

Polydeoxyribonucleotide, an adenosine-A2A receptor agonist, preserves blood testis barrier from cadmium-induced injury

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Cadmium (Cd) impairs the blood-testis barrier (BTB) with changes of its junctional complexes [1]. Polydeoxyribonucleotide (PDRN), an adenosine A2A agonist, has positive effects on male reproductive system [2]. We investigated the effects of PDRN on the morphological and functional Cd-induced changes in mice testes. Swiss mice were divided into four groups: control animals treated with 0.9% NaCl (1 ml/kg, i.p., daily); control animals treated with PDRN (8 mg/kg, i.p. daily), animals challenged with Cd chloride (CdCl₂) (2 mg/kg i.p, daily) and animals challenged with CdCl₂ and treated with PDRN. The experiments lasted 14 days. At the end of experiment, the testes were processed for biochemical, structural and ultrastructural evaluation. CdCl₂ increased pERK 1/2 expression and Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) levels, decreased testosterone (TE) and inhibin-B levels and induced structural damages in the extratubular compartment and in the seminiferous epithelium, with ultrastructural features of BTB disruption. Many TUNEL-positive germ cells were present in the peripheral parts of the tubules. CdCl₂ increased also tubular TGF-β₃ immunoreactivity and reduced claudin-11, occludin and N-cadherin immunoreactivity. PDRN administration reduced pERK 1/2 expression, FSH and LH levels, increased TE and inhibin-B levels, ameliorated germinal epithelium changes and protected BTB ultrastructure. Only few TUNEL-positive germ cells were present and the extratubular compartment was preserved, showing only a mild edema. Furthermore PDRN decreased TGF-β₃ immunoreactivity and enhanced claudin-11, occludin and N-cadherin immunoreactivity. We demonstrate, for the first time, a protective effect of PDRN on Cd-induced BTB damages in mice testes. We suggest that the A2A agonist may play an important role against environmental Cd, and in particular against its harmful effects on gametogenesis.

References

- [1] Minutoli et al. (2015) Flavocoxid protects against cadmium-induced disruption of the blood-testis barrier and improves testicular damage and germ cell impairment in mice. *Toxicol Sci* 148:311-329.
- [2] Minutoli et al. (2012) Effects of polydeoxyribonucleotide on the histological damage and the altered spermatogenesis induced by testicular ischaemia and reperfusion in rats. *Int J Androl* 35:133-144.

Keywords

Cadmium; PDRN; blood-testis barrier; pERK 1/2; TGF-β₃; immunohistochemistry; transmission electron microscopy.