Original Article

Does Periprostatic Block Increase the Transrectal Ultrasound (TRUS) Biopsy Sepsis Rate in Men with Elevated PSA?

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Abstract

Introduction: Periprostatic nerve block (PPNB) is a common local anaesthetic technique in transrectal ultrasound-guided (TRUS) prostate biopsy, but concerns remain over the increased theoretical risks of urinary tract infection (UTI) and sepsis from the additional transrectal needle punctures. This study reviewed our biopsy data to assess this risk. Materials and Methods: Retrospective data collected from 177 men who underwent TRUS biopsy between July 2007 and December 2009 in a single institution were analysed. PPNB was administered using 1% xylocaine at the prostatic base and apex and repeated on the contralateral side under ultrasound guidance. Complications, including UTI sepsis, bleeding per rectum and acute retention of urine (ARU) were noted. Every patient was tracked for the first 2 weeks for complications until his clinic review. Demographic profile, biopsy parameters and histological findings were reviewed. Univariate and multivariate analysis of possible risk factors for development of sepsis after TRUS biopsy were performed. Statistical analysis was performed using SPSS 17.0. Results: Ninety (51%) men received PPNB and 87 (49%) did not. The groups were matched in age (PPNB: mean 62.7 ± 5.8 years; without PPNB: mean 64.4 ± 5.7 years) and prebiopsy prostate specific antigen (PSA) levels (PPNB: mean 8.2 ± 3.9 ng/mL; without PPNB: mean 8.3 ± 3.7 ng/mL). The PPNB group had a larger prostate volume, with more cores taken (P <0.05). On univariate and multivariate analysis controlling for age, PSA, prostate volume, number of cores taken and histological prostatitis, PPNB was not a significant risk factor for sepsis. Sepsis rates were 5.6% in the PPNB group and 5.7% in the other group (P = 0.956). Overall prostate cancer detection rate was 33.3%. Conclusion: The risk of sepsis was not increased in patients who received PPNB, even though this group had larger gland volumes and more biopsy cores taken.

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Key words: Periprostatic nerve block (PPNB), Sepsis, Transrectal ultrasound-guided (TRUS) prostate biopsy

Introduction

The progressive increase in the number of biopsy cores taken during transrectal ultrasound-guided (TRUS) needle biopsy of the prostate over the past decade has necessitated the introduction of anaesthetic techniques to minimise patient discomfort and pain. The sextant biopsy strategy was the gold standard for several years until the late 1990s when several publications reported high false-negative rates from missed cancers.[1] This led to the introduction of extended-biopsy schemes in current use, which involved taking at least 10 to 14 cores. A study conducted at our own institution showed that a 10-core biopsy strategy gave better detection rates for prostate cancer and this has been put in practice since.[2]

Periprostatic nerve block (PPNB) was first reported by Dr Shinohara's group at UCSF in 1996.[3] Injections were done via a 7-inch 22 gauge spinal needle under ultrasound guidance into the region of the prostatic vascular pedicle at the base of the prostate just lateral to the junction between the prostate and seminal vesicle. Soloway and Öbek introduced additional apical injections in 2000.[4] A subsequent randomised, controlled trial reported by Schostak et al showed that prostatic biopsy caused more pain at the apex and transitional zone than in the proximal peripheral zones and injection at the apex resulted in lower pain scores.[5] Hence, depending on the PPNB method, between 2 and 8 additional transrectal needle punctures through the rectum may be needed.

We hypothesise that these additional punctures could potentially lead to a higher postbiopsy sepsis rate. Previous

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studies have reported increased minor complications (e.g. haematospermia, haematochezia, haematuria) with increase in number of biopsy cores.[6] We therefore reviewed our experience in PPNB in men undergoing TRUS biopsy to determine if the sepsis rate and infection risks were increased with the use of PPNB.

Materials and Methods

Retrospective chart review of 177 men who underwent TRUS biopsy at a single institution between July 2007 and December 2009 was performed. Indications for biopsy were elevated prostate specific antigen (PSA) levels between 4 and 20 ng/mL and/or abnormal digital rectal examination findings. Inclusion criteria were age between 45 and 75 years, and the number of biopsy cores were between 10 and 20. Institutional review board approval was obtained for this study (IRB no. 44/2009).

