Atrazine affects tissue homeostasis of the testis and efferent ductules of the adult rats exposed by long-term.

Elisângela Martins dos Santos[1]; Cleida Aparecida Oliveira[1]

[1]Department of Morphology, Universidade Federal de Minas Gerais, Cx. Postal 486, CEP 31.270-901, Belo Horizonte, MG – Brazil

Atrazine is an endocrine disruptor, affecting the reproductive system across vertebrates. Reproductive problems promoted by atrazine include testicular atrophy parallel to reduction of testosterone and increase in estradiol levels, besides reduction in 3-beta-hydroxysteroid dehydrogenase (3β-HSD), a key enzyme in testicular steroidogenesis. However, it remains unknown whether these testicular effects are reversible or permanent. Moreover, it is not known whether the effects of atrazine on the testes are primary or due to dysfunction in the efferent ductules, a major target for environmental endocrine disruptors. Therefore, the present study aimed to investigate whether the long-term effects of atrazine on testicular structure and 3β-HSD expression are reversible or permanent, as well as to determine the effects of atrazine on expression of aromatase, a key enzyme in estradiol biosynthesis, and on the efferent ductules morphophysiology. For this purpose, male adult Wistar rats were treated with 200mg/kg of atrazine for 7, 15 and 40 days, as well as 40-day treatment followed by recover for 75 days. Our results showed early reduction of 3β-HSD and later induction of aromatase expression in the rat testes. The testicular atrophy and reduction in 3β-HSD were more pronounced after the recovery period, thus suggesting prolonged and irreversible effects. After the recovery period, it called the attention the presence of macrophage-like cells positive for 3β-HSD in the testis. The identity of these cells was confirmed by using specific markers for induced (ED1/CD68) and resident (ED2/CD163) macrophages. There was a remarkable increase of 89%, 76% and 42% in resident $ED1^{-}/ED2^{+}$, transitory $ED1^{+}/ED2^{+}$ and induced $ED1^{+}/ED2^{-}$ sub-populations of macrophages, respectively. These macrophages were positive for 3β-HSD, thereby raising possibility for their involvement in local steroidogenesis. Moreover, exposure to atrazine caused changes in the efferent ductules, including increase on luminal diameter, reduction in epithelial height, as well as increase on aromatase expression, cell proliferation and apoptosis. These results reveal disorders on morphophysiology of the efferent ductules after atrazine exposure, suggesting that testicular changes caused by atrazine may indeed be secondary to dysfunctions in efferent ductules. Altogether, our findings further emphasize the adverse effects of atrazine as an endocrine disrupter on the male reproductive system and physiology, revealing the testis and efferent ductules as important target for the herbicide action.

Key words: Atrazine, Testes, Efferent Ductules, Steroidogenesis, Macrophages

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