Diagnosis and Treatment of Chronic Prostatitis

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Abstract: New topics in the diagnosis of prostatitis include the revised classification of prostatitis and the development of a symptom scoring system proposed by the U.S. National Institute of Health (NIH). The new classification features the inclusion of chronic prostatitis/chronic pelvic pain syndrome. The development of the symptom scoring system facilitated the comparison of treatment effects and clinical study results. Epidemiological research on chronic prostatitis-like symptoms has been conducted using this scoring system. The role of bacterial infection as a cause of chronic prostatitis/chronic pelvic pain syndrome has not been clarified. With respect to treatment of prostatitis, the administration of antibacterial agents is an established treatment for acute or chronic bacterial prostatitis, but there is no established treatment for chronic prostatitis/chronic pelvic pain syndrome. The paucity of large-scale randomized trials and the diversity of causes are preventing the establishment of treatment for this disease.

Key words: Prostatitis; Epidemiology; Questionnaire; Treatment

Introduction

Except for a limited number of cases caused by bacterial infection, prostatitis is not easy to diagnose and treat. The reasons for this difficulty include the diversity of causes and the lack of reliable test methods for confirming the presence of inflammation. This article reviews new topics related to the diagnosis and treatment of prostatitis.

Classification of Prostatitis

Recently, the National Institute of Health (NIH) in the U.S. proposed to classify prostatitis into 4 categories (Table 1). While the new system does not differ much from conventional classification of prostatitis, a new feature is the inclusion of abacterial prostatitis and prostatodynia in 1 category (Category III). The asymptomatic inflammatory prostatitis in Category

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the main complaints in those with chronic prostatitis are pain and discomfort. The questionnaire features questions concerning pain and discomfort during urination and after ejaculation, in addition to those in the perineum, testicles, penis, and lower abdomen.

A major difference from similar forms used previously in Japan is the inclusion of questions related to QOL. This enabled relatively easy comparison regarding how symptoms of chronic prostatitis affect the patient’s QOL. We translated the NIH questionnaire into Japanese and examined its validity and reproducibility.3) The results show that the score regarding pain or discomfort and that regarding QOL are clearly higher in patients with chronic prostatitis as compared with those with BPH and healthy adults. This result suggests that this type of questionnaire is useful for evaluating not only symptoms but also QOL of patients with chronic prostatitis. Our evaluation of reproducibility also provides satisfactory results. Thus, we conclude that this questionnaire can be applied for Japanese patients with chronic prostatitis. The Japanese Urological Association is currently evaluating the final Japanese version of the questionnaire.

It must be emphasized that this questionnaire is not intended for diagnosis of chronic prostatitis but for objective evaluation of symptoms and evaluation of treatment effects. This precaution is the same as that concerning the International Prostate Symptom Score (IPSS) for BPH. The IPSS is not used for the diagnosis of BPH.

### Epidemiology of Chronic Prostatitis-Like Symptoms

The prevalence and number of patients with chronic prostatitis-like symptoms in Japan have not been ascertained exactly. A study in Canada using the aforementioned questionnaire reported a prevalence of 9.7% among men in the age range of 20 to 79, although the definition as to what score indicates the

**Table 1 Classification of Prostatitis (NIH)**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I</td>
<td>Acute bacterial prostatitis</td>
</tr>
<tr>
<td>Category II</td>
<td>Chronic bacterial prostatitis</td>
</tr>
<tr>
<td>Category III</td>
<td>Chronic prostatitis/chronic pelvic pain syndrome</td>
</tr>
<tr>
<td>Category IIIA</td>
<td>Inflammatory</td>
</tr>
<tr>
<td>Category IIIB</td>
<td>Noninflammatory</td>
</tr>
<tr>
<td>Category IV</td>
<td>Asymptomatic inflammatory prostatitis</td>
</tr>
</tbody>
</table>

IV is defined based on histological diagnosis.

Without exception, acute bacterial prostatitis is caused by infection of Gram-negative bacilli, typically *Escherichia coli*. Chronic bacterial prostatitis in Category II is caused by Gram-negative bacilli and by some Gram-positive cocci. Category III is chronic prostatitis/chronic pelvic pain syndrome, which is subdivided into inflammatory and noninflammatory. The “inflammatory” Category IIIA refers to so-called chronic abacterial prostatitis, while the “noninflammatory” Category IIIB refers to chronic pelvic pain syndrome. Category III represents 80% of all prostatitis cases. Because the most important problems of diagnosis and treatment are associated with prostatitis cases in categories II and III, the following sections focus on the discussion of problems concerning these 2 categories.

