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# COMPARISON OF INTRAVESICAL HYALURONIC ACID INSTILLATION WITH DIFFERENT REGIMENS FOR INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME

Hypothesis / aims of study

Preliminary studies using intravesical hyaluronic acid instillation have been demonstrated to have benefit in the treatment of interstitial

cystitis/painful bladder syndrome (IC/PBS). A loading dose of four weekly instillation of 50ml (40 mg) hyaluronic acid followed by 5 monthly maintaining doses has been suggested. However, the optimal regimen has not been defined yet. Patients might feel improved during the first month, but gradually failed in the maintenance period. The aim of this study was to compare the clinical effectiveness of intravesical hyaluronic acid instillations with different regimens in patients with IC/PBS.

Study design, materials and methods

In this prospective, randomized, parallel study, 60 patients (age 16-77 years) who were diagnosed to have IC/PBS, were identified. All patients had undergone urine analysis, videourodynamic study, potassium chloride (KCL) test and cystoscopic hydrodistention with biopsy. The final diagnosis of IC/PBS was made based on cystoscopic findings of glomerulations and clinical symptoms. Thirty patients were assigned to receive intravesical instillation of 40 mg HA weekly in the first month and then monthly in the following 5 months (HA-9 group). Another 30 patients received intravesical instillation of 40 mg HA per 2 weeks for 24 weeks (HA-12 group). Symptom after HA treatments was assessed using Interstitial Cystitis Symptom and Problem Index (ICSI/ICPI), pain visual analog scale (VAS), functional bladder capacity(FBC), frequency, noturia, maximum flow rate (Qmax), voided volume, postvoid residual volume (PVR), and quality of life index(QoL-I) at 1,3 and 6 months. Efficacy analysis compared responders (moderately or markedly improved) according to the global response assessment (GRA) at 1,3 and 6 months, relative to overall baseline symptoms.

Results

All 60 patients were evaluable at 6 months. The ICSI/ICPI total score and QoL-I were significantly improved at 6 months in both groups (Table 1). The VAS, FBC and ICSI, ICPI score, however, were significantly improved only in HA-12 group (Table 2). Endpoint analysis at month 1, 3 and 6 revealed with moderately and markedly improved was similar in both groups. The measured variables all showed no significant change from baseline to 6 months between two groups.

Interpretation of results

Intravesical hyaluronic acid instillation improved IC/PBS symptoms and improved quality of life. Treatment either with initial four weekly loading doses plus maintaining five monthly doses or regular treatment biweekly for 12 times provided similar results. However, patients in the HA-12 group had better improvement in pain and symptom after treatment although the difference in treatment effect in this study was not statistically significant between two regimens.

Concluding message

No significant difference was noted in therapeutic effect between two regimens of HA instillation for IC/PBS patients. Both groups showed significant improvement in symptom score and QoL index.

Table.1 The changes of variables from baseline to 6 months in HA-9 group.

| HA-9 | Baseline | 1M | 3M | 6M | P value |
|---|---|---|---|---|---|
| **ICSI+ICPI** | 15.86±7.59 | 12.17±7.27 | 11.19±6.96 | 11.13±7.50 | 0.041 |
| **ICSI** | 8.27±3.37 | 6.89±3.17 | 6.80±3.28 | 6.69±3.52 | 0.067 |
| **ICPI** | 7.58±4.53 | 5.27±4.33 | 4.53±3.76 | 4.44±4.10 | 0.056 |
| **VAS** | 3.27±2.48 | 1.93±2.14 | 2.04±2.60 | 1.94±2.14 | 0.147 |
| **FBC** | 181.0±96.7 | 216.2±105. | 223.3±133.2 | 219.36±135.8 | 0.366 |
| **Frequency** | 10.13±4.23 | 9.44±4.66 | 9.90±4.83 | 10.19±4.49 | 0.852 |
| **Nocturia** | 2.24±1.64 | 2.07±1.36 | 2.29±1.38 | 2.31±1.49 | 0.188 |
| **Qmax** | 16.10±9.72 | 18.56±9.34 | 15.81±10.0 | 20.18±12.53 | 0.259 |
| **Volume** | 222.6±128.5 | 241.±151.9 | 214.6±179.4 | 278.1±200.1 | 0.268 |
| **PVR** | 35.17±56.27 | 36.89±54.9 | 41.77±52.8 | 22.80±21.0 | 0.424 |
| **QoL** | 3.20±1.18 | 2.24±0.83 | 2.29±0.90 | 2.44±1.03 | 0.010 |

Table 2. The changes of variables from baseline to 6 months in HA-12 group.

| HA-12 | Baseline | 1M | 3M | 6M | P value |
|---|---|---|---|---|---|
| **ICSI+ICPI** | 15.40±7.39 | 13.77±6.16 | 12.80±7.07 | 11.69±6.84 | 0.000 |
| **ICSI** | 8.10±3.37 | 7.40±2.97 | 6.95±3.33 | 6.54±3.07 | 0.001 |
| **ICPI** | 7.30±4.18 | 6.37±3.41 | 5.85±3.86 | 5.15±3.87 | 0.000 |
| **VAS** | 3.30±2.38 | 2.53±1.83 | 2.45±2.28 | 2.33±2.06 | 0.002 |
| **FBC** | 161.7±83.4 | 183.33±73.0 | 232.0±113.4 | 226.9±123.5 | 0.001 |
| **Frequency** | 10.47±5.25 | 9.13±2.85 | 9.10±3.34 | 7.92±2.06 | 0.060 |
| **Nocturia** | 2.87±1.63 | 2.63±1.56 | 2.65±1.63 | 2.31±1.18 | 0.157 |
| **Qmax** | 13.47±7.66 | 14.28±8.20 | 18.99±9.27 | 19.58±7.61 | 0.145 |
| **Volume** | 202.5±141.3 | 208.3±105.4 | 293.2±188.6 | 268.5±143.8 | 0.114 |
| **PVR** | 47.67±54.84 | 22.63±21.72 | 29.45±38.52 | 32.39±39.69 | 0.508 |
| **QoL** | 3.20±1.21 | 2.40±0.72 | 2.25±0.78 | 2.15±0.98 | 0.000 |


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|---|---|
| ***Specify source of funding or grant*** | **None** |
| ***Is this a clinical trial?*** | **No** |
| ***What were the subjects in the study?*** | **HUMAN** |
| ***Was this study approved by an ethics committee?*** | **Yes** |
| ***Specify Name of Ethics Committee*** | **Research Ethics Committee of Buddhist Tzu Chi General Hospital** |
| ***Was the Declaration of Helsinki followed?*** | **Yes** |
| ***Was informed consent obtained from the patients?*** | **Yes** |