UNIVERSITI PUTRA MALAYSIA

THE EFFECTS OF C5aR ANTAGONISM ON HISTOPATHOLOGICAL AND BLOOD PARAMETERS CHANGES FOLLOWING CHLORHEXIDINE-INDUCED CONTACT DERMATITIS IN MICE

SIONG JING JING

FPV 2015 71

THE EFFECTS OF C5aR ANTAGONISM ON HISTOPATHOLOGICAL AND BLOOD PARAMETERS CHANGES FOLLOWING CHLORHEXIDINE-INDUCED CONTACT DERMATITIS IN MICE

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A project paper submitted to the
Faculty of Veterinary Medicine, Universiti Putra Malaysia
In partial fulfilment of the requirement for the
DEGREE OF DOCTOR OF VETERINARY MEDICINE
Universiti Putra Malaysia
Serdang, Selangor Darul Ehsan.

MARCH 2015

It is hereby certified that we have read this project paper entitled "The Effects of C5aR Antagonism on Histopathological and Blood Parameters Changes Following Chlorhexidine-Induced Contact Dermatitis in Mice" by Siong Jing Jing and in our opinions it is satisfactory in term of scope, quality and presentation as partial fulfilment of the requirement for the course VPD 4901-Project.

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DEDICATION

Every challenging work needs self-effort as well as guidance of elders especially those who were very close to our hearts.

My humble effort I dedicate to the Al-mighty

God

All the support and care from my loving

Father and Mother

Along with all responsible and respected

Lecturers

As well as all guidance and assistance from

Laboratory staffs and friends

ACKNOWLEDGEMENTS

Praise the Lord for the blessing to give me courage and strength to finish this dissertation, for God has guided my path through this long way until now. I would never have the chance to finish this composition without the guidance of my supervisors, assistance from many staffs and friends and support from my family.

This work would not have the spirit that it has without the invaluable academic, educational, psychological, and financial support provided by my supervisor, Dr Mohd Hezmee b. Mohd Noor. I would like to thank him for his insight, patience and editing skills in helping me to structure and write this thesis. For this I am sincerely grateful.

I would like to express my deep gratitude to my co-supervisor, Prof. Noordin Mohamed Mustapha, for his guidance and experiences has raised me further up on the stairway to knowledge heaven.

I am also grateful to Cik Farhana for helping me a lot in my research. It would surely have a lot more difficulties during these weeks without her suggestions and aids. I would also like to thank En. Abdullah, Pn. Jamilah, Pn. Latifah and Dr. Mazlina and other laboratory assistances for the permission to do my research in the laboratory as well as giving advices and services in haematology results and histopathology results.

Finally, I would also like to thank my housemates, friends and my family members who are always supporting me and encouraging me with their best wishes.

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LIST OF ABBREVIATIONS

CD	contact dermatitis
CICD	chlorhexidine-induced contact dermatitis
ACD	allergic contact dermatitis
ICD	irritant contact dermatitis
C5L2	C5a receptor-like 2
C5aR	C5a receptors
IACUC	Institutional Animal Care and Use Committee
UPM	Universiti Putra Malaysia
H&E	haematoxylin and eosin
WBC	white blood cell

ABSTRAK

Abstrak daripada kertas projek yang dikemukan kepada Fakulti Perubatan Veterinar untuk memenuhi sebahagian daripada keperluan kursus VPD4901-Projek

KESAN ANTAGONIS C5aR PADA PARAMETER HISTOPATOLOGI DAN PERUBAHAN DARAH BERIKUTAN KONTAK CHLORHEXIDINE DENGAN KULIT MENYEBABKAN KERADANGAN KULIT DALAM TIKUS

Oleh

SIONG JING JING

2015

Penyelia: Dr. Mohd Hezmee Mohd Noor

Penyelia bersama: Prof. Noordin Mohamed Mustapha

Sepanjang beberapa dekad, chlorhexidine merupakan salah satu bahan disinfektan yang kerap digunakan dalam bidang perubatan sama ada untuk manusia atau haiwan. Namun, chlorhexidine telah didapati bahawa bahan ini akan mengakibatkan reaksi memudaratkan seperti hipersensitiviti dalam manusia, tetapi sama ada bahan ini

