

The conclusion of this study is the provision of *alprazolam* might decrease the number of Leydig cells, spermatogenic cells and decrease the number of thick epithelium of the seminiferous tubules of mice *Mus musculus* model of chronic stress.

## ABSTRAK

### PENGARUH ALPRAZOLAM TERHADAP JUMLAH SEL LEYDIG, JUMLAH SEL SPERMATOGENIK DAN TEBAL EPITEL TUBULUS SEMINIFERUS MENCIT *Mus musculus* MODEL STRES KRONIS

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**Latar belakang:** Prevalensi stres di masyarakat Indonesia mengalami peningkatan dari tahun ke tahun. Penggunaan obat hipnotik menjadi pilihan terapi. Penyalahgunaan obat hipnotik jenis *benzodiazepine* dalam *alprazolam* diidentifikasi sebagai permasalahan utama jenis narkoba. Ketergantungan *benzodiazepine* dapat mempengaruhi sistem saraf pusat yaitu neurotransmitter dopamin dan serotonin. Paparan *benzodiazepine* dapat menimbulkan gangguan keseimbangan protein pro-apoptosis dan anti-apoptosis, dengan ditandai peningkatan protein pro-apoptosis serta menurunnya protein anti-apoptosis seperti dalam sel Leydig. Stimulasi stres oksidatif akan mengaktifkan jalur apoptosis intrinsik.

**Tujuan:** melihat penurunan jumlah sel Leydig, jumlah sel spermatogenik dan tebal epitel tubulus seminiferus pada mencit jantan setelah diberikan paparan stres dengan metode CUMS, kemudian diberi terapi pengobatan *anti anxiety* dosis maksimal dari *alprazolam* 4mg/kg/bb.

**Bahan dan cara:** Hewan coba mencit (*Mus musculus*) galur *Balb-c* dilakukan proses aklimatisasi lalu randomisasi sampel pada tiga kelompok, yaitu kelompok kontrol negatif (K0), mencit tidak diberikan perlakuan ataupun obat, kelompok kontrol positif (K1), mencit diberi stressor metode CUMS selama masa spermatogenesis, kelompok perlakuan (K2), mencit diberi stressor dan obat *alprazolam* dengan merk dagang *alphanax* dosis maksimal 4 mg/kg/bb yang diberi dengan cara sonde lambung. Pengukuran dilakukan setelah testis mencit dipotong melintang dan dilakukan proses HE (*Hematoxylin-Eosin*). Penghitungan dilakukan dibawah mikroskop cahaya (*Olympus BX 41*).

**Hasil:** Uji Statistik pada variabel sel Leydig menunjukkan ada beda antar kelompok menggunakan uji *kruskal wallis*  $p=0,000$  ( $p<0,05$ ). Uji statistik pada sel spermatogenik, uji beda antar kelompok menggunakan uji ANOVA  $p=0,000$  ( $p<0,05$ ). Penghitungan tebal epitel tubulus seminiferous dilakukan dengan menarik ujung epitel menuju lumen. uji beda antar kelompok menggunakan uji ANOVA,  $p=0,000$  ( $p<0,05$ ).

**Kesimpulan:** pemberian *alprazolam* dapat menurunkan jumlah sel Leydig, jumlah sel spermatogenik dan menurunkan tebal epitel tubulus seminiferus pada mencit *Mus musculus* model stres kronis

**Kata kunci:** CUMS, *alprazolam*, sel Leydig, sel spermatogenik, tubulus seminiferus

## ABSTRACT

### THE EFFECT OF *ALPRAZOLAM* TO NUMBER OF LEYDIG CELL, SPERMATOGENIC CELL AND THE THICKNESS OF EPITHELIAL TUBULUS SEMINIFEROUS IN MICE *Mus musculus* STRESS CHRONIC MODEL

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**Background :** Infertility in marriage life, is one of the stress stimulated. The prevalence of stress in Indonesian people was increased and they will choose hypnotic drugs. Misuse hypnotic drugs types of *benzodiazepine* in *alprazolam* as their primary drug problem. *Benzodiazepine* dependence can also affect the central nervous system that interfere with neurotransmitters dopamine and serotonin. Oxidative stress caused by exposure to *benzodiazepine* can cause interference pro-apoptotic protein balance and anti-apoptotic, with a marked increase in pro-apoptotic protein and a decrease in anti-apoptotic proteins such as in the Leydig cells. Oxidative stress stimulation activates the intrinsic apoptotic pathway

**Objective:** to see a decrease in the number of Leydig cells, spermatogenic cell number and thickness of seminiferous tubule epithelium of male mice after exposure to the stress with cums method, and the mice would be given anti-anxiety medication therapy was *alprazolam* with maximum dosage.

**Materials and methods:** The research subject using male mice (*Mus musculus*) strain *Balb-c* had acclimatization process and randomize sampling. There were divided into three groups consisting of negative control group (K0), without stress and drugs when spermatogenesis time is positive control group (K1) and treatment group (K2), the mice get a daily *alprazolam* drugs (alganax) by gavage sonde with maximum dosage 4mg/kg/weight. The measurement's do after obtained from the testis that has been cut crosswise and do the Hematoxylin-eosin (HE). Calculations carried out under a light microscope (*Olympus BX 41*).

**Results:** Statistical test in Leydig cell showed that there was significant difference with *kruskal walis*  $p=0,000$  ( $p<0,05$ ). Statistical test in spermatogenic cell showed that there was significant difference with ANOVA  $p=0,000$  ( $p<0,05$ ). The calculation of the seminiferous tubule epithelial thickness is done by pulling the end towards the luminal epithelium). Statistical test showed that there was significant difference with ANOVA  $p=0,000$  ( $p<0,05$ ).