A day prior to biopsy, these patients received oral laxatives and prophylactic oral antibiotics. On the day of biopsy, a urine dipstix was performed to exclude obvious urinary tract infection. Additionally, intramuscular gentamicin was given according to body weight before commencement of biopsy. This practice is in accordance to a study conducted at our institution which showed that the use of dual antibiotics was effective in reducing postTRUS biopsy sepsis.[7]

Ninety men received PPNB during their biopsies. These biopsies were performed by a single operator. TRUS biopsies in this group were performed with an end-firing rectal probe with an 18G biopsy needle using a BK Medical Pro Focus 2202 ultrasound machine. All had PPNB with 10 mL of 1% lignocaine at bilateral prostate bases (junction of the prostate and seminal vesicle) and apices using a 22G needle through the ultrasound probe. No periprocedural analgesia was given for the other 87 patients.

We collected data on demographic profile, biopsy parameters (prebiopsy PSA level, prostate volume, number of cores taken), final histology and post procedure complications (sepsis, bleeding per rectum and acute urinary retention). Sepsis was defined as 2 or more of the following: pyrexia (temperature ≥38.5°C) within 1 week of TRUS biopsy, pulse rate: >90 beats per minute, respiratory rate: >20 breaths per minute and white blood cells (WBCs): >12,000 cells per mm^3 or <4000 cells per mm^3, requiring admission to any hospital, with no other clinically evident source of infection.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 17.0. Quantitative data were compared using independent samples test and Mann-Whitney U Test. Qualitative data were compared using Chi-square test. Multivariate analysis was performed using logistic regression. Level of significance was established at P <0.05.

Results

Of the 1130 men who underwent TRUS biopsy between July 2007 and December 2009, 108 received PPNB whilst the remaining 1022 did not. Of the 1130 men, 764 patients had incomplete data and were excluded for comparison, leaving 177 men who fit the inclusion criteria and were included in this study.

The 177 men were divided into 2 groups: group 1 with PPNB (n = 90), group 2 without PPNB (n = 87). Their demographic profile, clinical and biopsy parameters, and histological outcome were compared in Table 1.

Table 1. Demographic Profile, Clinical and Biopsy Parameters, Histological Outcome and Complications in 177 Men Who Underwent TRUS Biopsy

Biopsy Parameters	Group 1 (PPNB)	Group 2 (No PPNB)	*P* Value
No. of patients	N = 90 (50.8%)	N = 87 (49.2%)	
Age (years)			
Mean (± 2SD)	62.7 ± 5.8	64.4 ± 5.7	0.058
Median	63.0	64.0	
Range	52.0 to 75.0	51.0 to 75.0	
PSA (ng/mL)			
Mean (± 2SD)	8.2 ± 3.9	8.3 ± 3.7	0.622
Median	6.8	7.0	
Range	4.4 to 20	4.4 to 20	
Prostate volume (mL)			
Mean (± 2SD)	46.9 ± 22.1	38.0 ± 22.6	0.001
Median	41.9	32.0	
Range	20.8 to 140.0	11.0 to 155.0	
No. of cores			
Mean (± 2SD)	13 ± 2	11 ± 2	<0.001
Median	12	10	
Range	10 to 20	10 to 18	
Histology			
Prostate cancer (%)	39 (43.3)	20 (23.0)	0.004
Prostatitis/ inflammation (%)	24 (26.7)	26 (29.9)	0.634
Complications			
Sepsis (%)	5 (5.6)	5 (5.7)	0.956
ARU (%)	4 (4.4)	1 (1.1)	0.186
Rectal bleeding (%)	1 (1.1)	1 (1.1)	0.981

ARU: acute retention of urine; PPNB: periprostatic nerve block; PSA: prostate specific antigen; SD: standard deviation

The 2 groups were generally well matched in age and prebiopsy PSA levels. The mean age of patients in the group with and without PPNB were 62.7 ± 5.8 years (median 63.0 years, range 52.0 to 75.0 years) and 64.4 ± 5.7 years (median 64.0 years, range 51.0 to 75.0 years) respectively. The mean prebiopsy PSA level in the group with PPNB was 8.2 ± 3.9 ng/mL (median 6.8 ng/mL, range 4.4 to 20 ng/mL). In the group without PPNB, the mean PSA level was 8.3 ± 3.7 ng/mL (median 7.0 ng/mL, range 4.4 to 20 ng/mL).

