Premature ejaculation (PE) is regarded as the most common male sexual disorder. Previous studies reported that prostatic inflammation was highly prevalent in PE. However, the effect of antibiotic treatment of cases with PE and chronic prostatitis has not been extensively investigated. To examine the effect of antibiotic treatment in delaying ejaculation in patients with PE and chronic prostatitis, the study was carried out in my private chamber and at General Hospital N.Gong from June 2014 to December 2016. The study was performed with prior permission and the confidentiality was maintained. A total of 135 consecutive men attending of secondary premature ejaculation (SPE) were included in this study. Sequential microbiologic specimens were obtained from urine and prostatic fluids. Antibiotics were given for one month according to the results of their culture and sensitivity test. All patients were instructed to follow up in General Hospital N.Gong/Private chamber monthly for at least 4 months. At the end of the 4-month follow-up, another prostatic secretion analysis was performed. Based on expressed prostatic secretion culture and white blood cell (WBC) count, 84 (62.2%) were having chronic bacterial prostatitis. The remaining 51 (37.8%) patients had negative WBC count. Of the 84 patients with secondary premature ejaculation (SPE) and chronic bacterial prostatitis, 20 patients were left untreated and considered as a control group. All 64 patients with PE and chronic prostatitis continued the 1-month treatment duration. Following 1-month antibiotic treatment, all 64 patients with initially positive cultures had sterile final cultures (P < 0.05). Fifty one (79.68%) patients showed increases in their ejaculatory latency time and reported good control of their ejaculation and were considered treatment responsive. None of the control group patients experienced any improvement either in their prostatic infection condition or in their ejaculation time. The follow-up of treatment-responsive patients (N = 51) revealed no recurrence of PE with negative prostatic culture. Successful eradication of causative organisms in patients with PE and chronic prostatitis may lead to marked improvement in intravaginal ejaculatory latency time and ejaculatory control.

Keywords: Premature ejaculation; Prostatitis; Antibiotics

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Introduction
Premature ejaculation (PE) is regarded as the most common male sexual disorder, affecting 30-40% of sexually active men1,2 and perhaps as many as 75% of men at some points in their lives3.

Regrettably, there is no universal agreement on how to define or to diagnose PE.

The term PE is subject to several definitions according to the approach used. In the psychological approach, consensus on a definition of PE has never been reached because of conflicting ideas on the essence of the syndrome4. Another way to define PE is by quantitative measures such as the duration of ejaculatory latency or the number of thrusts before ejaculation. Definitions according to the time before ejaculation varied from 1 to 7 minutes after vaginal intromission4,5. These cutoff points were not derived by objective measurements but were subjectively chosen by the various investigators. Equally subjective cutoff points were proposed for the number of thrusts as a criterion for PE, namely, ejaculation within 8-15 thrusts4. Recently, the International Committee of the First Consultation on ED (erectile dysfunction) suggested strict criteria for definition of PE5.

Treatment of PE with behavioral therapy4,7 and pharmacotherapy with different drugs such as tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs) is widely used6. However, behavioral approaches and pharmacologic agents are both symptomatic therapies that may or may not help elucidate the causes of this sexual dysfunction7.

Psychological causes are commonly suspected as an etiology of PE10. On the other hand, organic causes, such as chronic prostatitis, have been also suggested as important causes of PE10. Screponi et al. investigated the prevalence of chronic prostatitis in patients with PE and reported that prostatic inflammation was found in 56.5% and chronic bacterial prostatitis in 47.8%
of the subjects with PE, respectively. These interesting findings were further confirmed that prostatic inflammation was found in 62% and chronic bacterial prostatitis in 52% of the 153 men with PE.

Lue et al. proposed an algorithm for the treatment of PE incorporating several management options. Men with lifelong PE should be managed with pharmacotherapy, while men with PE secondary to ED, other sexual dysfunction, or genitourinary infection should receive appropriate etiology-specific treatment. Concomitant behavioral therapy should be offered with the presence of evident contributing psychological factors. The effect of antibiotic treatment of cases with PE and chronic prostatitis has not been extensively investigated.

In this study, we aimed to examine, through a pilot study, the effect of antibiotic treatment in delaying ejaculation in patients with PE and chronic bacterial prostatitis (National Institute of Health [NIH] category II).

Methods and Measures
A total of 135 consecutive heterosexual men with a mean age of 39.2 ± 7.0 years with a range of 28-64 years attending in my private chamber and General Hospital in Narayangong and complaining of PE (all secondary type) were included in this study. Diagnosis of PE was based on the criteria set by the second consultation on sexual dysfunctions. This comprises three essential criteria: (i) brief ejaculatory latency; (ii) loss of control; and (iii) psychological distress in the patients and/or partner. Intravaginal ejaculatory latency time (IELT) of 2 minutes or less may qualify a man for the diagnosis, which should include consistent inability to delay or control ejaculation, and marked distress about the condition.

