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Effect of Thiamine Pyrophosphate on Oxidative Damage to the Oropharyngeal, Nasal and Cochlear Tissues Induced by Doxorubicin in Guinea Pigs

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SUMMARY*. Doxorubicin (DOX) inhibits the enzyme tyaminpyrophosphokinase (TPK). Hence the synthesis of thiamine pyrophosphate (TPP) which is the active metabolite of thiamine stops. This leads to oxidative damage. In the literature, no studies on the protective effect of TPP against doxorubicin-induced oropharyngeal, nose and cochlear oxidative damage were found. In this study was investigated whether DOX produces oxidative stress in the oropharyngeal, nose and cochlea of animals and it examines the protective effect of TPP against DOX toxicity on these tissues. Guinea pig experimental animals were divided into groups as the controls. One group was given DOX, another group was given TPP + doxorubicin (TDOX) and the final group was the healthy group (HG). The TDOX group (n = 6) received an intraperitoneal (ip) injection of 25 mg/kg TPP. The DOX (n = 6) and HG (n = 6) animals were given distilled water in the same way. TDOX and DOX animals were administered ip 5 mg/kg DOX one hour after the administration of TPP and distilled water once a day for seven days. At the end of this period, animals were sacrified with a high dose of anesthesia and the levels of malondialdehyde (MDA), myeloperoxidase (MPO), nitric oxide (NO), total glutathione (tGSH) and glutathione reductase (GSHRd) were determined in the removed oropharyngeal, nasal, and cochlear tissues. In addition, the TNF-α gene expression was measured. DOX was demonstrated to significantly increase the levels of MDA, MPO and NO and to reduce the levels of tGSH and GSHRd in the oropharyngeal, nasal and cochlear tissues of animals. TPP prevented the increase of the levels of MDA, MPO, NO and TNF-α with doxorubicin. TPP supressed the oxidative stress induced by DOXin the oropharyngeal, nasal and cochlear tissues. It can be suggested that TPP can be used against DOX toxicity

RESUMEN. Doxorubicina (DOX) inhibe la enzima tiaminopirofosfokinasa (TPK). Por lo tanto, la síntesis de tiamina pirofosfato (TPP), que es el metabolito activo de la tiamina, se detiene. Esto conduce a daño oxidativo. En la literatura no se encontraron estudios sobre el efecto protector de la TPP contra el daño oxidativo orofaríngeo, nasal y coclear inducido por doxorrubicina. En este estudio se investigó si DOX produce estrés oxidativo en la zona orofaríngea, la nariz y la cóclea de los animales y se examina el efecto protector de TPP contra la toxicidad de DOX en estos tejidos. Los animales experimentales (cobayos) fueron divididos en grupos como los controles. Un grupo recibió DOX, otro grupo recibió TPP + doxorrubicina (TDOX) y el grupo final fue el grupo sano (HG). El grupo TDOX (n = 6) recibió una inyección intraperitoneal (ip) de 25 mg/kg de TPP. Los animales DOX (n = 6) y HG (n = 6) recibieron agua destilada de la misma manera. A los animales de los gruposTDOX y DOX se les administraron ip 5 mg/kg de DOX una hora después de la administración de TPP y agua destilada una vez al día durante 7 días. Al final de este período, los animales fueron sacrificados y se determinaron los niveles de malondialdehído (MDA), mieloperoxidasa (MPO), óxido nítrico (NO), glutatión total (tGSH) y glutatión reductasa (GSHRd) en los tejidos orofaríngeos, nasales y cocleares. Además, se midió la expresión génica del TNF-α. Se demostró que DOX aumentaba significativamente los niveles de MDA, MPO y NO y redujo los niveles de tGSH y GSHRd en los tejidos orofaríngeo, nasal y coclear de los animales. TPP previno el aumento de los niveles de MDA, MPO, NO y TNF-α con doxorrubicina. TPP suprimió el estrés oxidativo inducido por DOX en los tejidos orofaríngeo, nasal y coclear. Se puede sugerir que TPP puede ser utilizado contra la toxicidad de DOX

KEY WORDS: cochlea, doxorubicin, oropharynx, oxidative stres, thiamine pyrophosphate.

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