BPH among Iranian men above 40 years is estimated to be 23.6%.⁶ BPH would present with LUTS. The progression of LUTS can result in AUR.¹ It is well-recognized by both urologists and pathologists that BPH and prostatitis can coexist.^{7,8} Twenty percent of patients with LUTS associated with BPH might also have symptoms suggestive of prostatitis.^{1,5} But, the relationship between BPH and prostatic inflammation, and how one can influence the presentation, diagnosis, treatment and treatment outcome of the other, is under controversy.⁹ Histopathologically, inflammation would be detected in most pathological speci-

ABSTRACT

Objectives: Almost 20% of patients with lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) might also have symptoms of prostatitis. But, the inter-relationship between BPH and prostatic inflammation, and how one can influence the other, is under controversy. The aim of our study was to determine the incidence of prostatic inflammation in BPH patients presented with acute urinary retention (AUR).

Methods: This cross-sectional study was conducted in a hospital at Guilan, the northern province of Iran. A total of 280 patients undergoing transurethral resection of the prostate (TURP) or open prostatectomy from 1999 to 2002 were enrolled. Histopathologic samples of prostate were examined for existence of acute and/or chronic intra-prostatic inflammation (ACI).

Results: Overall, 150 (53.6%) of patients undertook surgery for AUR and 130 (46.4%) for LUTS. Among them, 130 patients (46.4%) showed ACI in the pathologic examinations whereas 150 patients (53.6%) did not. The patients with AUR were significantly older than those with LUTS. ACI was significantly associated with AUR. The mean prostate weight was significantly higher in AUR group compared the LUTS group. Those patients who showed ACI according to pathologic examinations had heavier prostates than those who did not. The association of ACI and AUR should be considered in secondary prevention for BPH patients.

Conclusions: ACI may increase the degrees of urinary obstruction and AUR.

Keywords: Inflammation; Acute urinary retention; Benign prostatic hyperplasia.

Int J Prev Med 2011; 2(1): 28-31

mens of patients with BPH, who do not necessarily have symptoms of prostatitis.^{1,7} Incidental asymptomatic prostatic inflammation is defined in the USA National Institute of Health classification of prostatitis (category IV) and has been showed to be present in 43-98% of surgically resected prostates due to BPH.^{10,11} A sub-analysis of the medical therapy of prostatic symptoms (MTOPS) study suggested that inflammation detected in baseline prostatic biopsies was highly predictive of progression of BPH to AUR and the need for more invasive therapy.¹² If inflammation and BPH had a causal relationship, by derivation the incidence of inflammation would be higher in AUR, the most severe symptom in BPH than in those patients with BPH who do not present with AUR.¹

In the present study, we investigated the patients with BPH who were scheduled to undergo TURP or open prostatectomy with the aim of

determining whether the incidence of prostatic inflammation was significantly different in patients presented with AUR than in those presented with LUTS.

METHODS

This was a cross-sectional study done at a hospital in Guilan, the northern province of Iran. The studied population was consisted of patients undergoing TURP or open prostatectomy from 1999 to 2002.

Histopathologic prostatic samples from both groups were fixed in formalin and examined by two consultant histopathologists. Sections were stained with hematoxylin and eosin, and examined using light microscopy. ACI was diagnosed by the presence of edema, vascular congestion and numerous neutrophils within prostatic acini infiltrating the lining epithelium and extending to a lesser extent into the surrounding stroma. The term ACI was used for lymphocyte and plasma cell dominant stromal infiltrations with lesser admixture of neutrophils and macrophages.¹ The studied sample was consisting of 300 patients, of whom complete data was available for 280 patients. The patients who had bladder stones or prostate cancer or complained of prostatitis manifestations or any other pathology of prostate were excluded. Independent variables included age, presence of ACI, and prostate weight. Data were analyzed using SPSS by descriptive statistics and compare means. P value < 0.05 was considered significant.

RESULTS

Among 300 patients, 20 were excluded due to incomplete data. The mean age \pm SD of the patients was 66.87 ± 7.13 years, with the range of 45 to 85 years old. The mean \pm SD prostate

weight was 44.88 ± 9.50 g. Among the studied subjects, 150 and 130 patients (53.6% and 46.4%, respectively) undertook surgery due to AUR and LUTS, respectively; 130 out of 280 patients (46.4%) showed ACI in their pathologic exams and 150 patients (53.6%) did not (Table 1). T-test analysis showed that the patients who had AUR were significantly older than the patients who presented with LUTS (68.14 ± 6.97 and 65.41 ± 6.05 years, respectively) ($P < 0.05$) (Table 2). Also, patients with ACI were significantly older than patients without it (67.96 ± 6.34 and 65.92 ± 7.64 years, respectively; $P < 0.05$) (Table 1). Bivariate analysis showed that ACI was significantly associated with AUR ($P < 0.05$). The mean prostate weight was significantly higher in AUR group compared the LUTS group (48.08 ± 8.39 g versus 41.21 ± 9.13 g, respectively; $P < 0.05$) (Table 2). Also, patients who showed ACI according to pathologic exams had heavier prostates than those who did not showed ACI (46.86 ± 8.70 versus 43.23 ± 9.90 g, respectively; $P < 0.05$) (Table 1).

