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URINARY TRACT OBSTRUCTION

NLRP3 inhibition prevents BOO

Bladder outlet obstruction (BOO) in humans can result in inflammation, which is often followed by long-term alterations in bladder function that can lead to overactive bladder or fibrosis. Now, newly published research in rat models of BOO reveals that the NLRP3 inflammosome, which has been suggested to act as a transducer of cellular damage, is central to this process of inflammation.

Female BOO rats received either the NLRP3 inhibitor glyburide (10 mg/kg) or placebo for 12 days following outlet obstruction. BOO rats had significant increases in caspase-1 activity, bladder weight, Evan's blue extravasation, void pressure, duration of contractions and duration of voiding combined with significant decreases in volume voided, intercontraction intervals and flow rates compared with unobstructed, or sham-operated animals. BOO rats that received glyburide had similar levels of caspase-1 activity, extravasation, voided volume and intercontraction intervals to those of unobstructed or sham-operated animals and also had significant decreases in bladder weight and void pressure compared with BOO rats, indicating that many of the inflammation-induced effects of experimentally induced BOO are attenuated by NLRP3 inhibition; however, flow rates were similarly low compared with those of BOO control animals. Glyburide treatment also resulted in significant increases in both contraction and void duration compared with control animals, reflecting a normal voided volume in the presence of a reduced flow rate and demonstrating that NLRP3 inhibition cannot attenuate the primary effects of BOO.

The finding that BOO induces inflammation confirm a previously held general consensus on this relationship. These data also provide evidence that the NLRP3 inflammosome has an important role in bladder inflammation experienced after BOO. Findings of this research indicate that the NLRP3 inflammosome might be an important therapeutic target in patients with BOO.

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ORIGINAL ARTICLE Hughes, F. M. *et al.* The NLRP3 inflammasome mediates inflammation produced by bladder outlet obstruction. *J. Urol.* http://dx.doi.org/10.1016/j.juro.2015.12.068 (2015)