

# Application of hyperbaric oxygen in middle-aged and elderly patients with chronic prostatitis and depression

## Abstract

**Purpose:** This study aims to analyze the effects and safety of hyperbaric oxygen in middle-aged and elderly patients with chronic prostatitis and depression. **Methods:** A total of 120 middle-aged and elderly patients with chronic prostatitis and depression were enrolled at Qingdao's Jiaozhou Central Hospital. Before and after hyperbaric oxygen therapy, the symptom scoring scale (NIH) and Hamilton Depression Scale (ADMH) scores, testosterone levels, and clinical efficacy were all recorded, and the differences were analyzed using correlation analysis and an independent sample t-test. **Results:** Compared with patients before hyperbaric oxygen therapy, NIH-CPSI and AMDH scores were lower, and testosterone levels were higher, which was statistically significant ( $P < 0.05$ ). **Conclusion:** The effect of hyperbaric oxygen combination on patients with chronic prostatitis and depression is remarkable, and the level of testosterone is significantly improved, which can effectively improve their clinical symptoms and depressive symptoms and improve the quality of life for patients.

## Keyword

chronic prostatitis, Hyperbaric oxygen, Depressive patients

## Introduction

Chronic prostatitis is a common male reproductive system disease in urology. The prevalence of andrology diseases exceeds 56%, particularly among the middle-aged and elderly. Higher recurrence rates are common among patients who previously had chronic prostatitis after treatment[2]. 90% to 95% of cases of prostatitis are chronic nonbacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS, Class III), according to the National Institute of Diabetes and Digestive and Renal Diseases (NIDDK)/National Institutes of Health (NIH; Krieger et al., 1999[2]). The National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) is a valid metric widely applied in China to assess the severity of symptoms in individuals with chronic prostatitis [3]. Patients with CP/CPPS are said to have lower health-related quality of life (HRQOL) than those with other chronic illnesses (such as congestive heart failure and diabetes)[5]. Pelvic pain and lower urinary tract symptoms are the primary clinical manifestations of CP/CPPS, and low testosterone (TT) levels (3.5 ng/mL) are significantly correlated with these symptoms[6]. frequently causing male hypogonadism, delayed testicular dysfunction (LOH), sexual dysfunction, and sperm quality damage, especially ejaculatory issues (such as ejaculation precursors [EP] and ejaculation pain [EP]) plus infertility[7-8]. The Hamilton Depression Scale (HAMD) is frequently used to evaluate the signs of anxiety and depression because this could put the population under a lot of psychological strain and even result in mental illness [9-10]. Because depression and anxiety have been linked to prostate symptoms in CP patients, research has shown that these patients have significant psychological and organ function damage [11]. CP may be caused by the interaction of psychological factors with immune, neurological, and endocrine system dysfunction, according to some reports. The exact cause of CP is unknown[12]. This also contributes to the fact that empirical medication and symptomatic relief of symptoms are frequently used in its treatment [13], including antibiotics, anti-inflammatory drugs, hormones, immunotherapy, behavioral cognitive therapy, acupuncture, and moxibustion therapy, among others [14–17]. Antibiotics are the most widely used empirical treatment, but CP patients frequently do not have multiple positive cultures, which may be because antibiotics target unidentified pathogenic microorganisms or because the anti-inflammatory properties of the drugs

themselves result in a reduction of some inflammatory factors, such as IL-6 and IL-8 [18]. However, the regulation of inflammation can be resolved through other methods, such as enhancing immunity, so it is not recommended to use antibiotics in the absence of a positive culture[19]. For example, ciprofloxacin and tamsulosin did not significantly reduce CP/CPPS symptoms compared to placebo[20]. There are reports confirming a significant correlation between low testosterone levels (3.5 ng/mL) and prostatitis-like symptoms[21]. In recent years, testosterone replacement therapy [TRT] has been shown to improve the composition of metabolic syndrome and reduce prostatitis[22]. There are undeniable advantages for men with LOH in clinical, metabolic, increased erection hardness, and sexual desire[23, 24]. In patients with chronic prostatitis and hypogonadism, it can improve lower urinary tract symptoms, reduce pelvic pain, and significantly improve quality of life[25]. However, there are risks that can lead to prostate enlargement. Although the benefits outweigh the drawbacks, finding a new treatment method that is reliable, safe, widely available, less expensive, and has fewer complications remains one of the challenges that urologists are addressing.

