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·*Original Article*·

Transrectal ultrasonography in infertile patients with persistently elevated bacteriospermia

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Abstract

Aim: To identify and define prostate and seminal vesicle abnormalities in patients with chronic male accessory gland infection (MAGI) who failed to respond to antibacterial treatment. **Methods**: We selected 67 consecutive patients with MAGI and persistently elevated bacteriospermia ($\geq 10^6$ colony forming units [CFU]/mL) after three antibiotic courses. Fourteen infertile patients with initial chronic microbial ($\geq 10^6$ CFU/mL) MAGI who responded to antibacterial treatment ($< 10^3$ CFU/mL) served as a control group. All patients and controls underwent transrectal ultrasonography (TRUS) scans and semen analysis. Patients with low seminal plasma volume (< 1.5 mL) underwent both pre-ejaculatory and post-ejaculatory TRUS examination. **Results:** TRUS revealed multiple abnormalities indicative of: (i) bilaterally extended prostato-vesiculitis (group A: 52 cases, 77.6%) (nine of these patients also had micro-emphysematous prostate abscess); and (ii) prostato-vesiculitis with unilateral or bilateral sub-obstruction of the ejaculatory ducts (group B: 15 cases, 22.4%). Mean sperm concentration, total sperm number, ejaculate volume and pH value were significantly higher in group A than in group B. In addition, sperm forward motility and the percentage of normal forms were significantly worse than in controls, whereas leukocyte concentration was significantly higher in group A. Group B patients had all sperm parameters, but their pH values, significantly different from those of controls. **Conclusion:** Although antibiotic therapy is considered suitable when microbial MAGI is suspected, it is impossible to account for a poor response to antibiotics merely on the basis of conventional criteria (clinical history, physical and ejaculate signs). Thus, TRUS may be helpful in the follow-up of these patients. *(Asian J Androl 2008 Sep; 10: 731–740)*

Keywords: persistent bacteriospermia; prostato-vesiculitis; sub-obstruction of the ejaculatory ducts; micro-emphysematous prostate abscess; sperm parameters; ultrasound features

1 Introduction

Prostatitis is a common urological condition that many physicians find difficult to treat effectively. Acute bacterial prostatitis (category I, National Institute of Health

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[NIH] classification) has an abrupt onset characterized by fever, genitourinary and general signs and symptoms. The microbiological diagnosis of acute bacterial prostatitis is straightforward and easily accomplished. However, the microbiological diagnosis of chronic bacterial prostatitis (category II, NIH classification) is particularly challenging in an andrological setting, especially in infertile patients without symptoms (category IV, NIH classification) and with male accessory gland infection (MAGI) [1]. The occasional detection of bacteria in significant concentrations ($> 10^5$ colony forming units [CFU]/mL) in the semen specimen of these patients is followed by one or more courses of antibacterial therapy judged by bacteriological results and clinical symptoms [2, 3]. However, in a significant number of cases, bacteria are still present in the glandular prostate secretory system, despite antibiotic treatment [4]. This is the reason why chronic bacterial prostatitis is a subtle illness, characterized by relapsing and recurrent urinary tract infection (UTI).

We previously showed that the bacteriological cure rate is directly related to the extension of the inflammatory process, being very high (92.5%), after three antibiotic courses, in infertile patients with prostatitis alone, intermediate in patients with prostato-vesiculitis (70.4%), and low in patients with prostato-vesiculo-epididymitis (PVE) (52.0%) [3]. In that study [3], after initial suspicion of MAGI, the glandular site of infection was determined by scrotal (testicular and epididymal regions) and transrectal ultrasonography (TRUS). The ultrasonographical (US) diagnosis of MAGI was based on the presence of a significant number of ultrasound abnormalities limited to the prostate region or extended also to the seminal vesicles and the epididymis on one or both sides. In particular, in comparison with healthy men (proven recent fertility, lack of conventional MAGI criteria, and low bacteriospermia [$< 10^3$ CFU/mL]), prostatitis (diagnosis of one sexual inflamed accessory gland alone) was made in the presence of two or more of the following ultrasound signs: (i) glandular asymmetry; (ii) hypoechogenicity associated with oedema; (iii) hyperechogenicity associated with areas of calcification; and (iv) dilation of the periprostatic venous plexus [5]. However, the diagnosis of prostato-vesiculitis or PVE was corroborated by the combination with the above US signs of prostatitis (US score > 2) combined with two or more signs on the seminal vesicles and on the epididymis (prostato-vesiculitis: US score > 4; PVE: US score > 6) [5].

