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# CORRELATION OF GAP JUNCTIONAL PROTEIN EXPRESSION (CONNEXIN 43) AND ULTRASTRUCTURAL FEATURES IN THE UNSTABLE HUMAN DETRUSOR

## Aims of Study

Recent ultrastructural studies by Tse et.al[1] have demonstrated a relative abundance of ultraclose junctions compared with normal intercellular junctions in the detrusor muscle of patients with detrusor instability and sensory urgency. It is postulated that these may represent gap junctions capable of rapid electrical intercellular conduction and may allow any spontaneous trigger activity to spread and cause an involuntary detrusor contraction. Hampel et.al have demonstrated increased expression of Connexin-43, (the most common isoform of gap junctional proteins) in the obstructed rat bladder.[2] We were unable to confirm this in our preliminary study in patients with detrusor instability. [3] To further investigate the nature of these abnormal junctions, quantitative reverse transcriptase – polymerase chain reaction (RT-PCR) was carried out in human detrusor biopsy specimens to identify Connexin-43 expression and to correlate with findings on ultrastructural study.

## Methods

Detrusor muscle biopsies were obtained from 12 patients. 10 of these had urodynamically proven detrusor instability and 2 controls. Expression of Connexin 43 gene was measured by quantitative real time RT-PCR method with fluorogenic probes. Connexin 43 mRNA copies are normalized to 1000 copies of G3PDH (housing keeping gene) in each patient. The specimens were also examined by electron microscopy according to our previous protocol[1] to identify abnormal intercellular junctions.

## Results

Connexin-43 expression was found in all of the detrusor muscle samples. The level of connexin-43 expression was higher in patients with detrusor instability as compared to controls. Abnormal intercellular junctions were identified on ultrastructural study (electron microscopy) in both controls and patients with detrusor instability. However the mean ratio of abnormal to normal junctions was 5:1 in patients with detrusor instability and only 1:1 in controls.

## Conclusions

This study showed an increased level of connexin-43 expression in patients with urodynamically proven detrusor instability which correlates with the higher ratio of abnormal to normal intercellular junctions observed on ultrastructural study. The findings suggest that gap-junctional proteins may be involved in the pathogenesis of detrusor instability.

## References

1 Tse, V., Wills, E., Szonyi, G., Khadra, M.H. (2000) "The application of ultrastructural studies in the diagnosis of bladder dysfunction in a clinical setting", Journal of Urology 163 (2): 535-539.

2 Hampel C. Dolber P.C.. Bremer R.E. Schwinn D. A. Thűroff J.W. and Thor K.B. (2000) Increased expression of gap junctions (connexin 43) in rat bladder outlet obstruction. Journal of Urology “AUA Conference Proceedings, Atlanta Georgia USA” Abstract 215

3 McLachlan C, Tse V, Jusuf P, Wills E, Chan L (2001) “The role of gap junctional proteins (connexin 43) in the pathogenesis of detrusor instability” Abstract 32, Second World Health Organisation International Consultation on Incontinence, Paris July 2001