As an emerging discipline, hyperbaric oxygen therapy (HBOT) has distinct advantages as a safe, low-risk, and non-invasive treatment method that can be used as a primary or auxiliary treatment for a variety of medical conditions[26,27]. Can be used in bacterial, fungal, and viral infections[28]. It has achieved good results in reducing carbon monoxide poisoning, kidney damage, and ulcers in diabetes patients; reducing ultraviolet skin damage and radiation damage; improving wound healing; preventing ischemia-reperfusion injury; reducing inflammatory reactions; anti-aging; and improving immunity[29,30]. Previous studies have shown that hyperbaric oxygen combined with nursing can have good therapeutic effects on postpartum, acute cerebral infarction patients, and post-stroke depression [31,32]. It can also induce angiogenesis and restore erectile function and sexual desire in male patients [33]. The mechanism of action may be to increase oxygenation of blood and tissues to hyper physiological levels, improving neuronal function by reactivating metabolic or electrical pathways. [34] It may also be achieved by improving clinical symptoms to alleviate depression. At present, there is no relevant research on the efficacy of hyperbaric oxygen therapy for patients with chronic prostatitis and depression. Therefore, this study mainly analyzes the clinical efficacy and safety of hyperbaric oxygen therapy for middle-aged and elderly patients with CP/CPPS.

## **Materials and Methods**

### **1.1 General Information**

The study included 120 CP patients from Qingdao Jiaozhou Central Hospital. This study's inclusion criteria are as follows:

- 1) meets the diagnostic criteria of CP or CPPS, and the Hamilton Depression Scale (ADMH) score is 20 points;
- 2) The reason for the patient's medical treatment is frequent urination, incomplete urination, and discomfort from perineal pain and bloating. Some patients also have insomnia, weak erections, and premature ejaculation.
- 3) Sign an informed consent form for voluntary participation in the study;
- 4) Intervention measures such as clinical treatment have not been taken before seeking medical attention.

The exclusion criteria for the subjects of this study are:

- 1) The patient has urinary system stones or other serious organic diseases;
- 2) The patient is accompanied by functional liver and kidney dysfunction;
- 3) Contraindications to HBOT treatment include open chest wall trauma, multiple rib fractures, extensive and severe chest wall contusions, untreated malignant tumors, hypertension, etc.
- 4) The patient's clinical data is incomplete.

### **1.2 Method**

1.2.1 Blood samples from these 120 patients should be collected from 7:00 a.m. to 11:00 a.m. before and after 4 weeks of treatment. Use enzyme-linked immunosorbent assay to detect serum testosterone.

1.2.2 Group B was treated with an additional hyperbaric oxygen chamber; the treatment pressure was 0.2 kPa (2.0 TAT), and the pressure was increased for 20 minutes. After stabilizing, a mask was used for oxygen inhalation for 20 minutes, followed by a 10-minute rest before another mask was used for oxygen inhalation for 20 minutes. Finally, the pressure was reduced for 20 minutes, and the first treatment was completed. Once a day, continue treatment for 5 days and then rest for 2 days. Both groups of treatments lasted for 4 weeks.

1.2.3 Using the R language "corrplot" package to study the correlation between pre-treatment testosterone levels and other clinical traits; Conduct data analysis using SPSS to compare the differences in HAMD, NIH-CPSI scores, and testosterone levels between pre- and post-treatment patients and determine whether there are significant differences.

### 1.3 Observation indicators

(1) Compare the HAMD scores before and after 4 weeks of treatment: The content of the HAMD includes 24 items such as depression, guilt, and difficulty falling asleep, using a 5-level scoring method. A score of 0-4 indicates no, mild, moderate, severe, and extremely severe, respectively. A total score of <8 indicates no depressive symptoms, 8-20 indicates possible depression, 21-35 indicates certain depression, and >35 indicates severe depression.

(2) Compare the treatment effects of two groups: cured, with a decrease of 75% or more in HAMD score; significant effect, reducing HAMD score by 50% to 74%; effective, reducing HAMD score by 25% to 49%; invalid, reducing HAMD score by less than 25% [3].

(3) Compare the incidence of adverse reactions between the two groups: Record the adverse reactions during treatment, including headaches, dizziness, dryness, and gastrointestinal discomfort.

