

INTISARI

Latar Belakang: Stroke iskemik menginduksi stres oksidatif, kerusakan mitokondria, peradangan dan penuaan, akhirnya menurunkan fungsi kognitif. Vitamin D adalah hormon yang larut dalam lemak yang memiliki efek neuroprotektif untuk memperbaiki fungsi sistem saraf.

Tujuan: Penelitian ini mengkaji pengaruh pemberian vitamin D terhadap fungsi memori spasial, ekspresi mRNA p16, mRNA p21 sebagai *marker* penuaan seluler, dan ekspresi mRNA *nerve growth factor* (NGF) sebagai *marker neurotrophin* pada hippocampus tikus model iskemia cerebral global transien

Metode: Penelitian ini bersifat quasi eksperimental dengan post-test only control group design. Kami melakukan studi *in vivo* dengan model induksi bilateral common carotid artery occlusion (BCCAO) dan injeksi vitamin D selama 10 hari. Dua puluh empat tikus dibagi menjadi 4 kelompok ($n = 6$): SO (Sham Operation), BCCAO, VD1 (BCCAO + vitamin D 0,125 $\mu\text{g} / \text{kg}$), dan VD2 (BCCAO + vitamin D 0,5 $\mu\text{g} / \text{kg}$). Fungsi memori spasial diuji dengan Morris *water maze*. Penilaian dengan imunohistokimia untuk melokalisasi ekspresi p16. Ekspresi mRNA p16, p21 dan NGF dinilai dengan metode RT-PCR.

Hasil: Kelompok BCCAO memerlukan jarak tempuh lebih panjang untuk menemukan *platform* berdasarkan penilaian *learning phase*, penilaian *probe test* berdasarkan waktu yang dihabiskan di kuadran non target dibandingkan dengan kuadran target, kelompok BCCAO + vitamin D mempunyai total waktu lebih lama di kuadran target dibandingkan kelompok BCCAO. Deskripsi pewarnaan imunohistokimia pada sel piramidal CA1 hippocampus menunjukkan lokasi penuaan seluler yang terjadi di hippocampus. Ekspresi mRNA p16 dan mRNA p21 kelompok BCCAO + vitamin D lebih rendah dibandingkan dengan kelompok BCCAO. Ekspresi mRNA NGF kelompok BCCAO + vitamin D lebih tinggi dibandingkan dengan kelompok BCCAO.

Kesimpulan: Pemberian vitamin D memberikan efek terhadap kemampuan memori spasial yang lebih baik berdasarkan penilaian *learning phase* dan *probe test*. Hal ini disertai dengan ekspresi mRNA p16, mRNA p21 Lebih rendah dan ekspresi mRNA NGF lebih tinggi di hippocampus tikus model iskemia cerebral global transien.

Kata kunci: Vitamin D, penuaan seluler, *neurotrophin*, hippocampus, memori, iskemia cerebral global.

ABSTRACT

Background: Ischemic stroke induces oxidative stress, mitochondrial damage, inflammation and senescence, eventually decreases cognitive function. Vitamin D is a fat-soluble hormone that has neuroprotective effect to repair of the function nervous system.

Purpose: To study effect vitamin D in memory function, p16, p21 (senescence) and nerve growth factor (NGF) mRNA expression on hippocampus after transient global cerebral ischemic.

Methods: This study was a quasi-experimental with post-test only control group design. We performed in vivo study with induction bilateral common carotid artery occlusion (BCCAO) model and vitamin D injection for 10 days. Twenty-four rats were divided into 4 groups (n=6): SO (Sham Operation), BCCAO (transient global cerebral ischemic model not given vitamin D), VD1 (BCCAO + vitamin D 0.125 µg/kg), and VD2 (BCCAO + vitamin D 0.5 µg/kg). Spatial memory function was tested with Morris water maze. We performed Immunohistochemistry to localize p16 expression. p16, p21 and NGF mRNA Expression was assessed by RT-PCR method.

Results: The BCCAO group required longer distance to find the platform based on the learning phase assessment, probe test assessment based on time spent in the non-target quadrant compared to the target quadrant, the BCCAO + vitamin D group takes longer in the target quadrant than the BCCAO group. The immunohistochemical staining description of hippocampus CA1 pyramidal cells indicated the location of senescence occurring in the hippocampus. The expression of mRNA p16 and mRNA p21 of the BCCAO+vitamin D group was lower compared to the BCCAO group. The expression of the NGF mRNA BCCAO + vitamin D group was higher compared to the BCCAO group.

Conclusion: Vitamin D administration has an effect on better spatial memory skills based on learning phase assessments and probe tests. This was accompanied by lower p16 mRNA expression, lower p21 mRNA and higher NGF mRNA expression in the hippocampus of mice model transient global cerebral ischemia.

Keywords: Vitamin D, senescence, neurotrophin, memory, global cerebral ischemic