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PURINOCEPTOR EXPRESSION IN DETRUSOR INSTABILITY

Aims of study

The role of the purinoceptors in mammalian bladder has been previously investigated. ATP is known to act as a co-transmitter in functional experiments of the human pathological bladder. The aetiology of Idiopathic Detrusor instability (D.I.)is still unknown but recent work has shown the presence of significant atropine-resistance in the unstable bladder. We used a Novel RT-PCR technique to quantify the expression levels of the 7 P2X receptor subtypes in human bladder in oreder to perform a comparison between stable and unstable bladders.

Methods

TaqMan RT-PCR provides a system for the detection and analysis of gene expression. Female patients with Detrusor Instability (n=20) were recruited for cystoscopy and bladder biopsy with ethical approval. Control tissue was obtained from patients with stable bladders. Total RNA was extracted from each sample and 10ng of this used for individual PCR reactions. An ABI 7700 machine determined expression levels of the seven P2X genes/ng of total RNA.
Comparison of gene expression was performed between the DI bladder and control tissue. Since P2X1 is known to be smooth muscle specific, the smooth muscle protein, calponin, was used as a normalisation gene.

Results

In both sets of bladder, P2X1 was by far the predominant purinergic receptor at the RNA level, the remainder consistently present in the order P2X1>>P2X4>P2X7>>P2X5>P2X2>>P2X3=P2X6=0. The ratio P2X1/Calponin was used as a comparison of amount of P2X1 receptor per smooth muscle cell in the two types of bladder.
In the DI bladder P2X1 was reduced but the ratio was increased. P2X2 expression was also increased in the DI bladder whilst P2X4, P2X5 and P2X7 expression was reduced in the DI tissue compared with the control tissue.

Conclusion

P2X1 is the predominant receptor subtype in the adult human bladder. The P2X1/Calponin ratio is increased in DI tissue compared with control tissue indicating an up-regulation of P2X1 receptor per smooth muscle cell in the unstable bladder. This, along with functional studies presented in our other abstract, would indicate the possibility of a new target for the pharmacological manipulation of the unstable bladder.