(2) Compare the NIH-CPSI scores, clinical efficacy, and adverse reactions of patients before and after treatment. Evaluate the improvement of clinical symptoms and quality of life of patients in three aspects using the NIH-CPSI .the first aspect is to evaluate the location, frequency, and severity of the patient's pain. The second aspect is the evaluation of symptoms related to patient urination. The third aspect is to evaluate the patient's quality of life. The total score of the NIH-CPSI is 43 points. The lower the NIH-CPSI score of a patient, the lighter their clinical symptoms and the higher their quality of life. The clinical efficacy of patients can be divided into four levels: cured, significantly effective, effective, and ineffective. 1) Cure: After receiving treatment, the patient's clinical symptoms have greatly improved compared to before, and the patient's NIH-CPSI score is 0. 2) Significant effect: After receiving treatment, the patient's clinical symptoms improved significantly, and their NIH-CPSI score decreased by 51% to 99% compared to before treatment. 3) Effective: After receiving treatment, the patient's clinical symptoms improved, and their NIH-CPSI score was 25% to 50% higher than before treatment. 4) Invalid: After receiving treatment, the patient's clinical symptoms did not improve, and their condition even worsened. The NIH-CPSI score of the patient increased or decreased by less than 25% compared to before treatment. Total effective rate = (number of cured cases + number of significantly effective cases + number of effective cases) / total number of cases × 100%.

(3) Compare the total testosterone levels of patients before and after treatment.

### 1.4 Statistical methods

The data for this study was processed using statistical software IBM SPSS Statistics 26 and R language. The measurement data are all expressed as mean ± standard deviation ( $\bar{x} \pm s$ ). The normal distribution data is subject to the t-test, and the non-normal distribution data is subject to the non-parametric test. The counting data is expressed in percentage (%), using  $\chi^2$  Inspection.  $P < 0.05$  indicates a statistically significant difference.

## Results

The age range of these 120 patients is between 43 and 60 years old, with an average age of  $(51.26 \pm 3.46)$  years; The course of the disease ranges from 5.2 to 18.1 years, with an average course of  $(12.65 \pm 0.51)$  years. The average testosterone before clinical intervention was  $(7.2 \pm 2.8)$  ng/ml, and there was no statistically significant difference between the general data of these 120 patients before and after treatment ( $P > 0.05$ , see Table 1).

Figure 1 depicts the relationship between testosterone and clinical traits, as well as HAMD and NIH-CPSI scores prior to clinical intervention. Despite the lack of a significant correlation, we discovered a negative correlation between testosterone levels and HAMD and NIH-CPSI scores, confirming the link between low testosterone and prostatitis symptoms and a depressive mental state in patients.

After 4 weeks of treatment, the HAMD scores of both groups were lower than the pre-treatment scores. The NIH-CPSI score improved before and after treatment, and the testosterone level significantly increased after treatment, with a statistically significant difference ( $P < 0.05$ , Table 2, Figure 2-7)

Table 1 shows the relationship between testosterone levels and clinical parameters prior to intervention.

| Variables                       | Number of patients | Testosterone levels (ng/ml, mean $\pm$ SD) | P value |
|---------------------------------|--------------------|--|---------|
| Patients                        | 120                | $7.20 \pm 2.80$                            |         |
| Age <sup>a</sup>                |                    |  |         |
| $\leq 51$                       | 65                 | $7.27 \pm 2.77$                            | 0.920*  |
| $> 51$                          | 55                 | $7.23 \pm 2.75$                            |         |
| HAMD <sup>a</sup>               |                    |  |         |
| $\leq 29$                       | 81                 | $6.68 \pm 2.76$                            | 0.564*  |
| $> 29$                          | 39                 | $7.45 \pm 2.75$                            |         |
| Pain score <sup>a</sup>         |                    |  |         |
| $\leq 14$                       | 66                 | $7.05 \pm 2.60$                            | 0.394*  |
| $> 14$                          | 54                 | $7.49 \pm 2.93$                            |         |
| Urination score <sup>a</sup>    |                    |  |         |
| $\leq 7$                        | 65                 | $6.99 \pm 2.65$                            | 0.318*  |
| $> 7$                           | 55                 | $7.56 \pm 2.85$                            |         |
| life Quality score <sup>a</sup> |                    |  |         |
| $\leq 7.5$                      | 60                 | $7.68 \pm 2.90$                            | 0.076*  |
| $> 7.5$                         | 60                 | $6.82 \pm 2.54$                            |         |
| NIH-CPSI <sup>a</sup>           |                    |  |         |
| $\leq 28$                       | 66                 | $7.12 \pm 2.64$                            | 0.641*  |
| $> 28$                          | 54                 | $7.41 \pm 2.90$                            |         |