**Chronic Prostatitis-like Symptom Scores**

Questionnaires have been used for the evaluation of symptoms of chronic prostatitis, but unfortunately, there were no established forms for this purpose. Recently, a questionnaire form for scoring chronic prostatitis-like symptoms was developed by a group supported by NIH.2) A draft version that was translated into Japanese is also available.3) This questionnaire consists of 9 questions in total: 4 regarding pain or discomfort, 2 regarding urination, and 3 regarding the quality of life (QOL). In contrast to patients with benign prostatic hyperplasia (BPH) and healthy adults, the main complaints in those with chronic prostatitis are pain and discomfort. The questionnaire features questions concerning pain and discomfort during urination and after ejaculation, in addition to those in the perineum, testicles, penis, and lower abdomen.
presence of chronic prostatitis-like symptoms has not been concretely established.\(^5\)

When we analyzed our data using the same definition, the prevalence in the above age range was 5\%.\(^3\) If we assume that all patients with these symptoms have chronic prostatitis, the number of patients in Japan is estimated to be between 1 to 1.5 million.

**Diagnosis of Prostatitis**

Diagnosis of acute prostatitis can be made easily based on clinical findings. Most patients show evident systemic symptoms, including fever of 38°C or higher, pain on urination, and difficulty of urination. Urinary sediment tests show leukocytes and bacteria without exceptions. The causative bacteria are Gram-negative bacilli, in particular *Escherichia coli*. The prostate is swollen with marked tenderness. Prostatic massage is contraindicated, because it increases the risk of sepsis.

As mentioned above, chronic prostatitis is classified into Category II (chronic bacterial prostatitis) and Category III (chronic prostatitis/chronic pelvic pain syndrome). A four-glass test using first voided urine, midstream urine, expressed prostatic secretion (EPS) obtained by massage, and post-massage voided urine has conventionally been recommended for the purpose of diagnosing prostatitis in these categories. However, this test has rarely been used in daily clinical practice.

A simplified test called the two-glass test has been used recently. This test uses pre-massage (midstream) urine and post-massage voided urine. When either method is used, the presence or absence of inflammatory signs and bacteria in the EPS or post-massage voided urine is diagnostically important. Generally, the presence of inflammation is presumed when EPS or the sediment of post-massage voided urine contains at least 10 to 20 leukocytes in a \(\times 400\) field of view. If the number of leukocytes is smaller, the probability of inflammation is considered low, although there are some objections in this respect.

On the other hand, bacterial infection is inferred when at least \(10^3/m\) Gram-negative bacilli or \(10^4/m\) Gram-positive cocci are isolated. In the case of the two-glass test, the diagnosis as having chronic bacterial prostatitis requires a lack of inflammation and bacteria in pre-massage urine and the presence of both in post-massage voided urine. In the U.S., if the number of bacteria isolated from EPS or post-massage voided urine exceeds 10 times that of the first voided and midstream urine, the isolated bacteria are usually considered the causative bacteria. When the test did not show involvement of bacteria, patients are diagnosed as having category III disease. In addition, chronic abacterial prostatitis in Category IIIA is suspected if EPS or post-massage voided urine had inflammation, and chronic pelvic pain syndrome in Category IIIB is suspected otherwise.

The question remains that whether Category III prostatitis really lacks the involvement of bacterial infection or the inability to prove bacteria merely reflects the insufficient sensitivity of the test. In particular, involvement of bacterial infection cannot be ruled out when there is an inflammatory finding. Indeed, there is an argument that prostatic massage cannot yield bacteria from the prostatic ducts, as well as a study reporting that bacterial genes could be demonstrated in a fairly large percentage of cases without clinical isolation of bacteria.\(^6\)

More basic study is needed before we are able to rule out bacterial infection as the cause of inflammation observed in a case lacking clinical demonstration of bacteria.

With respect to the causes of chronic pelvic pain syndrome showing no isolatable bacteria and no signs of inflammation, our understanding is poor. While bacterial infection cannot be ruled out completely, the involvement of inflammation unrelated to bacterial infection, prostatic calculus, urinary disturbance, congestion of pelvic veins, and mental or psychological factors is also suspected.
Recently, interstitial cystitis is also suspected as a possible cause in some patients. It may also be possible that the development of symptoms may be mediated by the same mechanism.

