

## A RANDOMIZED CONTROLLED TRIAL OF BACILLUS CALMETTE-GUERIN AND BOTULINUM TOXIN-A FOR THE TREATMENT OF REFRACTORY INTERSTITIAL CYSTITIS

### Hypothesis / aims of study

Bacillus Calmette-Guerin (BCG) has been used for more than 20 years for treatment of superficial bladder carcinoma. It is proposed to exert its tumor prophylaxis by modulating the immune system (1). Hence, several researchers had evaluated the efficacy of intra-vesical BCG instillation in the treatment of IC with promising results (2). Botulinum Toxin (a presynaptic neuro-muscular blocking agent) has gained widespread acceptance for treatment of bladder overactivity, detrusor-sphincter dyssnergia and IC (3). The present work was designated to evaluate the use of intra-vesical BCG instillation, versus intra-vesical injection of Botulinum Toxin-A (BTX-A) in subjects with intractable IC.

### Study design, materials and methods

Thirty six patients who met the National Institute of Health-National Institute for Diabetes and Digestive and Kidney Diseases criteria for IC, and reported at least moderate pain and frequency for a minimum of six months, were randomly divided into two groups (cases:1,3,5.. & cases:2,4,6..). The first group (group I) received standard six weeks intra-vesical BCG instillations (2). The other subjects (group II) had received intra-vesical injection of 300 units of BTX-A (3). The patients were followed at routine intervals with questionnaires and voiding diaries. Adverse events were closely monitored in the treatment and follow up phases of the study.

### Results

During the follow up period, 23 and 22 weeks for both groups respectively, 11/16 (68.75%) and 14/16 (87.50%) continue to have an excellent response in all parameters measured. The global interstitial cystitis survey improved 71% & 92%, daily voids decreased 31% & 68%, nocturia improved 54% & 100%, pelvic pain decreased 81% & 96%, urgency decreased 71% & 100 % and dysuria decreased 82% & 92% in groups I & II respectively. Group II subjects showed statistically significant improvement compared to group I cases in all parameters.

### Interpretation of results

With about 2-year follow-up, 68.75% of BCG group cases and 87.50% of the BTX-A group subjects continue to experience a positive clinical response with no additional treatment for intractable interstitial cystitis. Overall well being improved 67 % and 84% with BCG and BTX-A responders during the follow up period respectively. Of the subjects who received BCG and did not respond, there was no worsening of the pre-treatment complaints. Furthermore, the minimal, self limited adverse effects reported with intra-vesical BTX-A injection, would not preclude its promising application in treatment of intractable IC.

### Concluding message

Although the safety profile of BCG was acceptable, the response rate for treatment of intractable IC was poorer in relation to BTX-A. On the other hand, though BTX has not yet been approved by the Food and Drug Administration, the intra-vesical injection of BTX-A, has proved, on clinical trials to be safe and effective therapy for treatment of intractable IC within 22 weeks follow up period.

### References

1. Clin. Exp. Immunol. 115:131 1999
2. J. Urol., 164:1912, 2000
3. Urol. Clin. N Am, 33:503, 2006

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**CLINICAL TRIAL REGISTRATION:** This clinical trial has not yet been registered in a public clinical trials registry.

**HUMAN SUBJECTS:** This study did not need ethical approval because Materials used in the present study are safely approved internationally for human application, as well as, its usage in painful bladder syndromes but followed the Declaration of Helsinki Informed consent was obtained from the patients.