

## INTISARI

**Latar Belakang:** Pada kondisi stroke iskemia terjadi pengurangan suplai darah secara tiba-tiba sehingga menyebabkan cedera reperfusi iskemia dan gangguan fungsional otak, termasuk hippocampus. Hippocampus merupakan area yang sangat rentan pada kondisi iskemia dimana gangguan pada area ini akan mengakibatkan gangguan proses belajar dan pembentukan memori. Vitamin D hormon yang larut dalam lemak yang memiliki efek neuroprotektif.

**Tujuan:** penelitian ini mengkaji pengaruh pemberian vitamin D terhadap fungsi memori spasial, ekspresi mRNA protein regulator apoptosis BAX, *inducible Nitric Oxide Synthase* (iNOS) dan *Superoxide Dismutase* (SOD2) pada hippocampus tikus model stroke iskemia serebral global transien.

**Metode:** Dua puluh empat Tikus Wistar (*Rattus norvegicus*) jantan (usia 3-5 bulan, berat badan 150-300 gram) dibagi secara acak menjadi 4 kelompok (n=6): SO (kontrol), BCCAO (iskemia serebral global transien tanpa vitamin D), VD1 (iskemia serebral global transien + injeksi vitamin D 0,125 µg/kgBB/hari), dan VD2 (iskemia serebral global transien + injeksi vitamin D 0,5 µg/kgBB/hari). Induksi iskemia serebral global transien dilakukan dengan *bilateral carotis communis artery occlusion* (BCCAO) selama 20 menit. Vitamin D diberikan secara injeksi intraperitoneal selama 10 hari. Fungsi memori spasial diuji dengan Morris *water maze* (MWM) mulai hari ke-3 setelah operasi. Tikus diterminasi pada hari ke-10, kemudian dilakukan isolasi jaringan hippocampus. Pewarnaan imunohistokimia SOD2 dilakukan pada sediaan hippocampus untuk melihat gambaran ekspresi SOD2. Ekspresi mRNA iNOS dan BAX dinilai dengan metode RT-PCR. Uji statistik menggunakan *one-way ANOVA* diikuti *post-hoc LSD*. Nilai  $p < 0,05$  dianggap signifikan secara statistik.

**Hasil:** Kelompok BCCAO memiliki lama waktu (detik) lebih rendah pada analisis uji probe MWM pada kuadran target dibandingkan dengan kelompok SO. Kelompok VD1 dan VD2 memiliki lama waktu yang lebih rendah dari pada kelompok BCCAO. Ekspresi mRNA BAX pada kelompok BCCAO lebih tinggi dibandingkan kelompok SO. Pada kelompok VD1 dan VD2 lebih rendah dibandingkan dengan kelompok BCCAO. Ekspresi mRNA iNOS pada kelompok BCCAO lebih tinggi dibandingkan kelompok SO. Pada kelompok VD1 dan VD2 lebih rendah dibandingkan dengan kelompok BCCAO. Ekspresi mRNA SOD2 pada kelompok BCCAO lebih rendah dibandingkan kelompok SO, sedangkan kelompok VD1 dan VD2 lebih tinggi dibandingkan dengan kelompok BCCAO.

**Kesimpulan:** Pemberian vitamin D memberikan efek fungsi memori spasial yang lebih baik, serta memberikan efek neuroprotektif terhadap hippocampus dengan mencegah stress oksidatif, menurunkan ekspresi iNOS dan ekspresi BAX.

**Kata kunci:** vitamin D, memori spasial, BAX, iNOS, SOD2, iskemia serebral global

## ABSTRACT

**Background:** In ischemic stroke conditions, there is a sudden reduction in blood supply, causing ischemia reperfusion injury, and functional disorders of the brain, including the hippocampus. The hippocampus is an area that is very vulnerable to ischemia conditions where disturbances in this area will result in impaired learning processes and memory formation. Vitamin D is a fat-soluble hormone that has a neuroprotective effect.

**Purpose:** This study aims to study the effect of vitamin D treatment on spatial memory function, mRNA expression of the apoptotic regulatory protein BAX, and inducible Nitric Oxide Synthase (iNOS) and Superoxide Dismutase (SOD2) in the hippocampus of a rat model of transient global cerebral ischemia stroke.

**Methods:** Twenty-four male Wistar rats (*Rattus norvegicus*) (age 3-5 months, body weight 150-300 grams) were randomly divided into 4 groups (n=6): SO (control), BCCAO (transient global cerebral ischemia without vitamin D), VD1 (transient global cerebral ischemia + 0.125 µg/kg BW/day vitamin D injection), and VD2 (transient global cerebral ischemia + 0.5 µg/kg BW/day vitamin D injection). Transient global cerebral ischemia induction was performed with bilateral common carotid artery occlusion (BCCAO) for 20 minutes. Vitamin D is given by intraperitoneal injection for 10 days. The spatial memory function was tested with a Morris water maze (MWM) starting on the 3rd day after the operation. Mice were terminated on the 10th day, then hippocampus tissue was isolated. SOD2 immunohistochemical staining was performed on hippocampus preparations to see an overview of SOD2 expression. iNOS and BAX mRNA expression were assessed by the RT-PCR method. Statistical test using one-way ANOVA followed by post-hoc LSD. The value of  $p < 0.05$  was considered statistically significant.

**Results:** The BCCAO group had a shorter time (seconds) in the analysis of the MWM probe test in the target quadrant than the SO group. The VD1 and VD2 groups had a longer time than the BCCAO group. BAX mRNA expression in the BCCAO group was higher than in the SO group. The VD1 and VD2 groups were lower than the BCCAO group. iNOS mRNA expression in the BCCAO group was higher than in the SO group. The VD1 and VD2 groups were lower than the BCCAO group. SOD2 mRNA expression in the BCCAO group was lower than in the SO group, while the VD1 and VD2 groups were higher than the BCCAO group.

**Conclusion:** Vitamin D improves spatial memory function and neuroprotective effect on the hippocampus by preventing oxidative stress, and reducing iNOS expression and BAX expression.

**Keywords:** vitamin D, spatial memory, SOD2, iNOS, BAX, global cerebral ischemia