Patients included in the study were complaining of PE for at least 6 months while having regular sexual activity with a female partner. Prior to inclusion in the study, all patients were asked to record their intravaginal ejaculatory latency time (IELT) for 1 month. All patients had IELT of 2 minutes or less, timed with a watch. None of the patients had any major psychiatric or somatic disorder, consumed any drug that can affect sexual function, or used antibiotics during the previous 3 weeks of the study. None of the patients had ED according to the Sexual Health Inventory for Men. Written informed consent was obtained before inclusion in this study.

General and local urogenital examinations were performed in all subjects. Sequential microbiologic specimens were obtained according to the standardized Meares and Stamey protocol. Urethral and midstream bladder urine, and expressed prostatic secretions (EPS) were collected, examined microscopically, and cultured. Prostatic inflammation was diagnosed if 10 or more white blood cells (WBCs) per high power field (HPF) were present in the expressed prostatic secretions (EPS).

Chronic nonbacterial prostatitis/chronic pelvic pain syndrome (NIH category III) was defined by the evidence of prostatic inflammation but negative cultures of urine and prostatic fluids. Prostatic infection was defined by a 10-fold greater colony count in the EPS than in the urethral urine sample.

In cases without a positive culture, antibiotic selection was guided by prostatic penetration, response to previous therapy and patient allergies and side effects. If interim cultures showed resistance to the chosen antibiotics, these were changed.

Antibiotics were given for 1 month according to the results of their culture and sensitivity test. To classify treatment responders from nonresponders, patients with an intravaginal ejaculatory latency time (IELT) of more than 2 minutes and who responded positively (Yes) to a direct question by one of the investigators "Do you feel that you have good control over your ejaculation during sexual intercourse?" were classified as treatment responsive, regardless of prostatic infection condition. Patients not fulfilling the aforementioned criteria were classified as treatment nonresponsive.

Following cessation of antibiotic treatment, all patients were instructed to continue recording their IELT and visit General hospital/private chamber monthly for at least 4 months for the follow-up and detection of any recurrence. At the end of the 4-month follow-up, an EPS analysis was performed.

Statistical comparison of continuous variables was conducted by an unpaired t-test and of category variables by the chi-squared test. Statistical significance was set at an alpha of 0.05.

Results
The demographic characteristics of all subjects included in the study. None of the 135 patients complained of symptoms suggestive of chronic prostatitis. Only six patients gave the history of medical treatment of PE in the form of SSRIs, with unsatisfactory results (table-I).

| Age (years) | 28-64 (mean 39.2 ± 7) |
| Marital status | All married |
| Education level | |
| Primary schooling | (27/135) 20% |
| High school degree | (76/135) 56.3% |
| University graduate | (32/135) 23.7% |
| General medical disorder (e.g., diabetes) or psychiatric disorder | N/A |
| Erectile dysfunction | N/A |
| Duration of complaint (mean ± SD, months) | 13.2 ± 2.7 |
| Symptoms suggestive of chronic prostatitis | N/A |

N/A = Not available
Based on EPS culture and WBC count, 84 (62.2%) out of 135 patients were having chronic bacterial prostatitis. The remaining 51 (35.2%) patients had negative WBC count. Most of the 84 patients with positive cultures with Gram-negative bacteria, with the most common being coagulase negative (table-II).

Table-II: Prevalence of prostatitis in all patients (N = 135).

<table>
<thead>
<tr>
<th>Organism</th>
<th>Culture-positive (urine and prostate)</th>
<th>Culture-negative (urine and prostate)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>WBC &lt; 10/HPF</td>
<td>WBC &gt; 10/HPF</td>
</tr>
<tr>
<td>E. coli</td>
<td>18 (21.42%)</td>
<td>25 (29.76%)</td>
</tr>
<tr>
<td>Enterococci</td>
<td>2 (2.41%)</td>
<td>3 (3.57%)</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>10 (12.1%)</td>
<td>15 (17.8%)</td>
</tr>
</tbody>
</table>
| *P > 0.05; inflammation vs. no inflammation; culture-positive vs. culture-negative.

At this stage of the study, we randomly selected 20 out of the 84 patients with PE and chronic prostatitis and considered them as a control group. Therefore, only 64 out of 84 patients with PE and chronic prostatitis were further treated with antibiotics, while the control group patients were left untreated. Antibiotics chosen on the basis of sensitivities included quinolones (53 patients), doxycycline (6 patients), and cephalosporin (5 patients). All 64 patients continued the 1-month treatment duration. There was no significant difference between the two groups (patient and control) regarding demographic data and prostatic culture results (table-III).

Table-III: Patient and control group results.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Control (N = 20)</th>
<th>Treatment responsive (N = 64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>9 (45%)</td>
<td>9 (22%)</td>
</tr>
<tr>
<td>Enterococci</td>
<td>3 (15%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>6 (30%)</td>
<td>6 (12%)</td>
</tr>
</tbody>
</table>
| *P > 0.05; **P < 0.05, vs. Baseline.

Following 1-month antibiotic treatment, all patients with initially positive cultures had sterile final cultures. Fifty one (79.68%) patients showed increase in their IELT (mean ± SD) 2.8 ± 0.2** and seminal plasma magnesium levels 18,29.

