THE EFFECT OF HALOTHANE INHALATIONAL ANAESTHETICS ON LIVER CELLS

(Experimental Study of Halothane Toxic Effect in BALB C Mice)

Thesis

Submitted as partial fulfilling of the requirement for
Master degree of Biomedical Science

Prepared by:
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APPROVAL SHEET

A thesis

THE EFFECT OF HALOTHANE INHALATIONAL ANAESTHETICS
ON LIVER CELLS
(EXPERIMENTAL STUDY IN BALB C MICE)

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DECLARATION

"I am here declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which to a substantial extent has been accepted for the award of any other degree or diploma of the university or other institute of higher learning, except where due acknowledge is made in the text"

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ABSTRACT

Background: Adverse effects of halothane on the liver range from liver dysfunction to hepatitis, and are more frequent following repeated use. Medical personals are in risk of chronic exposure of wasted halothane. However, there are limited literatures about this effect based on time exposure.

Objectives: To identify and analyze the liver cells changes of halothane exposure to liver cells of Balb/C mice.

Methods: This experimental study used randomized post-test only control group design in 30 male BalbC mice given 0.011 mg/weight halothane 3 hours daily for two weeks (group 1), four weeks (group 2), six weeks (group 3), six weeks followed by 2 weeks of halothane free (group 4), and without exposure (control group). The liver tissues were HE stained and observed for enlarge, karyorhexis, and karyolisis of the nucleus. Immunohistochemistry was undertaken to count the percentage of cytocrome-P450 stained brown colour and scored based on its intensity.

Results: The difference among groups and between each group were statistically significant ($p< 0.05$), except between group 2 and 4 ($p = 0.078$), and between group 3 and 4 ($p = 0.522$). The difference of cytocrome-P450 expression among groups was not statistically significant ($p = 0.266$).

Conclusion: There was statistically significant difference of abnormal liver cell nucleus changes in groups with different time of halothane exposure ($p = 0.000$) while no statistically significant difference of cytocrome-P450 expressions ($p = 0.266$) was found. The nucleus changes were gradually increased with the time of exposure.

KEYWORDS: Halothane, liver cell nucleus changes, cytocrome-P450

ABSTRAK

Pendahuluan: Efek samping halotan pada hepar bervariasi mulai dari disfungsi hepar hingga hepatitis, hal ini lebih sering terjadi pada penggunaan berulang. Tenaga medis berada pada risiko paparan kronik dari kebocoran halotan. Namun, hanya ada sedikit literatur mengenai efek ini berdasarkan waktu paparan.

Tujuan: Untuk mengidentifikasi dan menganalisis perubahan sel hepar karena paparan halotan pada sel hepar mencit Balb/C.

Metode: Penelitian eksperimental ini menggunakan desain *randomized post-test only control group* pada 30 mencit Balb/C jantan yang diberikan 0,011 mg/kgBB halotan 3 jam/hari selama 2 minggu (grup 1), 4 minggu (grup 2), 6 minggu (grup 3), 6 minggu diikuti 2 minggu bebas halotan (grup 4), dan tanpa paparan (grup kontrol). Jaringan hepar dicat HE dan diamati untuk pembesaran, karyoreksis, dan karyolisis pada nukleus. Immunohistokimia dilakukan untuk menghitung persentase cytochrome-P450 yang terwarnai coklat dan diskor berdasarkan intensitasnya.

Hasil: Perbedaan antar semua grup dan antar-grup signifikan secara statistik ($p<0,05$), kecuali antara grup 2 dan 4($p = 0.078$) serta antara grup 3 dan 4($p = 0.522$). Perbedaan ekspresi cytochrome-P450 antar semua grup secara statistik tidak bermakna ($p = 0.266$).

Kesimpulan: Terdapat perbedaan yang signifikan dari perubahan nukleus sel hepar abnormal pada grup dengan lama waktu paparan halotan yang berbeda ($p = 0.000$), sementara itu tidak ada perbedaan yang bermakna secara statistik pada ekspresi cytochrome-P450 ($p = 0.266$). Nukleus berubah secara bertingkat sebanding dengan lama waktu paparan.

KATA KUNCI: Halotan, perubahan nukleus sel hepar, cytochrome-P450