Pharmaceutical Technology Perspectives

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IIUM PRESS

INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA

Pharmaceutical Technology

Perspectives

Editor

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IIUM Press

Published by:
IIUM Press
International Islamic University Malaysia

First Edition, 2011

Perpustakaan Negara Malaysia Cataloguing-in-Publication Data

Muhammad Taher
Pharmaceutical Technology Perspectives
Muhammad Taher
Include index
Bibliography: p. 149

ISBN: 978-967-418-075-1

Member of Majlis Penerbitan Ilmiah Malaysia – MAPIM
(Malaysian Scholarly Publishing Council)

Printed by :
IIUM PRINTING SDN. BHD.
No. 1, Jalan Industri Batu Caves 1/3
Taman Perindustrian Batu Caves
Batu Caves Centre Point
68100 Batu Caves
Selangor Darul Ehsan

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CHAPTER 10

THE ROLE OF PHARMACOGENETIC VARIATION IN METOPROLOL CYP2D6 GENOTYPES POLYMORPHISM

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*Ticlopidine is used as an anti-platelet in patients with ischaemic heart disease. An in vitro study suggested that ticlopidine inhibited CYP2D6 and the widely used antianginal metoprolol is metabolized by this polymorphic enzyme. The objective of this study was therefore to investigate the effect of ticlopidine treatment into patients maintained on chronic metoprolol therapy. The study was approved by the Ethics Committee of International Islamic University Malaysia (IIUM) and strictly adhered to Malaysian Good Clinical Practice (GCP) guidelines. This was an open labelled Case Controlled Study where all the patients were screened for the inclusion /exclusion criteria. CYP2D6 genotyping were performed for *3,*4,*5,*6,*9,*10, *14, *17 and duplication. Two weeks after the screening visit, blood for metoprolol was taken at timed intervals together with serial measurement on blood pressures and heart rates. Subsequently the patients were given a standard dose of ticlopidine 250 mg twice daily for a period of one month. At the end of study period, blood for metoprolol was repeated together with serial measurement on blood pressures and heart rates. After 18 months, 87 patients completed the study. From our study, it was showed that the frequency of predicted Poor Metabolizer (PM) was low at 2.6%, where both patients had homozygous *4/*4 and majority of them (47.8%) belong to the allele *10, predicted Intermediate Metabolizer (IM). After ticlopidine treatment, there were increasing*