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ORIGINAL

Effects of cypermethrin on cytokeratin 8/18 and androgen receptor expression in the adult mouse Sertoli cell

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KEYWORDS
Cypermethrin;
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Abstract
Background: With the explosive population growth an increased use of land for cultivation purposes and the usage of biotechnologies in agriculture—such as pesticides—respond to the need for more efficient systems. However, improper application of pesticides has a negative effect on the environment, on exposed animals and on humans. Cypermethrin, a synthetic pyrethroid, is an insecticide with low risk to human and animal health and with broad insecticidal activity against a large number of pests. Studies in humans and animals show morphological and functional alterations in different organs exposed to cypermethrin. Pyrethroids are chemicals with structural similarity to pyrethrins and possess increased toxicity to insects over mammals.
Objective: This research analyzes the variations of the state of differentiation of Sertoli cells and androgen receptor expression in testes of healthy adult mice exposed to cypermethrin.
Material and method: Mice were divided into three groups: control 1 (untreated), control 2 (inoculated intraperitoneally with 0.1 ml of vegetable oil), and the experimental group 3 (inoculated with 1/5 of the lethal dose 50 (LD_{50} = 485 mg/kg) of cypermethrin).
Results: Cypermethrin exerts acute and chronic effects on Sertoli cells in the testis of the adult mouse. These effects are manifested by the significant increase in epithelial height and the dedifferentiation of Sertoli cells evidenced through the presence of the Ck 8/18-type intermediate filament—a characteristic of differentiating cells—especially considering the functional cyclicity of the testicular compartment.

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Conclusions: Cypermethrin significantly affects the structure and function of Sertoli cells through the cytoskeleton and the state of maturation.

PALABRAS CLAVE
Cipermetrina;
Citoqueratina 8/18;
Receptor de andrógeno;
Célula de Sertoli;
Espermatogenesis

Efectos de cipermetrina sobre la expresión de citoqueratinas 8/18 y el receptor de andrógenos en la célula de sertoli del ratón adulto

Resumen
Antecedentes: Con el crecimiento explosivo de la población, un mayor uso de la tierra con fines de cultivo y el uso de las biotecnologías en la agricultura—como pesticidas—responden a la necesidad de sistemas más eficientes. Sin embargo, la aplicación inadecuada de pesticidas tiene un efecto negativo sobre el medio ambiente, en los animales expuestos y en los seres humanos. La cipermetrina, un piretroide sintético, es un insecticida de bajo riesgo para la salud humana y animal, y con una amplia actividad insecticida frente a un gran número de plagas. Los estudios en seres humanos y animales muestran alteraciones morfológicas y funcionales en diferentes órganos expuestos a la cipermetrina. Los piretroides son sustancias químicas con estructura muy similar a las piretrinas, a menudo más tóxicas para insectos que para mamíferos.
Objetivo: La presente investigación analiza las variaciones del estado de diferenciación de las células de Sertoli y de la expresión del receptor de andrógeno en testículos de ratones adultos sanos expuestos experimentalmente a cipermetrina.
Material y método: Los animales fueron distribuidos en 3 grupos: control 1 (n= 3) sin tratamiento, control 2 (n = 15) inoculados con 0,1 ml de aceite vegetal vía intraperitoneal, y el grupo 3 y experimental (n = 15) inoculados con 1/5 de la dosis letal 50 (LD_{50}= 485 mg/kg) de cipermetrina.
Resultados: Se observó que la cipermetrina tiene efectos agudos y crónicos sobre las células de Sertoli en el testículo de ratón adulto. Estos efectos se demuestran por el aumento significativo de la altura epitelial, como también por una desdiferenciación de las células de Sertoli a través de la presencia de los filamentos intermedios tipo CK8/18, característico de células en diferenciación, más aun considerando la ciclicidad funcional del compartimiento testicular.
Conclusiones: La cipermetrina afecta significativamente a la estructura y la funcionalidad de las células de Sertoli, a través del citoesqueleto y el estado de maduración.

Introduction

Exposure to pesticides can have acute, chronic and long-term effects on people, animals and the environment.[1] Cypermethrin is a type II pyrethroid widely used in the management of livestock and the production of primary agricultural products (cotton, cereals, vegetables and fruits), as well as a controlling agent for vectors of infectious diseases in public health.[2] Research in animal models show that pyrethroids exert a significant adverse impact on organs and systems such as liver, brain, immune and reproductive systems.[3–6]

In the reproductive system of mice, cypermethrin decreases fertility, reduces the number of implantation sites and viable fetuses in females crossed with males previously exposed to cypermethrin,[7] while in males cypermethrin significantly reduces testosterone levels by inhibiting testicular steroidogenesis, thus deteriorating the normal spermatogenesis.[8]

Sertoli cells (SCs) are the supporting and nourishing cells for male germ cells.[9] Changes in their general and nuclear morphology might be associated with absent or weak expression of the androgen receptor (AR) during puberty.[10] Testes with total absence of AR expression show alterations in their development and function. The lack of androgen receptors in Sertoli cells affects the production and secretion of testosterone in Leydig cells, as well as the normal spermatogenesis.[11,12]

The number of SCs determines the size of the adult testis and daily sperm production; this relationship is established because each Sertoli cell sets the number of germ cells that it can sustain. The variation of these parameters provides a clear correlation with the number of functional somatic cells.[9]

Once the individual reaches reproductive maturity, SCs experience a radical change in their morphology and function: from an immature proliferative (fetal) state to a non-proliferative mature (adult) state. In laboratory

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