Table 1 Continuous variables are represented by the median a; The use of bold font to represent numerical values has statistical significance ( $P < 0.05$ ); P \*: Independent sample T-test; HAMD is the Hamilton Depression Scale. The NIH-CPSI score includes a pain and discomfort symptom score, a urination symptom score, and a quality of life score. The numerical expression is  $(x \pm s)$

Table 2 Changes in HAMD, NIH-CPSI scores, and testosterone levels in patients after hyperbaric oxygen therapy

|                                   | Testosterone level before treatment (ng/ml, mean $\pm$ SD) | Post-treatment testosterone levels (ng/ml, mean $\pm$ SD) | P value          |
|-----------------------------------|--|---|------------------|
| HAMD                              | 28.70 $\pm$ 2.50   | 5.10 $\pm$ 0.50   | <b>P&lt;0.05</b> |
| Pain and discomfort symptom score | 13.70 $\pm$ 3.40   | 6.60 $\pm$ 2.50   |                  |
| Symptom score for urination       | 7.20 $\pm$ 2.80  | 4.80 $\pm$ 1.70   |                  |
| Rating of quality of life         | 7.60 $\pm$ 1.30  | 4.90 $\pm$ 1.90   |                  |
| NIH-CPSI                          | 28.38 $\pm$ 4.30   | 14.78 $\pm$ 2.66  |                  |
| testosterone                      | 7.20 $\pm$ 2.80  | 11.60 $\pm$ 2.50  |                  |

Table 2 The use of bold font to represent numerical values has statistical significance (P<0.05); HAMD is the Hamilton Depression Scale; The NIH-CPSI score includes pain and discomfort symptom score, urination symptom score, and quality of life score; The numerical expression is (x  $\pm$  s).

