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ORIGINAL

Effect of anakinra, an interleukin one beta antagonist, on oxidative testicular damage induced in rats with ischemia reperfusion

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KEYWORDS

Anakinra;
Ischemia/reperfusion;
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Abstract

Background: It has been reported in the literature that proinflammatory interleukin-1 beta (IL-1 β) is increased in cases of testicular ischemia reperfusion (I/R) damage. This information suggests that anakinra, an IL-1 β antagonist, may be effective in testicular I/R damage.

Objective: In our study, we investigated the effect of anakinra on testicular I/R damage induced in rats with torsion/detorsion.

Methods: The 50 mg/kg anakinra + testicular torsion/detorsion (KTD-50) and 100 mg/kg anakinra + testicular torsion/detorsion (KTD-100) groups received an intraperitoneal (i.p.) injection of 50 mg/kg and 100 mg/kg of anakinra, respectively. In turn, the testicular torsion/detorsion (TTD) and sham operation (SOG) groups received a single dose of distilled water as a solvent 1 h before ketamine anaesthesia. After the testes of the TTD, KTD-50 and KTD-100 groups were subjected to torsion and detorsion for 4 h each, the rats were killed with a high-dose anaesthesia, and their testicles were removed and evaluated through biochemical, gene expression and histopathological examinations. The results were evaluated in comparison with those of the SOG group.

Results: The levels of malondialdehyde (MDA), myeloperoxidase (MPO) and IL-1 β showed significant increases in the TTD group, which underwent torsion/detorsion, compared to the KTD-50, KTD-100 and SOG groups. Conversely, the levels of glutathione (tGSH), glutathione peroxidase (GPO) and glutathione s-transferase (GST) were found to be significantly higher in the KTD-50, KTD-100 and SOG groups than in the TTD group.

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PALABRAS CLAVE

Anakinra;
Isquemia/reperfusión;
Testis daños;
Interleucina-1 β ;
Rata

Conclusion: Anakinra at a 100 mg/kg dose histologically suppressed better oxidative stress and tunica albuginea, germ cell, seminiferous tubule and interstitial damage in the testicular tissue compared to a 50 mg/kg dose. Experimental results indicate that anakinra might be beneficial in the attenuation of testicular I/R damage.

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Efecto de la anakinra, que es un antagonista de la interleucina 1 beta en oxidativo daño testicular, inducida en ratas con isquemia reperfusión

Resumen

Antecedentes: Se ha reportado en la literatura que citoquinas interleucina-1 beta (IL-1 β) es mayor en el daño de la isquemia reperfusión testicular (I/R). Esta información sugiere que la anakinra, que es un antagonista IL-1 β puede ser eficaz en daño testicular I/R.

Objetivo: En nuestro estudio se investigó el efecto de este medicamento en daño testicular I/R inducida en ratas con detorsion/torsión.

Métodos: KTD-50 grupo recibido intraperitonealmente (i.p.) inyección de 50 mg/kg y KTD-100 Grupo 100 mg/kg de anakinra, mientras TTD (control) y SOG (sham grupo operación) recibieron una dosis única de agua destilada como solvente, una hora antes de ketamina anestesia. Después de que los testículos de TTD, KTD-50 y KTD-100 grupos fueron sometidas a torsión y detorsion para cuatro por cuatro horas, las ratas fueron asesinados con altas dosis de anestesia, sus testículos fueron extraídos y evaluados a través de la expresión génica, bioquímicas e histopatológicas de exámenes. Los resultados fueron evaluado en comparación con la de SCG grupo.

Resultados: Los niveles de MDA, MPO y IL-1 β mostraron incrementos significativos en el grupo TTD/torsión detorsion administrados frente a-50, KTD KTD-100 y SOG grupos. Por el contrario, los niveles de tGSH, GPO y GST resultaron significativamente más altas en KTD-50 KTD-100 y grupos SOG de TTD en grupo.

Conclusion: La anakinra en 100 mg/kg dosis mejor histológicamente suprime el estrés oxidativo y la túnica albuginea, células germinales, túbulos seminíferos apretadamente enrollados intersticial y daño en el tejido testicular en comparación con la dosis de 50 mg/kg. Los resultados experimentales indican que la anakinra puede ser beneficiosa en la atenuación de los daños I/R testicular.

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Introduction

Testicular ischemia reperfusion (I/R) damage occurs as a result of the detorsion of torsioned testes. Despite early surgical intervention to recover the ischemic testicle, only 32% of testicles can be recovered successfully.¹ This is because while testicular torsion leads to ischemic damage, detorsion results in reperfusion damage.² Studies have shown that the damage detected in testicular biopsies following reperfusion is more severe than the damage in biopsies following ischemia alone.³ Despite the fact that even a single healthy testicle does not pose a problem for fertility, unilateral testicular torsion leads to infertility in 25% of cases, and the testicular damage, which may be seen at any age, increases as the degree and duration of the torsion increase.⁴ Free oxygen radicals are blamed for this I/R damage in the tissues.⁵ On the other hand, proinflammatory cytokines, such as interleukin one beta (IL-1 β), are reported to increase following testicular I/R damage.⁶ Recent studies proposed

that I/R damage is a complex pathological process beginning with the tissues becoming deprived of oxygen, progressing to a change in the oxidant/antioxidant balance in favor of oxidants and expanding with the inflammatory response.⁷ Therefore, it is thought that drugs showing antioxidant and anti-inflammatory impacts that antagonise especially the effect of IL-1 β might be beneficial in testicular I/R damage. Anakinra will be investigated in the present study to determine whether it has a protective effect against testicular I/R damage. It is the first biological agent approved to block the proinflammatory effects of IL-1 β in patients with rheumatoid arthritis.⁸ Anakinra has been reported to improve inflammatory symptoms rapidly.⁹

Hasturk et al. reported that the amount of malondialdehyde (MDA), which is a product of lipid peroxidation, was increased and the activities of enzymatic antioxidants were decreased in spinal cord damage experimentally induced in animals; in addition, the authors stated that anakinra prevented the increase of MDA and decrease of enzymatic

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