Premature ejaculation is a highly prevalent disorder; however, accurate population-based data are not available. Even though it is usually associated with fewer nuisances than ED, this disorder may be highly upsetting in some instances. The etiology of PE is uncertain in most cases, and likely includes a combination of organic and psychogenic factors. PE has been associated with low serum testosterone17 and seminal plasma magnesium levels18, hyperthyroxinemia19, major neurological disorders, and short frenum of prepuce, penile hypersensitivity and reflex hyperexcitability20,22. Recently, two studies reported a higher than normal prevalence of PE in patients with chronic prostatitis5,11.

Initial studies examining the effect of antibiotics in improving PE reported successful outcomes23,24. Our study demonstrated a highly positive effect of the use of culture-specific antibiotics in treatment of patients with PE and chronic bacterial prostatitis. The mechanism behind this dramatic effect of antibiotics on ejaculation time is not entirely clear. It is thought that prostatitis can foster in mild form for years without obvious or clear symptoms except for PE25. Sensory impairment occurring before orgasm is considered one of the pathogenetic mechanisms of PE26. Gospodinov 27 indicated that 64% of men complaining of PE were classified as having neurophysiologic PE. Prostatic inflammation may contribute to this concept by altering the sensation and modulating the ejaculatory reflex.

Chronic prostatitis in all our patients with PE was bacterial together with absence of prostatitis symptoms. This finding applies to both interesting and challenging, and requires further clarification. First, Schaeffer et al. reported poor correlation between inflammation and infection of prostate on one side and the severity of prostatitis symptoms on the other side in 278 patients with chronic prostatitis28. Furthermore, none of the Chronic Prostatitis Symptom Index (CPSI) measures, including subset for pain, urinary symptoms, and quality of life, were different for WBC subgroups. They concluded that the overall rank correlation between WBC and urinary symptoms was nonsignificant and weak. Another argument against the association of inflammation and symptoms is that category IIIB patients have symptoms but no inflammation, and conversely category IV patients have inflammation but no symptoms29. Second, whether the type of organism-bacterial or nonbacterial-has an effect on the development of PE is still to be investigated.

Interestingly, a 1-month antibiotic treatment of our patients with PE and chronic bacterial prostatitis resulted in marked improvement in both ejaculation time and prostatic infection. Metz and Pryor suggested that a long period may elapse from prostatitis infection and appearance of prostatitis related symptoms25.
reasonable to deduce that microorganisms causing chronic prostatitis may have a relatively long incubation period. We hypothesize that the high success rate of our short course of antibiotics in treating chronic prostatitis may be related to an apparently "early" interference during the pathogenesis of chronic prostatitis. This is also evidenced by the lack of prostatitis related symptoms in all treated patients. The lack of any improvement in ejaculation time or prostatic infection in the control group patients clearly demonstrates the beneficial effect of antibiotics in cases of PE and chronic bacterial prostatitis.

Several management options are available for PE following initial assessment and diagnosis. Behavioral therapy may augment pharmacotherapy to enhance relapse prevention. Pharmacological treatments for PE include use of SSRIs (e.g., paroxetine, sertraline, fluoxetine), topical local anesthetics (e.g., lidocaine), and phosphodiesterase type 5 (PDE-5) inhibitors (e.g., sildenafil). However, none of these drugs have received regulatory approval for treatment of PE, although clinical trial data support their use in individual cases. Interestingly, Lue et al. suggested that, specifically, men with PE with other sexual dysfunction or genitourinary infection should receive appropriate etiology-specific treatment. Our results do strengthen that genitourinary infection may be an important contributor to the development of PE. Unfortunately, assessment of prostatic infection is not currently a routine measure during evaluation of men with PE. However, our results suggest that the presence of prostatic infection should be considered and preferably, managed in cases of PE.

The absence of short-term recurrence of either prostatitis or PE in all 64 successfully treated patients adds to the advantages of antibiotics in the treatment of PE with chronic bacterial prostatitis. On the other hand, around 16% of PE patients with chronic prostatitis showed, in spite of infection clearance, no improvement of their ejaculatory complaint. It is assumed that other nonorganic factors may have contributed to these patients' PE condition.

An evident limitation in PE studies involving drug therapy is the lack of standardized and validated measurement to classify responders from nonresponders. In this study, we overcame this problem by using the criteria set by the second consultation on sexual dysfunctions as determinants of treatment response. However, the need for a valid and reliable diagnostic questionnaire to accurately define PE and assess its severity is indeed obvious.

We did not include transrectal ultrasonography (TRUS) of the prostate as a chronic prostatitis assessment tool because it is considered optional. Furthermore, the identification of prostatic calcifications and the heterogeneity seen in TRUS in some prostatitis patients will lead to unnecessary prostate biopsies. Pelvic imaging using ultrasound or computed tomography scan, or magnetic resonance imaging in selected patients can identify potentially treatable pelvic pathology.

Conclusion

Successful eradication of causative organisms of chronic bacterial prostatitis can lead to marked improvement in intravaginal ejaculatory latency time (IELT) and ejaculatory control in patients with PE. Further studies examining the effect of combination pharmacotherapy in delaying ejaculation time in patients with PE and chronic prostatitis are indeed encouraged.

References