The mean prostate volume was slightly larger in the group with PPNB. The mean prostate volume in the group with PPNB was 46.9 ± 22.1 mL (median 41.9 mL, range 20.8 to 140 mL) and that in the group without PPNB was 38.0 ± 22.6 mL (median 32.0, range 11.0 to 155.0 mL). This difference between the 2 groups was statistically significant ($P = 0.001$).

More cores were taken in the PPNB group. In the group with PPNB, mean was 13 ± 2 cores (median 12 cores, range 10 to 20 cores) compared to a mean of 11 ± 2 cores in the group without PPNB (median 10, range 10 to 18 cores). This difference in the number of cores taken was also statistically significant ($P < 0.001$).

The overall prostate cancer detection rate for both groups was 33.3%. The presence of focal prostatitis in biopsy specimens from both groups were similar (26.7% in the PPNB group, 29.9% in the group without PPNB).

Complications of TRUS biopsy were few and similar in both groups. Four patients from the PPNB group had postbiopsy acute retention of urine (ARU) (4.4%) compared to 1 patient from the group without PPNB (1.1%). One patient from each group had postbiopsy rectal bleeding. None of these patients required hospitalisation.

Of the 177 patients, 10 developed postTRUS biopsy sepsis. Five were from the group with PPNB and the other 5 were from the group without PPNB. This gives a sepsis rate of 5.6% and 5.7% respectively ($P = 0.956$). Of these 10 patients, 4 had evidence of prostatitis/inflammation in their biopsies.

Average length of stay during hospitalisation for postbiopsy sepsis was 3.2 days. Blood cultures and urine cultures grew *Escherichia coli* in 2 and 3 patients, respectively. One patient was neutropenic. The other patients had raised white blood counts and neutrophils, save one (normal WBC with raised neutrophils). None of the patients were hypotensive i.e. all had mean arterial pressure >60 mm Hg. All these patients received parenteral ceftriaxone (with or without a stat dose of gentamicin) till afebrile and were discharged with oral antibiotics according to culture sensitivities.

Univariate and multivariate analysis were performed to identify risk factors for sepsis. On univariate analysis, prostate volume alone was found to be a risk factor for sepsis ($P = 0.033$). PPNB is not a risk factor for sepsis ($P = 0.956$). Neither was age, PSA level, number of cores taken or prostatitis on histology.

Multivariate analysis, controlling for age, PSA level, number of cores taken, presence of histological prostatitis and PPNB, confirmed that only prostate volume is a risk factor for sepsis ($P = 0.006$)(Table 2).

Table 2. Univariate and Multivariate Analysis of Risk Factors for Sepsis

Risk Factors	Univariate (*P* Value)	Multivariate (*P* Value)
PPNB	0.956	0.782
Age	0.392	0.188
Prebiopsy PSA	0.886	0.544
Prostate volume	0.033	0.006
No. of cores	0.223	0.742
Prostatitis on biopsy histology	0.395	0.597

PPNB: Periprostatic nerve block; PSA: Prostate specific antigen

Discussion

TRUS biopsy of the prostate continues to be the most common diagnostic modality used by urologists worldwide for detection of prostate cancer. The technique used has undergone many evolutions over the years. Up to the late 1990s, the sextant biopsy strategy was considered the gold standard. This was surpassed by an extended biopsy scheme which involved taking at least 10 to 14 cores after several publications reported high false-negative rates from missed cancers.[1,8,9] These included biopsies from the apical region, where prevalence of cancer is now well recognised.[10] Biopsies that include this region yield a cancer detection rate in the region of 40% to 50%.[11] Newer techniques advocated include the use of saturation biopsy strategies.[12]

