UNIVERSITI TEKNOLOGI MARA

PREDICTORS FOR DRUG UTILIZATION AND DRUG RELATED PROBLEMS IN HOSPITALIZED NEONATES

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Thesis submitted in fulfilment
of the requirements for the degree of
Doctor of Philosophy
(Pharmacoepidemiology)

Faculty of Pharmacy

May 2018

ABSTRACT

Despite complex pharmacotherapy management in neonates, the epidemiology of drug utilization, drug related problems (DRPs) and their predictors in hospitalized neonates in Malaysia are unknown. Thus, the aims of this study were to examine the drug utilization profile, DRPs and their predictors in hospitalized neonates. A systematic review was conducted prior to the actual study to determine the prescribing patterns and methodologies used for reporting drug utilization in hospitalized neonates. Two projects were undertaken under this study. Project I was conducted at Hospital Sultanah Aminah, Johor Bahru. Project I was carried out in Medical Record Office (retrospective) and neonatal intensive care unit (NICU) and neonatal wards (prospective). Patients' medication charts, ward notes and laboratory data were reviewed daily and progress of the selected patients in the ward were documented. Logistic regression was used to analyse potential risk factors associated with use of ≥ 5 drugs and DRPs occurrence. As Adverse Drug Reaction (ADR) is a subset of DRPs, Project II was carried out at National Pharmaceutical Regulatory Agency (NPRA) using the data from the national pharmacovigilance database, QUEST2 system to examine the characteristics and prevalence of ADRs in neonates in contrast to other paediatric population. The systematic review revealed that neonates are exposed to a high number of drugs, with antiinfectives for systemic use being the most predominantly prescribed. Various methods have been used to quantify drug consumption in neonates but no study from Malaysia was identified. In project I, a total of 302 neonates were included in the study. The majority of neonates admitted to NICU and neonatal wards were preterm (63.2%, n=191) and LBW infants (64.6%, n=195). On average, the neonates were admitted for 28.4 days and there were 2715 drugs documented. Antiinfectives for systemic use (n=1235, 45.5%) were the most commonly prescribed drugs, with benzylpenicillin (n=293) and gentamicin (n=275) being the most predominant. Number of diagnoses or problems was found to be a significant predictors for neonates to be prescribed with ≥ 5 drugs. In total, 768 DRPs were identified for 265 patients, whom had at least one DRP. The overall incidence of DRPs was 87.7% and treatment safety which relates to adverse drug events had the highest frequency amongst the reported problems, 67.1% (n=515). A retrospective analysis of ADRs reports received by the national pharmacovigilance centre in project II found that antibacterial for systemic use were commonly associated with ADRs in Malaysian children with majority of them manifested through skin reactions. ADRs reported for neonates was lower than other children age categories. Inappropriate dose, 60.0% (n=572) and drug selection 21.4% (n=204) were the common causes for DRPs identified. The number of drugs prescribed was the only potential risk factor that was found to be significant for the occurrence of DRPs. Neonates are exposed to high number of drugs and are at risk of developing DRPs. Pharmacists should set priority for the preterm and LBW neonates who have multiple diagnoses and prescribed with multiple drugs in order to minimize the risks of DRPs and subsequently improve efficiency of clinical pharmacy services.

ACKNOWLEDGEMENT

Firstly, I wish to thank Allah for giving me the opportunity to embark on my PhD and for completing this long and challenging journey successfully. My deepest and sincere gratitude goes to my supervisors, Prof. Dr. Noorizan bt Abdul Aziz (Faculty of Pharmacy, Universiti Teknologi MARA, UiTM & School of Pharmacy, Management and Science University (MSU)) and Prof. Dr. Mohamed Mansor bin Manan (School of Pharmacy, KPJ Healthcare University College). Thank you for the unwavering guidance, encouragement and ideas in assisting me with this study.

