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Title (type in CAPITAL LETTERS, leave one blank line before the text): HIGH FREQUENCY NEUROMODULATION FOR THE TREATMENT OF INTERSTITIAL CYSTITYS: LONG TERM FOLLOW UP .

AIMS OF THE STUDY

Sacral root neuromodulation has an established role for the treatment of lower urinary tract dysfunction as urge incontinence, urgency frequency sindrome and urinary retention. Several authors have reported their experience about the treatment of interstitial cystitis using conventional parameters of stimulation with poor outcome at long term follow up. Aim of this paper is to report our experience with high frequency neuromodulation for interstitial cystitis (IC) .

## METHODS

Two patients who failed to respond conventional therapy for IC underwent a permanent implant of S3 foramen after a successful PNE test with conventional parameters ( 210  $\mu$ sec , 10 Hz ) . Within a few months both failed to respond to neuromodulation with relapse of symptoms and dramatic worsening in quality of life .

After unsuccessful trials to change parameters of stimulation we started with high frequency neuromodulation , although it's considered unsafe for peripheral nerves in animal models . Before starting the new course we obtained an informed consent from the patients , explaining them the potential risks deriving from this trial.

## RESULTS

Within a couple months both patients experienced a complete recovery , with normal bladder capacity , no pain and significative improvement in quality of life . Neurophysiologic studies demonstrated no damage in peripheric nerves and at 24 months follow up the improvement is stable and patients are very satisfied .

## CONCLUSION

Neuromodulation is effective to treat various voiding dysfunction and pelvic pain but the underlying mechanism of action is not known . Spinal c-fos gene is devoid of basal expression , being only activated when the sensory cells are exposed to noxious input mainly conveyed by afferent C - fibers . Pain and nociceptive sensation are mediated via C fiber and A $\delta$  fibers and the majority in fibers in a peripheral nerve are C fibers . Recently Shaker and Wang ( J.Urol , 161, Abstract 1061 & 1065, 1999 ) demonstrated as sacral root neuromodulation reduces c-fos gene expression in spinalized rats . It indicates that blockage of C afferent fibers is one of mechanism of neuromodulation . High frequency neuromodulation appears to be safe for peripheral nerves and probably works blocking C fibers like Transcutaneous Nerve Stimulation Therapy (TENS), but in a more selective and continuous way.

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