NLRP3 inflammasome involvement in the organ damage and impaired spermatogenesis induced by testicular ischemia and reperfusion in mice

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We investigated the role of NLRP3 inflammasome during testis ischemia and reperfusion injury (TI/R) in wild type (WT) and NLRP3 knock-out (KO) mice. WT and KO mice underwent 1 hour testicular-ischemia followed by 4 hours, 1 and 7 days of reperfusion or a sham TI/R. Furthermore, two groups of WT mice were treated, at the beginning of reperfusion and up to 7 days, with two inflammasome inhibitors, BAY 117082 (20mg/kgi.p.),or Brilliant Blue G (BBG; 45.5mg/kg i.p.) or vehicle .Animals were euthanized with a pentobarbital sodium overdose at 4hours, 1 and 7days and bilateral orchidectomies were performed. IL-1ß and IL-18 mRNA, caspase-1 and-3 expression,TUNEL assay evaluation and a histological examination of spermatogenesis were carried out in all groups. TI/R in WT mice increased caspase-1 and IL-1ß mRNA after 4 hours, and IL-18 mRNA at 1 day of reperfusion; there was also an increase in caspase-3 and in TUNEL-positive cells, a marked histological damage, and an altered spermatogenesis in WT mice in both testes after 1 and 7 days of reperfusion. KO TI/R mice, WT TI/R BAY 11-7082 and BBG treated mice showed reduced IL-1ß and IL-18 mRNA expression, blunted caspase-1 and -3 expression, minor histological damages, low TUNEL activity and preserved spermatogenesis. These data suggest that the activation of NLRP3 plays a key role in TI/R and its inhibition might represent a therapeutic target for the management of patients with unilateral testicular torsion.