In another study, we found that prostatitis, prostato-vesiculitis and PVE have a negative impact on sperm output and cause a chronic inflammatory response in terms of hyper-production of leukocyte-related reactive oxygen species (ROS) and elevated leukocytospermia, both of which are directly related to the extension of the inflammatory process [5]. Furthermore, scrotal US and TRUS were also helpful diagnostic aids to discriminate patients with unilateral or bilateral post-infectious inflammatory PVE, because sperm abnormalities, low seminal fructose levels and ROS hyper-production do not discriminate patients with unilateral or bilateral post-infectious inflammatory PVE [6]. In addition, although complete ejaculatory duct obstruction is a rare cause of male infertility, its main causes or abnormalities (midline cyst, Wolffian malformation, tuberculosis, previous genitourinary infection and idiopathic) are well-documented, and TRUS findings correlate well with vasography [7–9]. Incomplete or partial ejaculatory duct obstruction is diagnosed with increased frequency in male infertility with the advent of TRUS (mainly high resolution TRUS technology), and although there are no specific findings associated to this disorder, several clinical findings are highly suggestive of its presence [10–14]. For this reason, we found it worthwhile to evaluate the above and other ultrasound findings. Therefore, the present study was undertaken to evaluate whether TRUS is a valid diagnostic aid to identify the presence of prostate and/or seminal vesicle abnormalities in infertile patients with persistently elevated bacteriospermia ($\geq 10^6$ CFU/mL) after three antibiotic courses.

2 Subjects and methods

2.1 Subjects

We studied 67 consecutive patients (age range: 28–44 years), with primary infertility (median: 4 years; range: 3–11 years) and chronic, persistent microbial MAGI. The diagnosis of MAGI was made on the basis of the following conventional World Health Organization (WHO) criteria [15]: oligozoospermia (sperm concentration $< 20 \times 10^6$ cells/mL), asthenozoospermia (< 50% spermatozoa with forward progression, a and b categories) and/or teratozoospermia (< 30% spermatozoa with normal oval form) associated with one of the following combinations:

• History positive for UTI and/or sexual transmitted diseases (STD) or male accessory sex gland abnor-

malities at the physical examination (factor A) plus prostatic signs (factor B);

• History positive for UTI and/or STD or male accessory sex gland abnormalities at the physical examination (factor A) plus ejaculate signs (factor C);

• Prostatic sign (factor B) plus ejaculate signs (factor C);

• Presence of at least two ejaculate signs (two factors C).

We did not perform the four-glass test in these patients because the clinical history, symptoms and signs of poor-responsiveness after three antibiotic courses gave sufficient indication to diagnose the presence of microbial MAGI in these patients. In addition, the patients with MAGI enrolled should fulfill the following eligibility criterium before enrolment: persistent relapse (same germ species) or re-infection (different germ species) with elevated ($\geq 10^6$ CFU/mL) bacteriospermia after antimicrobial treatment.

Fourteen infertile patients with initial chronic MAGI and elevated bacteriospermia ($\geq 10^6$ CFU/mL) who reached a bacteriological cure ($< 10^3$ CFU/mL) after antimicrobial treatment, served as a control group. A written informed consent was collected from patients and controls.

2.1.2 Exclusion criteria

• Patients with non-obstructive or obstructive azoospermia (condition not recognized by the conventional WHO criteria for MAGI) [15];

• Elevated (> 10 mIU/mL) serum follicle stimulating hormone levels;

• History or presence of primary testicular disease (cryptorchidism, orchitis, varicocele) or testicular volume ≤ 12 mL;

• Potential confounder factors: smoking (all kinds of tobacco, starting from one cigarette/day), occupational chemical exposure;

• Treatment of other co-morbid diseases, during the 3 months before enrolment in this study.

2.1.3 Antibiotic treatment design

As recommended by the European Association of Urology (EAU) [16, 17], antibiotic treatment in chronic bacterial prostatitis has to be provided for 2 weeks after the initial diagnosis, then patients have to be re-assessed and antibiotic treatment continued for other two intermittent courses of 2 weeks each when a relapse or re-infection is detected. Furthermore, because the EAU encourage a duration of antibiotic treatment based on experience and expert opinion [18], we chose a treatment schedule that, in our experience, registered a bacteriological cure rate of 92.5% after three antibiotic courses in well-characterized (through ejaculate signs, physical examination, microbiological and ultrasound criteria) patients with prostatitis [3].