With the increasing number of cores being advocated in order to increase cancer detection rates, better pain relief is necessary. Various forms of analgesia have been proposed over the years.[13] PPNB was first introduced in 1996 by Nash et al.[3] Since then, many parties have advocated its routine use as this method seems effective in reducing periprocedural pain scores without significantly increasing complication rates.[4,14,15] Various infiltration sites have been described, most commonly at the base (neurovascular bundle region),[16] at the apex[17] or in combination.[18] Each method has been reported to be effective in providing pain relief although some studies have shown superior analgesia with infiltration at both base and apex.[17] Other methods of analgesia include intraprostatic administration of local anaesthesia,[19] perianal/intrarectal lidocaine-prilocaine cream,[20] intrarectal lignocaine gel,[21] sedation with intravenous propofol[22] or nitrous oxide inhalation,[23] and suppository diclofenac.[24]

In contrast to the available literature on PPNB as an effective method for analgesia in TRUS biopsy, there is a relative dearth of publications designed specifically to look at complications arising from PPNB, in particular, postprocedural sepsis. PPNB involves injecting a soluble anaesthetic agent through the highly colonised rectal wall, requiring additional needle punctures on top of the biopsy cores. Direct correlation between number of biopsy cores and fever/chills has been reported.[25] We believe a needle puncture through the rectum can serve as a conduit to facilitate bacterial translocation. As needle size is standardised for this procedure at our institution, additional needle passes traversing the rectum can increase the inoculum size and extent of bacterial translocation from the gastrointestinal tract.[26] We therefore hypothesise that giving PPNB could increase postTRUS biopsy sepsis rates. We agree that septic episodes occur less commonly than bacterial translocation. This discrepancy is one of the key research questions in this area. An altered host response can facilitate or increase the risk of sepsis, but is not a requisite as a sufficient inoculum of pathogenic bacteria could still trigger sepsis in an immunologically competent individual.

Our study shows that there is no significant difference in sepsis rates between both groups after uni- and multi-variate analysis. This was despite the PPNB group having a larger prostate volume, which proved to be an independent risk factor for sepsis. Öbek et al in their prospective randomised trial reported an increase in postTRUS fever in patients given PPNB (although not statistically significant).[27] However, other studies did not show a similar trend.[28,29] We concur that there is a paucity of literature to explain the mechanisms through which PPNB could increase sepsis rates. Thus, more studies on the host response to bacterial inoculation and translocation in the setting of TRUS biopsy are merited. This may improve sepsis rates together with other enhancements in antibiotic prophylaxis and enhance acceptance of TRUS biopsy as a primary modality for diagnosis of prostate cancer.

The overall cancer detection rate in our series was 33.3%. This is comparable to cancer detection rates for PSA levels from 4 to 20 ng/mL in Western countries[30] but high relative to other Asian series.[2]

The strengths of this current study include a single operator for the PPNB group, standardised periprocedural antibiotic prophylaxis, contemporary, matched control group and multivariate statistical analysis using logistic regression to control for confounding factors. We acknowledge several weaknesses in our study including a small number of patients, lack of control for comorbid conditions that may predispose to sepsis (e.g. diabetes mellitus) and lack of prospective randomisation.

The results from this study shows that PPNB has a good safety profile as it does not increase postbiopsy sepsis or other complication rates. Moving forward, this allows the move to explore transrectal saturation approaches for prostate biopsy. On another note, PPNB alone may not offer a completely pain-free experience for all patients. This is evident by the many studies done to elicit the best analgesic method (as discussed previously). Due consideration should be given by the surgeon to combine PPNB with other strategies (e.g. EMLA cream, suppository diclofenac) to further decrease pain and increase acceptance of biopsy amongst patients. Another possible area for improvement would be in the design of the rectal probe eg. thinner probes for smaller frame Asian patients to decrease anal ring distension which contributes significantly to discomfort during biopsy. All this will help in mapping the exact location of cancer within the prostate gland and thus guide ablative therapy using cryotherapy, RFA (radiofrequency ablation) and HIFU (high intensity focused ultrasound).

Conclusion

Our data suggest that the postTRUS biopsy sepsis and complication rates are not increased by the addition of PPNB. Its role in reducing discomfort during the biopsy procedure is thus strengthened by the understanding that there is no compromise in safety. There is scope to further explore and minimise the risk factors for sepsis and enhance the role of regular antibiogram to tailor the antibiotic prophylaxis for our patients undergoing TRUS biopsy.

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