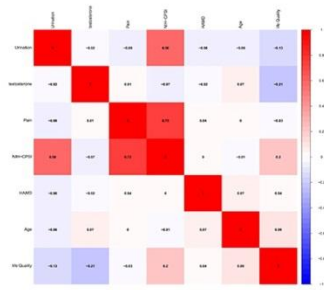


Fig 1

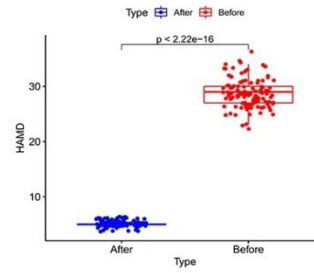


Fig 2

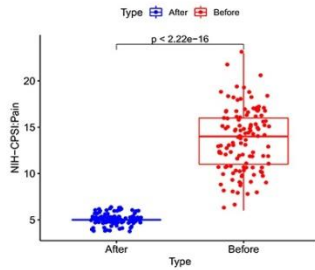


Fig 3

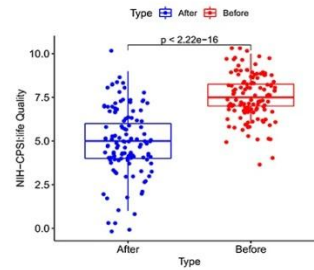


Fig 4

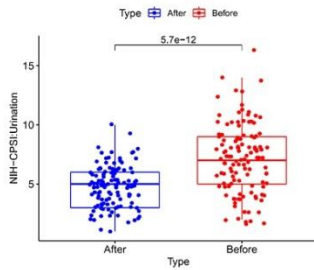


Fig 5

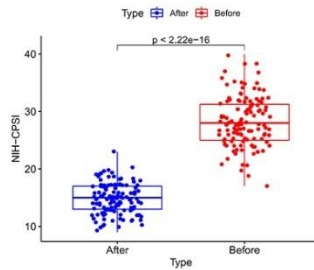


Fig 6

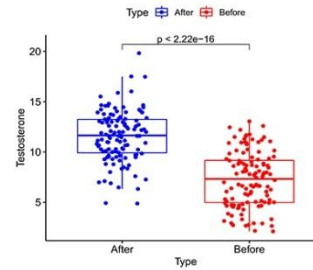


Fig 7

**Figure 1.** The relationship between testosterone and clinical traits

**Figure 2-7.** Box plots of the NIH-CPSI score, before and after treatment.

## Discussion

The term CP refers to prostate congestion and edema caused by a variety of factors. For example, sexual life is too frequent, the sedentary perineum is oppressed, unhealthy eating habits (such as excessive drinking, smoking, hot and humid accumulation from hot food, etc.), and prolonged exposure to low-temperature environments cause prostate vasospasm and contraction. cause prostate blood stasis [32]. After the age of 50, testosterone levels in male testicular veins decrease by about 1% per year. Low testosterone levels are closely related to early symptoms or a higher incidence of depression, indicating that male patients with low testosterone levels (particularly those aged 50–65) are more susceptible to depression [35]. The following points are included in the hyperbaric oxygen treatment principle for prostatitis combined with depression: (1) The use of hyperbaric oxygen increases the

variability of red blood cells, strengthens the inhibitory effect of the blood coagulation system, reduces blood viscosity, assists in the improvement of the regulatory function of microcirculation, and reduces prostate congestion and edema. To alleviate the clinical symptoms of the patient. (2) Hyperbaric oxygen can regulate local cerebral blood flow perfusion, increase cerebral oxygen supply, improve the excitability of the hypothalamus-pituitary thyroid system, and promote thyroid hormone and dopamine secretion; (3) Hyperbaric oxygen can stimulate neuronal metabolic recovery by increasing the activity of the pentose phosphate pathway in neuronal cells [33]. Hyperbaric oxygen can also help patients sleep better. Previous studies have shown that patients with CP/CPSP not only have clinical symptoms such as difficulty urinating, painful urination, and pelvic pain but also often have sexual dysfunction, erectile dysfunction, decreased libido, generalized anxiety disorder, and depression, which seriously affect the daily life and physical health of contemporary men. The etiology of prostatitis is often unclear, and treatment methods are diverse. Antibiotics and some invasive examinations and procedures are often accompanied by concurrent factors that are detrimental to the physical and mental health of patients. Seeking a new and reasonable treatment method can not only improve the clinical manifestations of CP and CPSP patients but also improve their quality of life. It is urgent to treat anxiety and depression.

We analyzed 120 middle-aged and elderly patients with chronic prostatitis accompanied by depression, ranging in age from 43 to 60 years old, who were diagnosed with CP/CPSP in the outpatient department. After HBOT treatment, there was a significant difference in the scores of HAMD and NIH-CPSI, as well as the changes in testosterone levels before and after treatment ( $P < 0.05$ ). The testosterone levels of the patients were significantly increased, and the erectile function and sexual desire of the male patients were significantly improved. The anxiety and depression conditions of the patients were effectively treated. In addition, our research scheme also shows its limitations, such as too few samples, a more concentrated geographical range of patients, uneven standards of patients in the questionnaire, and too strong subjectivity. However, through the clinical data we have collected, it has been proven that the treatment of patients with chronic prostatitis combined with hyperbaric oxygen has a significant effect, with significantly increased levels of testosterone, which can effectively improve their clinical and depressive symptoms and improve their quality of life. This may provide a new thinking plan for non-invasive treatment of patients with chronic prostatitis combined with depression.

**Conclusion:** In conclusion, chronic prostatitis is very common, and its symptoms are strongly correlated with low testosterone, sadness, and anxiety. Low testosterone levels can result in delayed testicular dysfunction (LOH), which can trigger or exacerbate psychological symptoms including anxiety and sadness. Hyperbaric medicine has the advantages of safe, low-risk, non-invasive sex therapy, which offers a new idea for the treatment of elderly Prostatitis patients with depression. It can effectively improve the clinical and depressive symptoms of chronic Prostatitis patients as well as their testosterone levels.

### **Ethics Approval and Consent**

This study was approved by The Research Ethics Committee of Qingdao Jiaozhou Central Hospital. The informed written consents were collected from all eligible patients and the entire study was performed based on the Declaration of Helsinki.

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