Levofloxacin or doxycyclin were chosen in relationship to the sensitivity tests prior to treatment (minimal inhibitory concentration < 1 μg/mL) and for their useful pharmakocynetic profile (excellent penetration into the prostate and seminal vesicles). All patients and controls underwent treatment with levofloxacin (500 mg p.o. every 12 h) or doxycycline (100 mg p.o. once daily) for 14 days per month over a 3-month period separated by 2-week washout period (the total treatment period was 6 weeks).

2.2 Methods

2.2.1 Ultrasound examination

All patients and controls underwent ultrasound examination following one day of sexual abstinence. The prostato-vesicular region was assessed using a transrectal 7.5 MHz biplan biconvex transducer. The ultrasound investigation was initially orientated to identifying the presence of lesions considered indicative of chronic infection as previously reported [5]. These ultrasound signs confirm the finding of other authors [10, 19–21]. This diagnostic procedure, applied to patients with an initial diagnosis of MAGI and elevated bacteriospermia ($> 10^5$ CFU/mL), offers the advantage of sub-classifying patients with MAGI into patients with prostatitis, prostato-vesiculitis and PVE as well as their unilateral or bilateral involvement [6].

In addition, a second post-ejaculatory TRUS (step IV, Table 1) was performed in the presence of: two or more abnormalities at the genital physical examination, TRUS signs of suspected ampullo-vesicular voiding disturbance and post-treatment persistent hypospermia (ejaculate volume < 1.5 mL) (Table 1). The first ultrasound investigation (step II, Table 1) allowed us to identify some anatomical abnormal findings in the prostate-vescicular region; the second (step IV, Table 1), performed in the immediate post-ejaculatory phase, helped to discriminate ampullo-vesicular voiding disturbance due to a likely (unilateral or bilateral) sub-obstruction of the ejaculatory ducts.

2.2.2 Semen analysis and cultures

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Table 1. Diagnostic work-up of patients with persistently elevated bacteriospermia (poor responders to antibiotics) and severe hypospermia (semen plasma volume < 1.5 mL): diary of the clinical examination. TRUS, transrectal ultrasonography.

Steps	Sexual abstinence
First examination	
Step I: Semen analysis and culture	3–5 days
Second examination	
Step II: TRUS (baseline condition)	1 day
Step III: Ejaculation (semen analysis not performed)	1 day
Step IV: post-ejaculation TRUS	1–2 hours
Third examination	
Step V: Semen analysis and culture	3–5 days

During pre-treatment and after the third course of antibiotic administration, all patients (those who failed to respond to antibacterial treatment) and controls (those who registered a bacteriological cure) underwent at least two semen analyses, performed according to the WHO guidelines [22], following 3–5 days of sexual abstinence, for the assessment of sperm parameters, physical–chemical properties (volume, pH) and seminal leukocyte concentration.

The concentration of leukocyte was determined by morphological identification with conventional immunocytochemical staining [22] using an anti-alkaline phosphatase monoclonal antibody CD45 (Dako Italia, Milan, Italy), as previously reported [5, 6]. Leukocyte concentration was evaluated by counting the number of red-stained round cells in 20–30 microscopic high-power fields (× 40 objective) under light microscopy. The total number of positive cells in duplicate spots was recorded, averaged and multiplied by the dilution factor (× 200) to produce the number of leukocytes per milliliter of semen [23].

In addition, an aliquot from all samples was cultured aerobically and anaerobically following a 1:2 dilution in saline solution, according to previously published standard bacteriological methods [3, 24]. To minimize methodological errors, the same investigators, in a blinded fashion, performed all seminal analyses (E.V. and R.C.) and TRUS scans (S.L.V. and A.A.).

2.3 Statistical analysis

Semen parameters are the mean of two consecutive semen specimens. Results were reported as median (10th and 90th percentiles) and were analyzed by analysis of variance followed by Duncan's multiple range test. The changes in the pre-treatement and post-treatment variables among groups were analyzed using the Wilcoxon test. The clinical and microbiological findings between groups A and B were analyzed using the χ^2-test or Fisher's exact test, as appropriate. The SPSS 9.0 software for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical evaluation. A statistically significant difference was accepted when $P < 0.05$.

