

ORIGINAL ARTICLE

Significance of Transrectal Ultrasonography in Infertile Patients with Persistently Elevated Bacteriospermia

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ABSTRACT

Objective: To establish the significance of transrectal ultrasound 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 50 consecutive patients with MAGI and persistently elevated bacteriospermia ($\geq 10^6$ colony forming units [CFU]/mL) after three antibiotic courses. All patients underwent transrectal ultrasonography (TRUS) scans and semen analysis.

Results: TRUS revealed hyperechogenicity with areas of calcifications in 90% (n=45) of patients with MAGI.

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.

Keywords: persistent bacteriospermia; male infertility, chronic prostatitis, transrectal ultrasound,

INTRODUCTION

Clinicians find difficult to treat prostatitis which is a common urological condition. Acute bacterial prostatitis (category I, National Institute of Health [NIH] classification) is characterized by fever, pelvic discomfort or pain and lower urinary tract symptoms. The diagnosis of acute bacterial prostatitis on microbiological basis is simple and easy. However, the diagnosis of chronic bacterial prostatitis (category II, NIH classification) is difficult and challenging, especially in asymptomatic infertile patients [1]. In the semen specimen of these patients the detection of bacteria in significant concentrations ($> 10^5$ colony forming units [CFU]/mL) is treated by one or more courses of antibacterial therapy monitored by bacteriological results and clinical symptoms [2, 3]. However, despite proper antibiotic treatment in a significant number of cases, bacteria are still present in the glandular prostate secretory system, [4]. That's why chronic bacterial prostatitis is a persistent ailment, characterized by relapsing and recurrent urinary tract infection (UTI).

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 prostates-vesiculitis (70.4%), and low in patients with prostates-vesiculo-epididymitis (PVE) (52.0%) [3]. In that study, after initial suspicion of MAGI, the glandular site of infection was observed by transrectal ultrasonography

(TRUS). The ultrasonographical (US) diagnosis of MAGI was determined on the presence of ultrasound abnormalities limited to the prostate gland or extended also to the seminal vesicles and the epididymis unilaterally or bilaterally.

In another study, it was found that prostatitis, prostatovesiculitis 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, TRUS was also helpful in 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

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presence [10–14]. 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.

SUBJECTS AND METHODS

Study Design

It is a cross-sectional quantitative study

Participants

We studied 50 consecutive patients (age range: 28–44 years), with primary infertility (median: 4 years; range: 3–11 years) and chronic, persistent microbial MAGI. These patients were presented in Department of Urology, Nawaz Sharif Social Security Hospital, Lahore. The diagnosis of MAGI was made on the basis of the 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: -

1. History positive for UTI and/or sexual transmitted diseases (STD) or male accessory sex gland abnormalities at the physical examination (factor A) plus prostatic signs (factor B)
2. History positive for UTI and/or STD or male accessory sex gland abnormalities at the physical examination (factor A) plus ejaculate signs (factor C)
3. Prostatic sign (factor B) plus ejaculate signs (factor C)
4. 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 criteria before enrolment: persistent relapse (same germ species) or re-infection (different germ species) with elevated ($\geq 10^6$ CFU/mL) bacteriospermia after antimicrobial treatment. A written informed consent was collected from patients.

Exclusion criteria

1. Patients with non-obstructive or obstructive azoospermia (condition not recognized by the conventional WHO criteria for MAGI) [15];
2. Elevated (> 10 mIU/mL) serum follicle stimulating hormone levels
3. History or presence of primary testicular disease (cryptorchidism, orchitis, varicocele) or testicular volume ≤ 12 mL;
4. Potential confounder factors: smoking (all kinds of tobacco, starting from one cigarette/day), occupational chemical exposure;
5. Treatment of other co-morbid diseases, during the 3 months before enrolment in this study.

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 reinfection 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 doxycycline were chosen in relationship to the sensitivity tests prior to treatment (minimal inhibitory concentration < 1 μ g/mL) and for their useful pharmacokinetic profile (excellent penetration into the prostate and seminal vesicles). All patients 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).

METHODS

Ultrasound examination

All patients and controls underwent ultrasound examination following one day of sexual abstinence. The prostatic-vesicular region was assessed using a transrectal high frequency probe (7.5 MHz) while the patient was in left lateral decubitus position. The ultrasound investigation was initially orientated to identifying the presence

of findings considered indicative of chronic infection. These ultrasound signs confirm the finding of other authors. 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 and prostatic-vesiculitis as well as their unilateral or bilateral involvement.

RESULTS

Transrectal ultrasonography identified multiple features indicative of prostate and seminal vesicle infections in all patients, but no abnormalities were found by digital rectal examination (DRE). TRUS revealed hyperechogenicity with areas of calcifications in 90% ($n=45$) of patients with MAGI. In particular, 30 out of 50 patients (61.5%) had an underlying disease, while a negative history of coincidental diseases was recorded in the remaining 20 patients. All patients had either unchanged or exacerbated clinical symptoms and/or unchanged or increased seminal white blood cells (WBC) numbers following antimicrobial treatment.

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 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 $> 10^6$ /mL and a significant number of ultrasound abnormalities [5].

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. Since the introduction of broad-spectrum antibiotics, a prostate abscess, rarely encountered, may manifest itself as a micro-physematous 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. 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 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.

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 seems 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, 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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