

CHRONIC ABACTERIAL PROSTATITIS

Background

Chronic abacterial prostatitis, or chronic pelvic pain syndrome (CP/CPPS), is a prevalent, yet poorly understood entity characterized by pelvic or perineal pain, irritative voiding symptoms, and sexual dysfunction. It is the most common urologic diagnosis in men less than 50 years of age. Chronic abacterial prostatitis accounts for more than 90–95% of clinical prostatitis. The impact of this condition on health status and quality of life is significant, as CP/CPPS patients demonstrate impaired quality of life and daily functioning impairment. Despite its prevalence and sickness impact, little remains known about its etiology and treatment.

The pathogenesis of CP/CPPS is still poorly understood but neurologic, immunologic, and endocrine dysfunctions have been proposed to be involved in disease development. Recently, evidence indicating an autoimmune component in the pathogenesis of CP/CPPS has begun to emerge. Patients with CPPS often have white blood cells in expressed prostatic secretions (EPS), implicating inflammation as a potential etiologic mechanism. In these patients, inflammatory infiltrates are exclusively mononuclear, consisting predominantly of lymphocytes, with a

virtual absence of neutrophils, basophils, eosinophils, and mast cells.

These evidence are further supported by the observation that patients with CP/CPPS show higher levels, compared to controls, of seminal plasma proinflammatory cytokines, such as interleukin 1b, IL-6, and tumour necrosis factor a, and chemokines such as IL-8.

Pathology Model

In order to induce a chronic inflammation in prostatic cells mimicking CP/CPPS, activated macrophages (derived from human monocytes)-conditioned medium will be applied to normal human prostatic cells. The U937 monocyte cell line will be cultured in appropriate medium. To achieve macrophage differentiation and cytokine production, cells will be treated with phorbol acetate at a final concentration of 16 nM for 16 h. After allowing the cells to rest for 2–3 h, lipopolysaccharide (LPS) will be added (10 ng/ml), and the cells will be incubated for 24 h. The human prostatic normal cells (RWPE-1) will be put in communication with activated macrophages for 4 wks, in order to induce chronic inflammation, either in the presence or absence of CLIENT's compounds.



Inflammation

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Readouts

The following parameters will be taken into consideration:

- Quantitative evaluation of cell vitality
- Quantitative evaluation of cell proliferation
- Quantitative evaluation of caspase activity
- Quantitative evaluation of inflammatory mediators by multiplex ELISA
- Quantitative evaluation of oxidative stress by Total ROS analysis