3 Results

Transrectal ultrasonography identified multiple features indicative of prostate and seminal vesicle infections in all patients, even in those whose MAGI was initially suspected [15], but no abnormalities were found by digital rectal examination (DRE). In particular, two main chronic pathological conditions were detected: (i) bilateral prostato-vesiculitis with or without micro-emphysematous prostate abscess (group A) (Figure 1); and (ii) prostato-vesiculitis and unilateral or bilateral sub-obstruction of the ejaculatory ducts (group B) (Figure 2).

Fifty-two patients (age range: 28–44 years) (77.6%) (group A) had ultrasound abnormalities suggestive of a bilaterally extended prostate-vesicular infection. A micro-emphysematous prostate abscess (presence of a hypoechoic area with thick walls) was also observed in nine of these patients (Table 2). The other 15 patients (age range: 28–42 years) (22.4%) (group B) showed signs indicative of prostato-vesiculitis complicated with an ampullo-vesicular voiding disturbance probably due to a sub-obstruction of the ejaculatory ducts as a result of pre-ejaculatory and post-ejaculatory TRUS (Table 2).

Controls (age range: 25–42 years) showed US signs of a less extended prostato-vesiculitis and no signs of unilateral or bilateral sub-obstruction of the ejaculatory ducts. In particular, they had more than two of the following ultrasound signs of prostatitis: (i) gland asymmetry (unilateral enlargement) (n = 6) or bilateral (extended to both prostate lobes) glandular enlargement (n = 8); (ii) areas of hypoechogenicity always are smaller than 30% of the peripheral and superior gland zone (n = 14); and (iii) areas of hyperechogenicity always are smaller than 25 × 25 mm present in the transitional gland zone (n = 14). Furthermore, controls also had more than two of the following ultrasound signs of vesiculitis; (iv) uni-

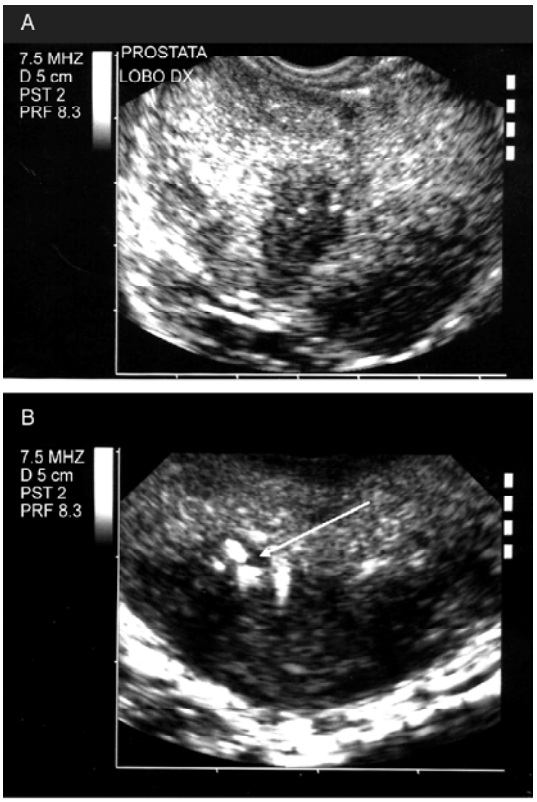

Figure 1. (A): Representative photographs of patients with ultrasound aspects of prostate abscess (group A). (B): The presence of hypo-anechoic areas (arrow) surrounded by hyperechoic area is suggestive of a micro-emphysematous abscess.

