INTISARI

Pengembangan Hewan Model *Alzheimer's disease* dengan *Trimethyltin* dan Studi Nanopartikel BUMSC-CM sebagai Neuroprotektan *Alzheimer's disease*

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Alzheimer's disease (AD) merupakan penyakit neurodegeneratif dengan penurunan fungsi kognitif progresif. Pengembangan hewan model AD penting untuk mempelajari patogenesis dan mengevaluasi kandidat terapi baru. *Bovine umbilical mesenchymal stem cell-conditioned media* (BUMSC-CM) yang kaya metabolit dan eksosom berpotensi sebagai agen neuroprotektan, terutama bila dikombinasikan dengan nanopartikel yang dapat menembus *blood-brain barrier* (BBB). Penelitian ini bertujuan mengembangkan hewan model AD dan menganalisis potensi neuroprotektan nanopartikel BUMSC-CM (NP-BUMSC-CM). Model AD dikembangkan menggunakan strain mencit C3H jantan dengan kelompok kontrol negatif dan kontrol positif yang diberi trimethyltin (TMT) 2,5 mg/kg intraperitoneal. Parameter meliputi pemeriksaan darah, uji perilaku *radial arm maze*, proteomik, dan histopatologi otak. Analisis statistik pengembangan hewan model AD menggunakan *unpaired t-test.* Evaluasi efek neuroprotektan NP-BUMSC-CM dilakukan melalui isolasi sel BUMSC, karakterisasi metabolit BUMSC-CM, fabrikasi NP-BUMSC-CM, dan pemberiannya pada model AD. Hewan uji dibagi menjadi tujuh kelompok: kontrol negatif, kontrol positif, donepezil 3 mg/kg, NP-BUMSC-CM 0,1 ml, BUMSC-CM 0,1 ml, NP-BUMSC-CM 0,2 ml, dan BUMSC-CM 0,2 ml. Parameter yang dinilai meliputi profil metabolit, ekspresi caspase-9 dan caspase-3, serta morfologi dan viabilitas sel piramidal hipokampus. Data dianalisis statistik menggunakan *One Way* ANOVA dilanjutkan dengan uji *post-hoc* Bonferroni. Induksi TMT menyebabkan tingginya nilai PCV, MCV, leukosit, neutrofil, melemahnya fungsi kognitif, dan munculnya biomarker protein AD seperti *amyloid beta,* protein tau, ApoB, dan ApoE. Pengamatan histologis terlihat adanya *neurofibrillary tangles* dan degenerasi sel piramidal. BUMSC-CM mengandung asam amino isoleusin, leusin, valin, lisin, dan triptofan. Pemberian NP-BUMSC-CM belum optimal dalam menekan ekspresi caspase-9 dan caspase-3 serta mempertahankan viabilitas sel piramidal dibanding BUMSC-CM dan donepezil. Kesimpulannya, induksi TMT menghasilkan hewan dengan karakteristik AD, namun NP-BUMSC-CM belum efektif sebagai neuroprotektan pada hewan model AD

Kata kunci: *Alzheimer's disease,* mencit C3H, neuroprotektan, NP-BUMSC-CM, *trimethyltin*

ABSTRACT

Development of Alzheimer's Disease Animal Model with Trimethyltin and Study of BUMSC-CM Nanoparticles as Neuroprotectant for Alzheimer's Disease

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive decline. The development of AD animal models is essential for studying its pathogenesis and evaluating potential therapeutic agents. *Bovine umbilical mesenchymal stem cell-conditioned medium* (BUMSC-CM), rich in metabolites and exosomes, has potential as a neuroprotective agent, particularly when combined with a nanoparticle-based delivery system capable of crossing the blood-brain barrier (BBB). This study aimed to develop an AD animal model and evaluate the neuroprotective potential of nanoparticle-encapsulated BUMSC-CM (NP-BUMSC-CM). Male C3H mice were divided into two initial groups: a negative control and a positive control included hematological profiles, behavioral performance using the radial arm maze test, proteomic analysis, and brain histopathology. Statistical analysis for model development used an unpaired *t-test*. Evaluation of NP-BUMSC-CM neuroprotective effects involved BUMSC isolation, metabolite characterization of BUMSC-CM, NP-BUMSC-CM fabrication, and administration to AD model mice. The animals were divided into seven groups: negative control, positive control, donepezil 3 mg/kg, NP-BUMSC-CM 0,1 ml, BUMSC-CM 0,1 ml, NP-BUMSC-CM 0,2 ml, and BUMSC-CM 0,2 ml. The parameters assessed included metabolite profiles, caspase-9, and caspase-3 expression, and hippocampal pyramidal cell morphology and viability. Statistical analysis was performed using One-Way ANOVA followed by Bonferroni post-hoc test. TMT induction high level of PCV, MCV, leukocyte, and neutrophil counts, cognitive impairment, and the appearance of AD related protein biomarkers such as amyloid beta, tau protein, ApoB, and ApoE. Histologically, neurofibrillary tangles and pyramidal cell degeneration were observed. BUMSC-CM contained amino acids such as isoleucine, leucine, valine, lysine, and tryptophan. Administration of NP-BUMSC-CM was not optimal in suppressing caspase-9 and caspase-3 expression or maintaining pyramidal cell viability compared to BUMSC-CM and donepezil. In conclusion, TMT induction produced mice with AD-like characteristics. However, NP-BUMSC-CM has not yet demonstrated effective neuroprotective activity in the AD animal model.

Keywords: *Alzheimer's disease,* C3H mice, neuroprotection, NP-BUMSC-CM, trimetyltin.