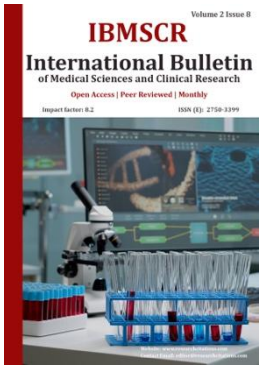

STAGE-BASED THERAPEUTIC APPROACHES TO BLADDER LEUKOPLAKIA: CLINICAL OUTCOMES

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Abstract: Treatment of bladder leukoplakia at various stages presents significant challenges [4, 7, 10, 11, 12, 14]. According to domestic and international literature, both conservative and surgical methods are used in the management of bladder leukoplakia. When choosing a treatment method, it is necessary to consider the patient's age, the severity of clinical manifestations, and the stage of the disease [1, 5, 8, 16].

According to the literature, the treatment of bladder leukoplakia should be etiopathogenetic [1, 3, 6, 10, 12, 15, 17]. In addition, symptomatic therapy of the disease is necessary [2, 5, 8, 9, 13]. Etiopathogenetic methods include antiviral, immunomodulatory, and hormone replacement therapy.

Surgical treatment methods for bladder leukoplakia include transurethral resection (TUR) of affected areas of the bladder mucosa or laser excision of altered mucosal areas following prior biopsy [2, 5, 8, 9, 13]. Transurethral vaporization of the altered bladder mucosa also occupies a specific place in the treatment of bladder leukoplakia [1, 3, 6, 10, 12, 15, 17].

Objective: To identify optimal treatment methods for bladder leukoplakia at different stages.

Materials and Methods: Patients were selected from those hospitalized in the urology department of Andijan State Medical Institute named after Yu. Otabekov between 2016 and 2019. A total of 45 women suffering from bladder leukoplakia were examined. Patients were divided into three groups according to biopsy results and subsequent treatment methods. Appropriate treatment was administered to each group:

- **Group I:** Conservative treatment
- **Group II:** Transurethral resection of altered areas of the bladder mucosa
- **Group III:** Transurethral coagulation of altered areas of the bladder mucosa

Results: Morphological examination of biopsy material established the stages of leukoplakia. The first stage of bladder leukoplakia was characterized by metaplastic changes in the transitional epithelium, detectable only by histological examination. Amid typical transitional epithelium, nests and fields of stratified squamous epithelium were visible. The number of cell layers increased by 1.5–2 times; the upper layers acquired a polygonal shape characteristic of squamous epithelium with vesicular nuclei containing multiple nucleoli. Histochemical studies revealed abundant glycogen and prokeratin in the cytoplasm of these cells.

The second and third stages were characterized by epithelial changes visible during cystoscopy as whitish patches on the bladder mucosa. Histologically, the mucosal fragments from these areas predominantly showed metaplastic stratified squamous epithelium with vertical differentiation. The lower layers consisted of smaller hyperchromatic polygonal cells. Toward the surface, cells increased in size, became paler due to glycogen and keratin

accumulation, and the surface layer accumulated varying amounts of keratohyalin. This indicated metaplastic keratinizing squamous epithelium, histologically and immunologically indistinguishable from native squamous epithelium.

Treatment:

- Group I: 20 women with first-stage leukoplakia received conservative therapy (antibacterial treatment, bladder instillations with antiseptic solutions, etc.).
- Group II: 10 women with second- and third-stage true leukoplakia underwent transurethral resection of affected mucosal areas.
- Group III: 15 women with second- and third-stage leukoplakia underwent transurethral coagulation of affected mucosal areas.

Among the study cohort, signs of active lower urinary tract inflammation (leukocyturia, bacteriuria) were detected in 3 (15%) patients in Group I, 5 (50%) in Group II, and 5 (33%) in Group III. The most common pathogen was gram-negative flora (Escherichia coli), found in 2 (10%) of Group I, 1 (10%) of Group II, and 3 (20%) of Group III. Staphylococcus saprophyticus was identified in 6 (13%) women. Antibacterial therapy was initiated based on the identified pathogen. For gram-negative flora (E. coli), fluoroquinolones were used (ciprofloxacin 500 mg twice daily for 10 days). For gram-positive flora, a combination of aminoglycosides and fluoroquinolones was applied (amikacin 1 g IM once daily for 7 days, and ofloxacin 200 mg twice daily for 10 days). Repeat bacteriological examination after 14 days confirmed pathogen elimination. In 4 (9%) patients, additional therapy with levofloxacin 500 mg once daily for 10 days was required. Follow-up urine culture after 12 days revealed no pathogenic flora.

All women with viral infection received antiviral therapy. Hormone replacement therapy was administered locally in cases of hypoestrogenism, following consultation with a gynecologist-endocrinologist: Ovestin suppositories 500 mg once daily for 30 days, then 250 mg once daily for 20 days. Immunostimulatory therapy with Polyoxidonium (0.6 mg IV once daily for 7 days) was also administered.

Surgical Treatment: TUR and transurethral coagulation were performed on Groups II and III, respectively.

Post-Treatment Observations: After treatment, 3 (15%) of Group I, 2 (20%) of Group II, and 2 (13%) of Group III continued to experience lower abdominal pain requiring additional conservative therapy. Pain management was conducted by neurologists and psychotherapists based on patients' mental state.

Patients were observed for 6 months. By the end of the observation period, nearly all patients reported resolution of pain. Complaints of pain, frequent, and difficult urination disappeared in all groups, a statistically significant result. Statistical analysis showed the best outcomes in Group III compared to Group II. Pain analysis before and after treatment also confirmed superior results in Group III (TUR coagulation) using McNemar's test ($p<0.05$).

Urodynamic Outcomes: At 6 months, comprehensive urodynamic studies revealed improved well-being, decreased lower urinary tract symptoms, increased bladder functional capacity, higher maximum urine flow rates, and increased volume at first urge to urinate. These values were closest to normal in Group III (TUR coagulation).

Conclusion:

Conservative therapy is indicated for first-stage bladder leukoplakia; surgical treatment (TUR or transurethral coagulation) is indicated for second- and third-stage leukoplakia.

The optimal surgical method is transurethral coagulation due to faster recovery of transitional epithelium and quicker restoration of normal urination.

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