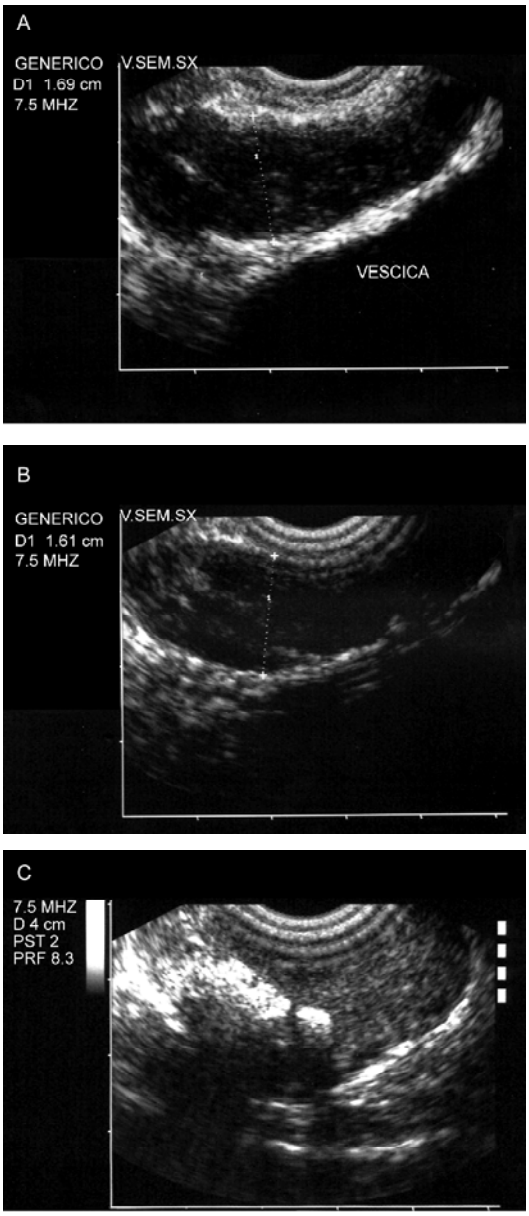

Figure 2. Representative photographs of the seminal vesicles before (A) and after (B) ejaculation in a patient with unilateral subostruction of the ejaculatory duct (group B). The same patient showed the presence of multiple micro-calcifications on the prostate left lobe extending to the montanum region (C). No reduction of the left seminal vesicle diameter was observed after ejaculation.

lateral (n = 8) or bilateral (n = 6) enlargement (median 15.8 mm, range 14.8–16.2 mm) and asymmetry (one vesicle > 15.8 mm or > 2.5 mm compared to the contro-lateral); (v) thickening and calcification of the glandular epithelium; and (vi) polycyclic areas separated by septi, unilaterally (n = 8) or bilaterally (n = 6). In addition, the control group showed a mean difference of the vesicular antero-posterior diameter before and after ejaculation of 3 mm, which overlaps a value of 2 mm already reported (mean width of the seminal vesicles of 13 mm before and 11 mm after ejaculation) [11].

The clinical history, symptoms and signs, as well as results of the bacterial cultures of the patients enrolled, are summarized in Table 3. No statistical significant differences were detected between groups A and B (Table 3). Clinical history and symptoms were relatively more marked, although not significantly different, in patients of group A. In particular, 32 out of 52 patients (61.5%) had an underlying disease, while a negative history of coincidental diseases was recorded in the remaining 20 patients. In contrast, mainly group B patients showed some signs, such as a painful DRE reflex in the epididymal cauda of the same side of the examined prostate lobe

Table 2. Ultrasound-based major diagnostic categories and relative signs in patients with persistently elevated bacteriospermia (poor responders to antibiotics). APD, anterior-posterior diameter; SV, seminal vesicles; TRUS, transrectal ultrasonography.

Ultrasound diagnosis	Ultrasound signs	Frequency (%)
Bilateral prostato-vesiculitis with/without micro-emphysematous prostate abscess (group A: *n* = 52, 100%)	Presence of more than two of the following US signs of prostatitis:	
	·Bilateral glandular enlargement;	86.5 (*n* = 45)
	·Bilateral and extended (> 30% of the peripheral and superior gland zone) area of hypoechogenicity associated with oedema;	100.0 (*n* = 52)
	·Bilateral and extended (> 25 × 25 mm, present in the transitional gland zone) hyperechogenicity associated with other calcification spots;	100.0 (*n* = 52)
	·Hypoechoic area (median 5.5 mm, range 4.0–11.5 mm) with thick walls.	17.3 (*n* = 9)
	Associated with two or more of the following US signs of vesiculitis:	
	·Bilateral enlargement (median 16.3 mm, range 15.8–19.7 mm) and asymmetry (one vesicle > 15.8 mm or > 2.5 mm compared to the controlateral;	100.0 (*n* = 52)
	·Thickening and calcification of the glandular epithelium;	15.4 (*n* = 8)
	·Polycyclic areas separated by septi (present bilaterally).	100.0 (*n* = 52)
Ampullo-vesicular voiding disturbance due to a likely (uni-bilateral) sub-obstruction of the ejaculatory ducts (at dynamic pre-ejaculatory and post-ejaculatory TRUS) (group B, *n* = 15, 100%)	Comparing pre-ejaculatory and post-ejaculatory TRUS, we found with various frequencies, the following echo-morphological changes:	
	(i) Prostate gland:	
	·Microcalcific aggregates and/or hyperechoic clods (in both prostate lobes or only homolaterally in the ampullo-vesicular tract showing signs of stasis).	80.0 (*n* = 12)
	(ii) SV:	
	·APD in one or both SV (within the normal range or higher in the pre-ejaculatory scan), unmodified in the post-ejaculatory scan;	86.7 (*n* = 13)
	·SV with persistent polycyclic areas separated by septa in the post-ejaculatory scan;	40.0 (*n* = 6)
	·SV with persistent lumpy shape and increased APD in post-ejaculatory scan;	73.3 (*n* = 11)
	·SV with normal echo-morphology and APD, slightly modified in the post-ejaculatory scan.	33.3 (*n* = 5)
	(iii) ejaculatory ducts and deferential ampullae:	
	·Pre-stenotic dilation of at least one (four out of 13) or both ejaculatory ducts;	86.7 (*n* = 13)
	·This ejaculatory duct dilation was more clearly visible in the post-ejaculatory phase;	86.7 (*n* = 13)
	·Hyperechoic thickness of periductal tissues with internment of the ejaculatory duct with restricted lumen;	33.3 (*n* = 5)
	·Hyperechoic small area (obstructive lithiasic concretion) at the substenotic ejaculatory duct level;	26.7 (*n* = 4)
	·Hypo-echogenicity at the ejaculatory duct level (with meaning of debris);	13.3 (*n* = 2)
	·Mono or bilateral ampullar dilation.	33.3 (*n* = 5)

