

**UNIVERSITI TEKNOLOGI MARA**

**A STUDY OF THE FACTORS AFFECTING  
INTOLERABILITY TOWARDS CHOLINESTERASE  
INHIBITORS IN ELDERLY PATIENTS WITH  
DEMENTIA  
(THE FACED STUDY)**

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## AUTHOR'S DECLARATION

I declare that the work in this dissertation was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This topic has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

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## ABSTRACT

The first line symptomatic treatment for AD is ChEIs. Study on factors that associated with intolerability towards ChEIs in elderly with dementia among Malaysian is still lacking. Study aimed to identify factors associated with intolerability towards ChEIs and to introduce genotyping to identify genetic factor that may influence intolerability. Factors analysis were based on retrospective record-review and prospective cross-sectional laboratory analysis for genotyping among patients in GMOC, HKL. Patients' aged 60 years and above with the first exposure with ChEIs were included. Intolerability define as stopping the drug or reducing the dosage because of adverse effects. The intolerability found to be 42.9 %. Sociodemographic factors was not a predictor of intolerability. Drug and SE is the main factors that affecting intolerability. FACED study found patients who were intolerant were at 53 times chance having intolerability at initiation dose regime (OR=53.48, 95 % CI 6.717-425.883,  $p<0.001$ ), use of concomitant CYP3A4 substrate having 11 times chances of intolerability (OR=11.05, 95 % CI 1.256-97.146,  $p=0.030$ ) and patient who developed CNS SE were 7 times risk develop intolerability (OR=7.14, 95 % CI 1.672-30.504,  $p=0.008$ ). For clinical factor, by increasing 1 mmol/L of serum FBG, the chances of intolerability can be reduce by 70 % (OR=0.30, 95 % CI 0.126-0.700,  $p=0.050$ ). Genotyping identified the most frequent genetic polymorphism were allele \*4 (88.8 %), \*10 (55.6 %) and \*14 (11.1 %). Four intolerants' are IM but one patient is an EM and does having risk factor as identified earlier and taking CYP2D6 inhibitor agent. This study serve as a new data for our local population. It provide an additional knowledge for pharmacist to play a role in planning for modification of therapy to improve management in dementia patient who requires ChEIs.

Keywords : cholinesterase inhibitor, dementia, intolerability, side effect

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