DISCUSSION

After Mishra et al study,¹ this was the first study carried out in Asia showed that ACI is specifically more reported in patients present with AUR than LUTS. The overall incidence of ACI in the present study was 46.4%, which was lower than that reported in the study of Mishra et al (51%)¹ and also some other studies.^{7,11} As Mishra et al said in their study, the reason might be an underestimation of inflammation in histopathologic sections. But, this phenomenon would be attributable to all samples in both groups, and therefore is unlikely to influence the validity of the last results.¹ The present study showed that the weight of prostates with ACI was almost

Table 1. The differences between patients with and without ACI

Patients Characteristics	Category 1	Category 2	P
	ACI	No ACI	
Number (%)	130 (46.4)	150 (53.6)	
Age(years) (mean \pm SD)	67.96 ± 6.34	65.92 ± 7.64	< 0.05
prostate weight (g) (mean \pm SD)	46.86 ± 8.70	43.23 ± 9.90	< 0.05

Table 2. The differences between patients with AUR or LUTS

Patients Characteristics	Category 1	Category 2	P
	For AUR	For LUTS	
Surgery			
Number (%)	150 (53.6)	130 (46.4)	
Age (years) (mean \pm SD)	68.14 ± 6.97	65.41 ± 6.05	< 0.05
prostate weight (g) (mean \pm SD)	48.08 ± 8.39	41.21 ± 9.13	< 0.05

3.7 g higher than the prostates without ACI. This difference of the weights between the two groups may be due to several reasons, including the experience and speed of the sonologist, but the most important reason might be related to the higher degrees of BPH present in ACI. This can support the argument that ACI might be a factor in the pathogenesis of BPH.

In the present study, a high incidence of ACI was reported in BPH patients and ACI was significantly more prevalent in patients whose presentation was AUR (the most severe symptom in BPH). This supports the hypothesis that patients with ACI are more likely to show AUR symptoms than those without it. The obstruction in symptomatic BPH is hypothesized to be caused by a combination of dynamic and static components. The dynamic component of obstruction is determined by the tone of the prostate and bladder neck smooth muscle, and the static component is related to the mechanical obstruction caused by the enlarged gland.^{1,7} Symptoms of BPH would progress despite medical therapy with α -blockers which balance dynamic component.^{1,13} Similarly, anti-androgen therapy (against static component) is only moderately effective.^{14,15} Some patients deteriorate even on combined therapy.¹⁶ Thus, there should be other causative factors exists for BPH, one of which could be inflammation.

Histological evidence of prostatic inflammation is often present in biopsy, surgical and autopsy samples. Inflammation in autopsy samples of prostates is reported as high as 5-15.3% in patients over 60 years of age,¹⁷ while McNeal found inflammation in 40 of 91 (44%) prostates samples obtained at autopsy.¹⁸ Evidence of prostatic inflammation was noted in 45% of aspiration biopsy specimens taken because of suspicion of carcinoma.¹⁹ Kohnen and Drach mentioned that up to 98% of surgically resected prostates removed for BPH contained at least some foci of significant inflammatory reaction.¹¹ Some of the studies⁷ have confirmed the histological association of prostatic inflammation and BPH, while others^{20,21} have characterized some of the specific inflammatory cells associated with BPH. A study by Sauver et al showed that using daily NSAIDs was inversely associated with onset of moderate and severe urinary symptoms, low maximum flow rate, increased prostate volume and elevated prostate specific antigen (PSA). Results suggested that using NSAIDs may prevent or delay development of BPH.² NSAIDs may inhibit proliferation and induce apoptosis

in hyperplastic cells.²² This mechanism may have therapeutic effect on BPH. In a similar study, Falahatkar et al showed that nocturia improved or disappeared in 82.5% of BPH patients who received Celecoxib.²³ If prostate inflammation truly has a role in the development and progression of benign prostatic hyperplasia, including AUR, the hypothesized role of NSAIDs in AUR must be challenged in a randomized trial (you did not mention anything about the role of NSAIDs in your introduction or method; so it is not appropriate to mention it in discussion).

CONCLUSION

The main finding of the present study was that ACI may be associated with more advanced urinary obstruction. This might have an implication in the future medical management of BPH, considering the extent of attention which is currently paid to therapy directed with the aim of reducing the size of the prostate and thus, to reduce the risk of AUR. Use of NSAIDs in BPH patients may probably decrease risk of urinary retention through reduction of edema and inflammation in the prostate, although randomized trials are suggested to support this.

Conflict of interest statement: All authors declare that they have no conflict of interest.

Source of funding: Guilan University of Medical Sciences.