and vesicular region.

All patients had either unchanged or exacerbated clinical symptoms and/or unchanged or increased seminal white blood cells (WBC) numbers following antimicrobial treatment. The ineffective response in terms of bacteriological cure was a result of a relapse of the same bacterial species in 40 out of 67 patients (59.7%) and a re-infection with a different bacterial species in the remaining 27 patients (40.3%). Sperm culture results after treatment showed a similar prevalence of Gram negative and Gram positive bacteria, in groups A and B, respectively (Table 3). The pathogens present in group A patients, who also had micro-abscess, were Gram negative bacteria, including Klebsiella (3 cases), Proteus spp (1 case), *Escherichia coli* (1 case), Citrobacter (1 case), Pseudomonas (1 case) or anaerobic bacteria, including

Table 3. Clinical data of patients with persistently elevated bacteriospermia (poor responders to antibiotics). Values in parentheses represent the features found in nine patients in group A, who had prostato-vesiculitis and micro-emphysematous prostate abscess following transrectal ultrasonography. Group A: bilateral prostato-vesiculitis by transrectal ultrasonography. Group B: unilateral or bilateral sub-obstruction of the ejaculatory ducts, by transrectal ultrasonography. The percentages of clinical (total positive history, sperm cultures) data were not significantly different ($P > 0.05$, χ^2 or Fisher's exact tests) between groups A and B. Symptoms were relatively more marked, although not significantly different, in group A patients.

	Group A (n = 52)	Group B (n = 15)
Clinical history	32 (61.5%)	8 (53.3%)
Diabetes and previous urinary infection	3	0
Prior urinary infection alone	4 (1)	2
Congenital urogenital abnormalities:	3 (1)	3
Hypospadias	1 (1)	2
Muller prostate cyst	0	1
Bilateral spermatocele and kidney polycysts	2	0
Dialysis for chronic renal failure	1	0
Chronic HCV infection related hepatitis	1	0
Alcohol intake	2	0
Food intolerance	9 (3)	1
Bowel pathologies	9 (2)	2
Symptoms and signs		
Slight persistent fever	3 (1)	0
Pollakiuria and dysuria	4 (1)	3
Leukocytosis and/or leukocyturia	3 (1)	1
Abdominal complaints	8 (2)	3
Fluctuation area in the prostate	2 (1)	0
Localized pain during digital rectal examination	8 (2)	3
Purulent urethral discharge	5	0
Painful digital examination reflexed to cauda epididymis (corresponding to the same side as the examined prostate lobe)	2	9
Suprapubic pain	8	1
Perineal pain	9 (2)	6
Leukocytospermia ($> 1 \times 10^6$ cells/mL)	52	15
Bacteriospermia ($\geq 10^6$ colony forming units [CFU]/mL)	52	15
Sperm cultures		
Total Gram negative	23 (44.2%)	6 (40.0%)
Escherichia coli	8 (1)	3
Klebsiella species	6 (3)	2
Proteus species	4 (1)	1
Citrobacter freundii	2 (1)	0
Pseudomonas aeruginosa	3 (1)	0
Total Gram positive	20 (38.5%)	6 (40.0%)
Enterococcus	14	3
Staphylococcus haemolyticus	4	1
Staphylococci aureus	2	1
Anaerobes	9 (17.3%)	3 (20.0%)
Bacteroides species	7 (2)	2
Peptococcus	2	1

Bacteroides species (2 case). The presence of anaerobic bacteria was similar in both groups.

