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Resumo	Lipopolysaccharide (LPS) is a component of gram-negative bacteria wall that elicits inflammatory response in the host through the toll-like receptor 4 (TLR4) activation. In the lower urinary tract (LUT), bacteria-derived LPS has been associated with lower urinary tract symptoms (LUTS); however, little is known about the effects of LPS in the urethral smooth muscle (USM). In the present study, we evaluated the functional and molecular effects of LPS in mouse USM in vitro, focusing on the LPS-induced TLR4-signaling pathway. Male C57BL6/JUnib and TLR4 knockout mice (TLR4 KO) were used. The USM contraction was performed in the presence of LPS (62.5-500 µg/mL), indomethacin (10 µM), L-NAME (100 µM), and TAK 242 (1 µM). The RT-PCR assay for the IL-1β, NF-kB, and COX-2 genes was also evaluated in the presence of LPS (125 µg/mL) and caspase 1 inhibitor (20 µM). Our results showed that LPS reduces mouse USM contraction elicited by phenylephrine and vasopressin. This LPS-induced urethral inhibitory effect was not reversed by the TLR4 inhibition or its absence in the TLR4 KO mice. Conversely, indomethacin (but not L-NAME) reversed the LPS-induced USM hypocontractility. Molecular protocols indicated upregulation of IL-1β, NF-kβ, and COX-2 mRNA upon LPS incubation, which were blunted by caspase 1 inhibition. Our data showed that LPS reduced mouse USM contraction independently of TLR4 activation, involving caspase 1 and IL1β, NF-kB, and COX-2 gene overexpression. Therefore, this alternative pathway might be a valuable target to reduce the LPS-induced urethral dysfunction under infection and inflammatory conditions.
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