REFERENCES

1. Mishra VC, Allen DJ, Nicolaou C, Sharif H, Hudd C, Karim OM, et al. Does intraprostatic inflammation have a role in the pathogenesis and progression of benign prostatic hyperplasia? *BJU Int* 2007; 100(2): 327-31.
2. St Sauver JL, Jacobson DJ, McGree ME, Lieber MM, Jacobsen SJ. Protective association between nonsteroidal antiinflammatory drug use and measures of benign prostatic hyperplasia. *Am J Epidemiol* 2006; 164(8): 760-8.
3. Verhamme KM, Dieleman JP, Bleumink GS, van der Lei J, Sturkenboom MC, Artibani W, et al. Incidence and prevalence of lower urinary tract symptoms suggestive of benign prostatic hyperplasia in primary care; the Triumph project. *Eur Urol* 2002; 42(4): 323-8.
4. Verhamme KM, Dieleman JP, Bleumink GS, Bosch JL, Stricker BH, Sturkenboom MC. Treatment strategies, patterns of drug use and treatment discontinuation in men with LUTS suggestive of benign prostatic hyperplasia: the Triumph project. *Eur Urol* 2003; 44(5): 539-45.

5. Nickel JC. The overlapping lower urinary tract symptoms of benign prostatic hyperplasia and prostatitis. *Curr Opin Urol* 2006; 16(1): 5-10.
6. Safarinejad MR. Prevalence of benign prostatic hyperplasia in a population-based study in Iranian men 40 years old or older. *Int Urol Nephrol* 2008; 40(4): 921-31.
7. Nickel JC. Prostatic inflammation in benign prostatic hyperplasia; the third component? *Can J Urol* 1994; 1(1): 1-4.
8. Nickel JC, Downey J, Young I, Boag S. Asymptomatic inflammation and/or infection in benign prostatic hyperplasia. *BJU Int* 1999; 84(9): 976-81.
9. Chronic Prostatitis Workshop. Proceedings of the National Institute of Diabetes and Digestive and Kidney Diseases; 1995 Dec 7- 8; Maryland; USA.
10. Di Silverio F, Gentile V, De Matteis A, Mariotti G, Giuseppe V, Luigi PA, et al. Distribution of inflammation, pre-malignant lesions, incidental carcinoma in histologically confirmed benign prostatic hyperplasia: a retrospective analysis. *Eur Urol* 2003; 43(2): 164-75.
11. Kohnen PW, Drach GW. Patterns of inflammation in prostatic hyperplasia: a histologic and bacteriologic study. *J Urol* 1979; 121(6): 755-60.
12. Roehrborn CG, Kaplan SA, Noble WD, Slawin KM, McVary KT, Kusek JW. The impact of acute or chronic inflammation in baseline biopsy on the risk of clinical progression of BPH. Results from the MTOPS study. *J Urol* 2005; 173(Suppl abstract): 1277.
13. Emberton M, Elhilali M, Matzkin H, Harving N, van Moorselaar J, Hartung R, et al. Symptom deterioration during treatment and history of AUR are the strongest predictors for AUR and BPH-related surgery in men with LUTS treated with alfuzosin 10 mg once daily. *Urology* 2005; 66(2): 316-22.
14. Stoner E. The clinical development of a 5 alpha-reductase inhibitor, finasteride. *J Steroid Biochem Mol Biol* 1990; 37(3): 375-8.
15. Oesterling JE. LHRH agonists. A nonsurgical treatment for benign prostatic hyperplasia. *J Androl* 1991; 12(6): 381-8.
16. McConnell JD, Roehrborn CG, Bautista OM, Andriole Jr. GL, Dixon CM, Kusek JW, et al. The long-term effect of doxazosin, finasteride, and combination therapy on the clinical progression of benign prostatic hyperplasia. *N Engl J Med* 2003; 349(25): 2387-98.
17. Moore RA. Inflammation of the prostate gland. *J Urol* 1937; 38: 173-82.
18. McNeal JE. Regional morphology and pathology of the prostate. *Am J Clin Pathol* 1968; 49(3): 347-57.
19. Maksem JA, Johenning PW, Galang CF. Prostatitis and aspiration biopsy cytology of prostate. *Urology* 1988; 32(3): 263-8.
20. Theyer G, Kramer G, Assmann I, Sherwood E, Preinfalk W, Marberger M, et al. Phenotypic characterization of infiltrating leukocytes in benign prostatic hyperplasia. *Lab Invest* 1992; 66(1): 96-107.
21. Steiner G, Gessl A, Kramer G, Schollhammer A, Forster O, Marberger M. Phenotype and function of peripheral and prostatic lymphocytes in patients with benign prostatic hyperplasia. *J Urol* 1994; 151(2): 480-4.
22. Zha S, Yegnasubramanian V, Nelson WG, Isaacs WB, De Marzo AM. Cyclooxygenases in cancer: progress and perspective. *Cancer Lett* 2004; 215(1): 1-20.
23. Falahatkar S, Mokhtari G, Pourreza F, Asgari SA, Kamran AN. Celecoxib for treatment of nocturia caused by benign prostatic hyperplasia: a prospective, randomized, double-blind, placebo-controlled study. *Urology* 2008; 72(4): 813-6.