INTISARI

PENGARUH PEMBERIAN KETAMIN DOSIS SUBANESTESI SESUDAH INDUKSI STRES BUATAN TERHADAP KOGNISI PADA TIKUS WISTAR

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Latar Belakang : Stres merupakan respon adaptif tubuh dalam menghadapi disrupsi atau gangguan. Respon tubuh terhadap stres bertujuan menjaga homeostasis tubuh. Stres berkepanjangan memicu aktivasi aksis HPA (*Hypothalamus Pituitary Adrenal*) dan sistem saraf otonom sehingga mempengaruhi aktivitas organ di tubuh. Kondisi stres dapat menyebabkan berbagai gangguan di tubuh seperti gangguan kognisi dan tingkah laku. Gangguan kognisi akan mempengaruhi proses pembelajaran (*learning*) dan pembentukan memori. Aktivasi berlebihan dari hormon stres memicu terjadi eksotoksisitas yang berakibat pada kerusakan sel. Hal ini disebabkan oleh aktivasi berlebihan dari reseptor NMDA (*N-Metyhl-D-Aspartate*) oleh glutamat. Ketamin yang dikenal sebagai obat anestesi memiliki mekanisme kerja secara antagonis non-kompetitif pada reseptor NMDA. Pemberian ketamin diharapkan dapat mengobati gangguan kognisi yang timbul akibat stres sehingga terjadi perbaikan fungsi pembelajaran dan memori.
Tujuan : Mengetahui efek pemberian *post-treatment* ketamin dosis subanestesi dalam mengobati gangguan kognisi pada tikus Wistar yang diinduksi stres buatan.
Metode : Penelitian *quasi experimental* dengan rancangan *posttest only with control group design.* Subjek penelitian menggunakan tikus Wistar jantan berusia 3-4 minggu yang berjumlah 18 ekor. Subjek dibagi menjadi tiga kelompok yakni netral, kontrol dan *post-treatment*. Subjek diberi perlakuan induksi stres buatan selama 7 hari dan kemudian diinjeksikan ketamin dosis subanestesi (5 mg/kgBB) secara intraperitoneal. Fungsi kognitif dinilai melalui uji *Morris water maze* dengan mengukur waktu latensi tikus Wistar ketika mencapai platform.
Hasil : Penilaian fungsi kognitif dilakukan dalam tiga kali percobaan yang teridiri dari 3 kelompok yakni netral, kontrol dan *post-treatment*. Rata-rata waktu latensi (detik) tiap kelompok secara berurutan pada percobaan 1 : 48,25 vs 99,94 vs 111,28 ($p = 0,539$); percobaan 2 : 23,21 vs 53,92 vs 24,59 ($p = 0,382$); percobaan 3 : 22,45 vs 49,49 vs 21,83 ($p = 0,266$).
Kesimpulan : Pemberian ketamin *post-treatment* dosis subanestesi (5 mg/kgBB) setelah induksi stres belum dapat mengobati gangguan fungsi kognitif.
Kata Kunci : Stres, kognisi, reseptor NMDA, eksitotoksisitas, ketamin, dosis subanestesi, *Morris water maze*

ABSTRACT

EFFECT OF KETAMINE IN SUBANESTHETIC DOSE ADMINISTRATION AFTER STRESS INDUCTION RELATED TO COGNITION IN WISTAR RATS

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Background : Stress is the body's adaptive response in facing distraction. The body's response to stress is aimed keeping homeostasis of the body. Prolonged stress triggers the activation of HPA (Hypothalamus Pituitary Adrenal) axis and autonomic nervous system thereby affecting the activity of the organs in the body. Stressfull condition can cause various problems in the body such as cognition impairment and behavioral disorder. Cognition disturbances will affect the process of learning and memory formation. Excessive activation of stress hormones trigger the excitotoxicity that results in cell death. This is associated with excessive activation of N-methyl-D-aspartate (NMDA) receptor by glutamate. Ketamine is known as anesthetic drug with mechanism of action as noncompetitive antagonist at NMDA receptor. Administration of ketamine is expected to treat cognition impairment due to stressful condition that resulting in improvement of learning function and memory formation.

Objective : To know the effect of ketamine administration in subanesthetic dose after stress induction in treating cognition impairment of Wistar rats.

Method : This research was quasi experimental study with posttest only with control group design. The subjects were eighteen male Wistar rats aged 3-4 weeks. Subjects were divided into three groups : netral, control and post-treatment. Subjects were given intraperitoneal injection of subanesthetic ketamine (5 mg/kgBB) after stress induction for 7 days. Cognitive function was assessed with Morris water maze test. Data was collected by measuring the latency time of Wistar rat to reach the hidden platform .

Results : The assessment of cognitive function was conducted in three times trial that consisted of thee groups: netral, control and post-treatment. The mean latency time (seconds) of each groups in the 1st trial : 48,25 vs 99,94 vs 111,28 (p = 0,539); 2nd trial : 23,21 vs 53,92 vs 24,59 (p = 0,382); and the 3rd trial : 22,45 vs 49,49 vs 21,83 (p = 0,266).

Conclusion : Administration of subanesthetic ketamine (5 mg/kgBB) after stress induction in post-treatment group could not treat cognitive function impairment.

Keywords : Stress, cognition, NMDA receptor, excitotoxicity, ketamine, subanesthetic dose, Morris water maze