boleh menghasilkan tindak balas yang sama pada haiwan masih tidak jelas. Dalam kajian ini, kami akan menyiasat tentang kesan antagonis C5aR pada parameter histopatologi dan perubahan darah berikutan kontak chlorhexidine dengan kulit menyebabkan keradangan kulit dalam tikus. Tikus secara rawaknya dibahagikan kepada empat kumpulan untuk menyebabkan chlorhexidine kontak dermatitis atas kulit dan rawatan Dexamethasone, Histamil, komponen pelengkap C5a reseptor antagonis PMX205 dan air masin natrium klorida diberikan kepada kumpulan masing-masing. Sampel-sampel darah diambil untuk menghasilkan keputusan hematologi manakala sampel kulit diambil untuk penilaian keputusan histopatologi . Kemungkinan hasilan serum IgE dalam darah melalui tindak balas alahan pula dikesan dengan teknik ELISA. Keputusan yang diperolehi daripada kajian ini menunjukkan bahawa rawatan chlorhexidine kontak dermatitis dengan C5aR antagonis telah berjaya mengurangkan keterukan luka yang serupa dengan anti-histamine dan rawatan corticosteroid berdasarkan pemarkahan lesi kulit secara kasar dan penilaian histopatologi. Keputusan hematologi untuk darah tidak menunjukkan apa-apa perubahan ketara berbanding dengan normal. Sebagai ringkasan, C5aR percanggahan menyediakan rawatan alternatif kepada chlorhexidine kontak dermatitis.

Kata Kunci: *chlorhexidine, chlorhexidine kontak dermatitis, C5aR antagonis*

ABSTRACT

An abstract of the project paper presented to Faculty of Veterinary Medicine in partial fulfilment of the course of VPD 4901-Project

THE EFFECTS OF C5aR ANTAGONISM ON HISTOPATHOLOGICAL AND BLOOD PARAMETERS CHANGES FOLLOWING CHLORHEXIDINE-INDUCED CONTACT DERMATITIS IN MICE

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For decades, chlorhexidine has been used in the medical field for its disinfectant properties. Yet, chlorhexidine is found to illicit hypersensitivity reactions in human, but whether it can produce the same reaction in animals remain unclear. In this study, we investigate the effects of C5aR antagonism on histopathological and blood parameters changes following chlorhexidine-induced contact dermatitis in mice.

Mice were randomly divided into four groups for chlorhexidine induced contact dermatitis and given treatments of Dexamethasone, Histamil, complement component C5a receptor antagonist PMX205 and saline. Blood samples were taken for haematology while skin samples were taken for histopathology analysis. The viability of serum IgE for allergy reaction is detected by ELISA technique. Results obtained from the study indicate that treatment of chlorhexidine-induced contact dermatitis by C5aR antagonist has managed to reduce the severity of the lesions similar to anti-histamine and corticosteroid treatment based on the gross skin lesion scoring and histopathological evaluation. The blood parameters did not showed any significant changes compared to normal. As a summary, C5aR antagonism provides an alternative towards the treatment of chlorhexidine-induced contact dermatitis.

Key Words: *chlorhexidine, chlorhexidine-induced contact dermatitis, C5aR antagonist*

1.0 INTRODUCTION

For decades, chlorhexidine has been highly utilized in the medical field for its broad-spectrum efficacy, microbricidal properties and low costs. Although exposure to chlorhexidine is very common in the health-care settings, sporadic cases of contact dermatitis (CD) occur regularly and are well documented, especially in the health-care workers in the medical and surgical environment. Chlorhexidine is found to illicit hypersensitivity reactions in human, but whether it can produce the same reaction in animals remain unclear. Studies have shown that IgE-mediated chlorhexidine allergy may lead to type I allergy reactions, extending from mild symptoms to anaphylaxis in human (Garvey et al., 2007). Currently topical corticosteroid is one of the most favoured treatments for cases of CD (Cohen & Heidary, 2004; Krautheim, Jermann, & Bircher, 2004). However, prolonged use of corticosteroid may not be warranted for chronic cases due to several complications such as polydipsia, polyuria, liver problems, muscle atrophy and susceptibility to skin and bladder infections (Koch, Torres, & Plumb, 2012). Therefore it is necessary to search for different methods to reduce the treatment of this disease with minimal side effects. A complement system is responsible to assist in the antibody action toward destroying the pathogen and eliminate the antigen-antibody complexes. Out of the complement components, C5a is important as an inflammatory mediator in most of the diseases. Hence, as an inflammation mediator, the idea of using the C5a antagonism to reduce and prevent the inflammation process can be manipulated in treating contact dermatitis (CD).

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