Sperm parameters, including cytological and physical-chemical properties, after three antibiotic courses were unmodified or significantly worse than those found in the pre-treatment (data not shown) for patients in groups A and B. Following antimicrobial treatment, group A patients had mean sperm concentrations, total sperm numbers, ejaculate volumes and pH values significantly higher than those found in patients in group B (Table 4). In comparison with the values registered in the controls, group A patients had significantly lower sperm forward motility, and percentage of normal forms, whereas WBC concentration was significantly higher. The subset of group A patients with a concomitant micro-emphysematous prostate abscess had sperm values overlapping those found in group A (data not shown). All the examined sperm parameters of group B patients were significantly different from those of the controls, except for the pH values (Table 4).

4 Discussion

Chronic bacterial prostatitis, defined also as a subacute infection, may manifest itself with a combination of pelvic pain and voiding symptoms, and is characterized by recurrent UTI. Treatment failures are common in prostatitis. It was been hypothesized that altered pharmacokinetics in the inflamed prostate gland might account for the treatment failure of clinically diagnosed chronic bacterial prostatitis [24]. In a chronically inflamed prostate gland, another difficulty in eradicating bacteria relates to the fact that micro-organisms are protected within infection-induced microcolonies and biofilms and, therefore, grow firmly attached to the inflamed ductal and acinar walls [25].

In infertile patients with bacteriospermia > 10^5/mL and a significant number of ultrasound abnormalities indicative of prostatitis, prostato-vesiculitis and PVE, we found an excessive inflammatory response in terms of increased WBC concentration and ROS hyper-production in the ejaculate of these patients [5]. Furthermore, we have shown that the bacteriological cure rate after the three antibiotic courses was directly related to the extension of the inflammatory process, being high (92.5%) in patients with prostatitis alone, low in patients with prostato-vesiculitis (70.4%) and even lower in patients with PVE (52.0%) [3]. Recently, Gutierrez *et al.* [26] reported a poorer antibiotic-independent, clinical response in patients with abnormal prostate ultrasound findings and DRE examination, and with Gram negative bacterial infection, although symptoms diminished or disappeared.

Table 4. Sperm variables in patients with persistently elevated bacteriospermia (poor responders to antibiotics) and in a group of patients responsive (< 10^3 colony forming units [CFU]/mL) to antibiotics (controls). Values are expressed as median (10th and 90th percentiles). *n*, number of patients; Pre-T, pre-treatment; Post-T, after three courses of antibiotic treatment. Group A: bilateral prostato-vesiculitis by transrectal ultrasonography. Group B: unilateral or bilateral sub-obstruction of the ejaculatory ducts, by transrectal ultrasonography. [a]$P < 0.05$ compared with Group B (analysis of variance followed by Duncan's test); [b]$P < 0.01$ compared with Post-T matched-values in controls (analysis of variance followed by Duncan's test).

Sperm variables	Group A (n = 52)		Group B (n = 15)		Controls (n = 14)	
	Pre-T	Post-T	Pre-T	Post-T	Pre-T	Post-T
Cytological						
Sperm density ($\times 10^6$/mL)	48 (8, 96)[a]	45 (6, 84)[a]	12.0 (1, 18)[b] 11.4 (1, 15)[b]	13 (1, 19)[b] 12.6 (1, 17)[b]	45 (12, 89)	52 (15, 101)
Total sperm count ($\times 10^6$)	108 (27, 164)[a]	92 (21.3, 155)[a]	8 (0, 14)[b]	8 (0, 15)[b]	99 (26, 161)[b]	143 (43, 225)
Forward motility (%)	11 (5, 15)[b]	12 (5, 15)[b]	15 (11, 22)[b]	16 (11, 22)[b]	14 (6, 19)	1.8 (1.2, 2.6)[b]
Normal forms (%)	18 (12, 25)[b]	19 (14, 27)[b]			20 (15, 30)[b]	25 (19, 35)
Leukocyte count ($\times 10^6$ cells/mL)	3.0 (1.9, 6.6)[b]	2.1 (1.4, 3.4)[b]	3.4 (1.4, 5.2)[b]	1.8 (1.2, 2.6)[b]	3.1 (1.3, 4.5)[b]	0.7 (0.5, 1.0)
Physico-chemical						
Ejaculate volume (mL)	2.2 (1.4–3.1)[a]	1.7 (1.5–2.2)[a]	0.7 (0.3–1.2)[b]	0.8 (0.3–1.5)[b]	2.3 (1.6–3.3)[a]	2.8 (1.8–4.1)
pH	8.4 (8.0–8.7)[a,b]	8.3 (7.8–8.7)[a,b]	7.1 (7.0–7.4)[b]	7.1 (7.0–7.4)[b]	8.0 (7.4–8.4)[a]	7.8 (7.4–8.1)

