

## Role of L-Arginine-NO pathway on Temporal and Gender Variation of Thiamine Analgesia

Gülçiçek Dagli, *Eda Aypar Mutlu*, Nurettin Abacıoğlu

Departmento Pharmacology, Faculty of Pharmacy, Gazi University 06330 Etiler Ankara, Turkey

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The aim of this study was to investigate the potential involvement of L-arginine-NO pathway on temporal and gender variation of thiamine analgesia on mouse parabenzoquinone (PBQ) writhing test.

Experiments were performed on mice of both sexes (Swiss-albino) synchronized to 12:12 light-dark (LD) (HALO at 07:00). PBQ writhing test was used at two different times of day (09:00 and 21:00). 15 minutes before PBQ (2.5 mg/kg i.p) administration animals were injected with saline (0.1 ml/10g), thiamine ( $ED_{50}=0.11$  mg/kg), morphine ( $ED_{50}=0.13$  mg/kg), L-NAME (75 mg/kg), L-arginine (2.0 mg/kg), thiamine+morphine, thiamine+L-NAME, thiamine+L-arginine, morphine+L-NAME, morphine+L-arginine, thiamine+morphine+L-NAME or thiamine+morphine+L-arginine subcutaneously.

After PBQ administration number of writhes were counted. Results were shown as normalized (arcsin transformation) % antinociception values. Parametric and nonparametric ANOVA was used for statistical analysis. Although there was no temporal and gender difference between thiamine groups, male groups of thiamine+L-NAME showed day-night variation. On 09:00-male group treated with L-NAME exhibited an enhanced antinociceptive response when compared with Thiamine+L-NAME combination. However, on 09:00-female group thiamine+L-arginine administration lead to a higher anti-nociceptive effect than thiamine. Results of this study indicate that L-arginine-NO pathway may have a role on day-night and gender variation of thiamine analgesia.