



## The Effect of Thiamine Pyrophosphate and Tocilizumab Alone and in Combination upon Ethanol-Induced Peripheral Neuropathy and Neuropathic Pain in Rats

Bilge EKİNCİ<sup>1\*</sup>, Bahadır SULEYMAN<sup>2</sup>, Renad MAMMADOV<sup>2</sup>, Murat CANKAYA<sup>3</sup>, Gulce Naz YAZICI<sup>4</sup>, Zeynep SULEYMAN<sup>5</sup>, Cagatay Nusret DAL<sup>1</sup>, Emine Esra ERGUL<sup>1</sup>, Didem ONK<sup>6</sup> & Halis SULEYMAN<sup>2</sup>

<sup>1</sup> Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Erzincan Binali Yildirim University, 24030, Erzincan/Turkey

<sup>2</sup> Department of Pharmacology, Faculty of Medicine, Erzincan Binali Yildirim University, 24030, Erzincan/Turkey

<sup>3</sup> Department of Biology, Faculty of Arts and Sciences, Erzincan Binali Yildirim University, 24030, Erzincan/Turkey

<sup>4</sup> Department of Histology and Embryology, Faculty of Medicine, Erzincan Binali Yildirim University, 24030, Erzincan/Turkey

<sup>5</sup> Department of Nursing, Faculty of Health Sciences, Erzincan Binali Yildirim University, 24100, Erzincan/Turkey

<sup>6</sup> Department of Anesthesiology and Reanimation, Faculty of Medicine, Erzincan Binali Yildirim University, 24030, Erzincan/Turkey

**SUMMARY.** The aim of the study to determine the effects of thiamine pyrophosphate (TPP) and tocilizumab (TCZ) either alone or in combination on ethanol-induced neuropathic pain and peripheral neuropathy in rat nerve tissues, biochemically and histopathologically. Albino Wistar male rats were divided into five groups as the healthy (HG), ethanol alone (EtOH), TPP + ethanol (TPE), TCZ + ethanol (TCE), and TPP + TCZ + ethanol (TPTE) groups. TPE (n = 6), TCE (n = 6) and TPTE (n = 6) groups were injected with 20 mg/kg TPP, 8 mg/kg TCZ, and 20 mg/kg TPP+8 mg/kg TCZ intraperitoneally (respectively). Distilled water were given the HG (n = 6) and EtOH (n = 6) groups. One hour after the drugs and distilled water were administered, 35% ethanol was administered orally by lavage at a 5 g/kg dose to the TPE, TCE, TPTE, and EtOH groups. Paw pain thresholds of animals were measured using Basile Algesimeter. TPTE, which suppressed the decrease of the pain threshold with ethanol more significantly than TPP and TCZ. The best inhibitor of MDA increase and inhibit the reduction of tGSH by ethanol was listed as TPTE > TPE > TCZ. The potency of suppressing the increase in cytokine production with ethanol was listed as TPTE > TCE > TPE. In conclusion, the results indicate that TPP+TCZ may be more beneficial than TPP and TCZ alone in treating ethanol-related neuropathic pain.

**RESUMEN.** El objetivo del estudio es determinar los efectos bioquímicos e histopatológicos del pirofosfato de tiamina (TPP) y el tocilizumab (TCZ), ya sea solos o en combinación, sobre el dolor neuropático inducido por etanol y la neuropatía periférica en tejidos nerviosos de ratas. Las ratas macho albinas Wistar se dividieron en cinco grupos como los grupos sanos (HG), etanol solo (EtOH), TPP + etanol (TPE), TCZ + etanol (TCE) y TPP + TCZ + etanol (TPTE). A los grupos TPE (n = 6), TCE (n = 6) y TPTE (n = 6) se les inyectaron 20 mg/kg TPP, 8 mg/kg TCZ y 20 mg/kg TPP+8 mg/kg TCZ por vía intraperitoneal (respectivamente). Se administró agua destilada a los grupos HG (n = 6) y EtOH (n = 6). Una hora después de administrar los fármacos y el agua destilada, se administró etanol al 35% por vía oral mediante lavado a una dosis de 5 g/kg a los grupos TPE, TCE, TPTE y EtOH. Los umbrales de dolor en las patas de los animales se midieron usando Basile Algesimeter. TPTE, que suprimió la disminución del umbral del dolor con etanol más significativamente que TPP y TCZ. El mejor inhibidor del aumento de MDA e inhibir la reducción de tGSH por etanol fue catalogado como TPTE > TPE > TCZ. La potencia de suprimir el aumento de la producción de citoquinas con etanol se enumeró como TPTE > TCE > TPE. En conclusión, los resultados indican que TPP+TCZ puede ser más beneficioso que TPP y TCZ solos en el tratamiento del dolor neuropático relacionado con el etanol.

**KEY WORDS:** ethanol, neuropathic disease, peripheral neuropathy, thiamine pyrophosphate, tocilizumab, rat.

\* Author to whom correspondence should be addressed. E-mail: bilgeekinci48@gmail.com