In the present study, a comprehensive clinical and US examination, conducted in selected patients without confounding factors (non-smokers and patients not exposed to occupational chemical exposure), helped us to subdivide patients with initial suspected MAGI diagnosis and persistent elevated bacteriospermia into two main groups: those exhibiting signs of bilaterally extended prostato-vesiculitis with or without micro-emphysematous prostate abscess (group A); and those with TRUS signs of prostato-vesiculitis complicated with unilateral or bilateral sub-obstruction of the ejaculatory ducts (group B). The presence of micro-abscesses in the prostate gland in a fraction (n = 9) of group A patients was associated with the detection of Gram negative aerobes and occasionally obligate anaerobic bacteria, which suggested a pathogenesis via intra-prostate reflux. The lower frequency of Gram positive aerobes and occasionally obligate anaerobic bacteria, in comparison to culture data reported by others [21, 27], might be due to our comparatively younger population and the low frequency of some risk factors (e.g. high alcohol intake and diabetes) that could cause autonomic neuropathy and, therefore, also disturbances of prostato-vesiculo-ductal voiding, and/or of underlying systemic disease (patients with dialysis for chronic renal failure or chronic HCV-related hepatitis). Since the introduction of broad-spectrum antibiotics, a prostate abscess, rarely encountered, may manifest itself as a micro-emphysematous abscess (< 10 mm). Given that few symptoms may be indicative of the presence of a prostate micro-abscess, only diagnostic imaging studies and optimal management, including pharmacological drainage with antibiotics, may lead to its diagnosis.

We hypothesized that the ultrasound abnormalities suggestive of PV with/without micro-abscess and PV with ejaculatory duct sub-obstruction found in the patients with persistent infection were the clinical expression of chronic PV, which pathogenetically did not extend retrocanalicularly, or rather just locally with a final picture of a complicated PV, which involves the prostate gland with the formation of a micro-abscess (group A patients) or a sub-obstruction of the ejaculatory ducts (group B patients). Clinical history and physical examination did not result in discrimination of the two different underlying abnormalities found in these patients with elevated and persistent bacteriospermia. The resulting voiding dysfunction of the inflamed gland, the host inflammatory response [3, 4, 19, 28] and a persistent bacteriospermia, accounted for group B patients having the worst sperm parameters, including a persistent leukocytospermia with values higher than those found in the group of antibiotic-responsive patients.

Low percentages (5%–10%) of patients under observation in specialized clinics have been reported to have bacterial prostatitis [29]; yet these percentages become higher when they are referred to patients observed for male infertility in andrological clinics. Diagnostic imaging studies, such as TRUS, might be of help. Recently, we commented on the poorly reproducible US abnormalities of the prostate and seminal vesicles [6], as well as the low frequency and typology of ultrasound prostate and vesicular abnormalities reported by Schipper *at al*. [30], postulating that the cohort of patients studied had prevalent signs of prostatitis or at most of prostato-vesiculitis. The inclusion of patients with PVE could have led to the observation of a higher percentage of vesicular US abnormalities and to better indication of the importance of vesicular ultrasound assessment.

Therefore, although discordant opinions exist on the use of TRUS scan as a diagnostic tool for a complete site-diagnosis [5, 6, 9, 19–21], TRUS scan seem to be helpful in the follow-up of chronic microbial MAGI. Indeed, TRUS made it possible for us to distinguish at least two categories of patients (groups A and B), whose unresponsiveness might be explained by the severe ultrasound abnormalities. In such cases, an adequate drainage of the inflamed areas, complicated in some cases by the additional presence of micro-abscess (< 10 mm), probably calls for an alternative therapeutic strategy, such as increasing the duration of the treatment and/or searching for a more appropriate pharmacological synergy (e.g. through a combined regimen of antibiotics and one or more non-steroidal anti-inflammatory compounds) [32] or curing an underlying disease, such as diabetes or bowel inflammation.

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