I would like to express my sincere appreciation to the Medical Record Office staffs of Hospital Sultanah Aminah (HSA), Johor Bahru for the hospitality and assistance during sampling of the project I. I would also like to extend my gratitude to Dr Mohd Nizam bin Mat Bah, Consultant Paediatrician and staffs of NICU and neonatal wards for the assistance during the study. Special thanks to my fellow pharmacists' colleagues and friends at HSA for helping me with this project. I also would like to thank the staffs of the National Pharmaceutical Regulatory Agency (NPRA), especially Mr. Tan Ann Ling, Mrs Nurul Huda bt Hamdan and Miss Wo Wee Kee for providing the facilities, information and technical assistance during the project II.

My special thanks to Dr Long Chiau Ming (School of Pharmacy, KPJ Healthcare University College) for his tireless effort in reviewing all the manuscripts published during my study. Not forgetting, Prof Dr Kamaruzaman bin Jusoff (Faculty of Resources Science & and Technology, UNIMAS) and Associate Prof, Dr A'edah bt Abu Bakar, (Faculty of Pharmacy, UiTM) for reviewing the published manuscripts on project II and systematic review, respectively. I would also like to thank Dr Mohd Zuli bin Jaafar, Senior Lecturer at Faculty of Applied Sciences, UiTM (Jasin) for his kind assistance and guidance in setting the format of the thesis using the MZJ Formatting Method. I would also like to acknowledge Dr Shamsuritawati bt Sharif, Senior Lecturer at School of Quantitative Sciences, Universiti Utara Malaysia for her advice on statistical method used in this study.

I owe thanks to a very special person, my husband, Mohd Faisal bin Hamid for his unfailing love, support and understanding during my pursuit of PhD. To all my wonderful children, Hakim, Danial, Haziq, Aisyah and my late son, Harith, thank you so much for your unending inspiration. Finally, my heartfelt gratitude goes to my beloved parents (Rosli bin Pin and Roswita bt Zahid) and family for their endless love, moral support and prayers for me to complete this entire journey. Alhamdulillah.

TABLE OF CONTENTS

CHAPTER ONE
INTRODUCTION

1.1 Background of the Study

Neonatal period is the most vulnerable time for the child. During this first 28 days of life, the risk of death is strikingly high and it has been reported that neonatal deaths accounts for nearly 45% of all under 5 child death every year. Prematurity, asphyxia and birth trauma are the main causes of neonatal death (WHO, 2016). Reducing child mortality is an urgent agenda and it has become one of the United Nation Millennium Development Goals (MDGs) which was set in 2000. The MDGs which was adopted worldwide have galvanized efforts to substantially reduced the child mortality and the rate of neonatal death have decreased by 47 percent between 1990 and 2015, from 36 to 19 deaths per 1000 live birth (UNICEF & WHO, 2015). The decline in neonatal mortality rate was also witnessed in Malaysia. The neonatal mortality rate has dropped from 6.8 per 1000 live births in 1995 to 3.9 per 1000 live births in 2014 (Ministry of Health Malaysia, 1995, 2016). Medical innovations in the management of neonates, particularly those born preterm has dramatically increased the survival of these critically ill newborns. It is imperative for the healthcare practitioners to address this issue so as to ensure these neonates surpassed this critical period of their life (Howson, Kinney, & Lawn, 2012).

Those preterm neonates who survived are mostly sick babies who will eventually admitted to the wards for survival support due to severe prematurity or management of congenital diseases and peri/post-natal complications. These neonates are often presented with multiple comorbidities due to immature organs which warrant them for intensive and highly specialized medical care with high exposure to drugs (Neubert, Lukas, & Leis, 2010). Despite its wide spread use, the majority of drugs prescribed for neonates have not undergone sufficient study to receive Food Drug Administration (FDA) labelling which indicate the safety and effectiveness of the drug when applied to this population (Booth & Sturgess, 2012; Dessì, Salemi, Fanos, & Cuzzolin, 2010; W. Du et al., 2006; Sanghera, Chan, & Khaki, 2006). Due to limited