**Treatment of Prostatitis**

In the final section, we discuss the treatment of prostatitis. As mentioned above, the causative bacteria of acute prostatitis are mostly Gram-negative bacilli. Accordingly, parental antibacterial agents that have antibacterial activity against these bacteria (e.g., second and third generation cephems, carbapenem, and monobactam) are used for treatment. Since fever is alleviated usually within 3 to 5 days, antibacterial chemotherapy using oral antibacterial agents (fluoroquinolones and new oral cephems) is followed for 2 to 3 weeks. In the case of acute aggravation of chronic bacterial prostatitis, prolonged antibacterial chemotherapy may be needed even after the disappearance of acute symptoms.

Chronic bacterial prostatitis is basically caused by bacterial infection. Whether the causative bacteria are Gram-negative or Gram-positive, treatment should be based on antibacterial chemotherapy.

A large number of antibacterial agents are currently covered by the national health insurance for use in prostatitis. Those frequently used for chronic bacterial prostatitis include tetracycline antibiotics (doxycycline and minocycline) and various new quinolones. These antibacterial agents show relatively good drug penetration to prostatic tissue. New quinolones are used most frequently, because of their advantage in drug penetration to prostatic tissue and antibacterial activity against possible causative bacteria. While antibacterial chemotherapy is usually used for 4 weeks, many patients require a treatment period of 12 weeks. Prostate massage in parallel with antibacterial chemotherapy may be effective.

Chronic bacterial prostatitis is often complicated with obstruction of prostatic ducts, reflecting its nature as a so-called biofilm disease. Treatment can sometimes be difficult, and the presence of urination disturbance, prostatic calculus, etc. must be considered in such cases. While sympathetic alpha-receptor blockers (alpha-blockers) and TURP are sometimes needed in these cases, the effectiveness of these treatments has not been established.

As compared with chronic bacterial prostatitis in Category II, the treatment of chronic prostatitis/chronic pelvic pain syndrome in Category III is more likely to be difficult. Various regimens have been attempted for the treatment of this disease, and this fact may be ironically viewed as a reflection of the lack of definite therapies. A major problem is the fact that few large-scale controlled trials have been conducted on this disease.

The effectiveness of several treatment methods has been confirmed in a small number of cases, but data have not been accumulated to establish evidence. Since a questionnaire for the objective evaluation of chronic prostatitis-like symptoms has been developed, we now can take a more scientific approach to the treatment of this disease. If not, we will have to repeat the process of trial and error that continued for decades in the past.

As discussed above, inflammatory category (IIIA) of chronic prostatitis/chronic pelvic pain syndrome (Category III) does not show isolatable bacteria. However, antibacterial agents are usually used as the initial therapy at least temporarily.

The antibacterial agents used in this disease are new quinolones, and the therapy is continued usually for 2 to 4 weeks. Combinations with plant extracts or antiinflammatory agents such as NSAIDs may be effective, but these combinations have not been confirmed to enhance the action of antibacterial agents. Among plant extracts, in vitro effects of Cernilton® have been reported. This preparation is attractive for inhibition of proinflammatory cytokines, but it has not been examined whether this activity is generated in clinical
setting. In addition, prostate massage, hot sitz bath, and other treatments can be effective in some patients, as well as life guidance such as avoidance of drinking, long sitting, and fatigue.

When treatment extends over a long period, it is desirable to discontinue antibacterial therapy and continue other methods of treatment. If symptoms do not respond to these treatments, alpha-blockers, Chinese herbal medicines, antidepressants, etc. may be used. However, it should be noted that none of these treatments has been established. In particular, the effectiveness of alpha-blockers has not been established, although some reports have indicated the clinical efficacy of these agents and there is a possibility that some patients with disturbance of urination mechanisms were included in the disease of this category.

The treatment for chronic pelvic pain syndrome in Category IIIB is even more empirical than that for Category IIIA. In addition to the treatments for Category IIIA, psychosomatic approaches, skeletal muscle relaxants, and other methods are attempted. Recently, prostate thermotherapy has been reported to be effective in Category III prostatitis. Future study in this direction is expected.

As discussed above, the methods for treatment of chronic prostatitis other than acute and chronic bacterial prostatitis have not been established. Because of a large number of patients with the disease, more clinical studies are crucial.

REFERENCES


