Efek Propofol terhadap Cedera Otak Traumatik pada Tikus Sprague-Dawley : Kajian Ekspresi dan Konsentrasi HIF-1alfa, IL-1beta, IL-6 dan Revised Neurobehavioral Severity Scale = The Effects of Propofol on Traumatic Brain Injury in Sprague Dawley Rats: A study of HIF -1alpha, IL-1beta, IL-6 Expression and Concentrations also Revised Neurobehavioral Severity Scale

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Abstrak

Latar Belakang Neuroinflamasi adalah kaskade pada cedera otak traumatik (COT) yang memiliki waktu lebih panjang dibandingkan kaskade lain sehingga memberikan kesempatan intervensi untuk mencegah kerusakan lebih lanjut. Berbagai penelitian telah dilakukan untuk mengetahui patofisiologi neuroinflamasi COT, namun belum semua diketahui dengan jelas. Tujuan penelitian ini untuk mengungkapkan alur kaskade neuroinflamasi akibat COT dengan mempelajari ekspresi dan konsentrasi HIF-1, IL-1, dan IL-6 di otak tikus COT yang diberi intervensi propofol. Metode Studi eksperimental in vivo ini menggunakan 51 tikus Sprague Dawley (SD) dan dilakukan pada bulan Maret 2019 – Maret 2021 di Fakultas Kedokteran Universitas Indonesia (FKUI) dan Fakultas Kedokteran Hewan Institut Pertanian Bogor (FKH IPB). Tikus dibagi 5 kelompok perlakuan (kontrol negatif/KN, Sham/S, propofol/P, COT/C dan COT yang diberi propofol/CP). Kelompok KN tidak diberi perlakukan dan Kelompok S diberi plasebo (NaCl). Manipulasi COT menggunakan model Marmarou weight-drop. Pada Kelompok P dan CP, tikus diberi propofol secara kontinu. Fungsi neurologis dan gangguan biokimia diperiksa dengan revised neurobehavioral severity scale/NSS-R. Ekspresi serta konsentrasi HIF-1, IL-1, IL-6 diperiksa dengan qRT-PCR, ELISA, dan imunohistokimia. Hasil Pada observasi hingga 5 hari, penurunan NSS-R lebih cepat pada Kelompok CP dibandingkan kelompok C. Uji Kruskal-Wallis pada ekspresi IL-6 Subkelompok Observasi 24 Jam menunjukkan perbedaan bermakna dan dengan post hoc Mann-Whitney didapatkan perbedaan bermakna pada Kelompok S dengan CP (1,48±0,52 vs. 3,29±0,7; p=0,011), P dengan CP (1,83±0,55 vs. 3,29±0,7; p=0,001), dan C dengan CP (1,81±0,49 vs. 3,29±0,7; p<0,001). Pada uji statistik, HIF-1 dan IL-1 tidak berbeda bermakna antar kelompok. Terdapat korelasi positif antara ekspresi dan konsentrasi HIF-1 dengan IL-1 dan IL-6 terutama di jaringan otak tikus kelompok P, C, dan CP. Kesimpulan Propofol memperbaiki fungsi neurologis model tikus COT, meningkatkan ekspresi IL-6 namun tidak memengaruhi ekspresi serta konsentrasi HIF-1 dan IL-1.

.....Background Neuroinflammatory is the cascades in TBI that has a longer time than other cascades, thus providing an opportunity for intervention to prevent further damage. Various studies have been conducted to investigate the pathophysiology of TBI and the management, but none have been clarified. The purpose of this study was to investigate changes in neurological function, expression, and concentration of HIF-1, IL-1, and IL-6 in the brain tissue of TBI rats given propofol intervention. Methods This was an in vivo experimental study using 51 Sprague Dawley (SD) rats in March 2020 – March 2021 at the Faculty of Medicine, University of Indonesia and the Faculty of Veterinary, Bogor Agricultural University. Rats were divided into five groups (negative control/NC, Sham/S, propofol/P, TBI/T, and TBI given propofol/TP). TBI manipulation using the Marmarou weight-drop model. The KN group was not treated. Group S was given

placebo treatment. In the P and TP groups, the rats were given propofol continuously. Neurological function and biochemical alterations of the experimental animal were examined using NSS-R; HIF-1, IL-1, and IL-6 expression and contents by means of qRT-PCR, ELISA, and immunohistochemistry. Result In the 5-day Observation Sub-group, the improvement in the NSS-R value in the TP group occurred faster than in the T group. The results of Kruskal-Wallis test on the IL-6 expression of the 24-hour Observation Subgroup showed a significant difference, then continued with Mann-Whitney post hoc, the results obtained group S with TP (1.48±0.52 vs. 3.29±0.7; p=0.011), P with TP (1.83±0.55 vs. 3.29±0.7; p=0.001), and T with TP (1.81±0.49 vs. 3.29±0.7; p<0.001). In the statistical analysis of HIF-1 and IL-1, no significant differences were found between groups. There was a positive correlation between the expression and concentration of HIF-1 with IL-1 and IL-6, especially in the brain tissue of rats in groups P, T, and TP. Conclusion Propofol improves neurological function in TBI rats, causing increased IL-6 expression but it does not affect expression and concentration of HIF-1 and IL-1.