A COMPARATIVE STUDY OF AN INTEGRATED PHARMACEUTICAL CARE PLAN AND A ROUTINE CARE IN BRONCHIAL ASTHMA

A Thesis Submitted in Partial Fulfillment of the Requirements for Master Degree in Pharmaceutical Science (Clinical Pharmacy)

Submitted By

Rana Rasheed Farrag

BSc in Pharmacy (2008)
Ain Shams University

Under The Supervision of

Prof. Manal EL Hamamsy

Professor of Clinical Pharmacy,
Faculty of Pharmacy,
Ain Shams University

Prof. Mamdouh Zaki

Professor of Clinical Pharmacy, Faculty of Pharmacy, Ahram Canadian University

Prof. Taher EL-Naggar

Professor of Chest Diseases, Faculty of Medicine, Ain Shams University

Ain Shams University Faculty of Pharmacy (Cairo - Egypt)

2014

ABSTRACT

Background:

Bronchial asthma is a chronic chest disease constituting a serious public health problem all over the world. Unfortunately it is still too often poorly controlled and evidence-based guidelines are still insufficiently implemented. A paradigm shift for asthma care implies that the level of asthma control should be continuously monitored and that treatment should be adjusted according to the patients' current asthma-control status. Pharmacists could assist to achieve and maintain asthma control by providing patient education and medical supervision .

Aim: The study compares the effect of asthma care by clinical pharmacist intervention versus routine care on asthma control.

Patients and Methods:

A 2-month randomized, controlled trial was conducted in outpatient clinics of Ain Shams University Hospitals, Cairo, Egypt. Patients were randomly assigned to receive routine care (n=30) or a pre-defined pharmacist intervention (n=30). This intervention mainly focused on patient education, improving inhalation technique and medication assessment. Primary outcome was the level of asthma control, as assessed by the Asthma Control Questionnaire (ACQ).

Results:

By the end of the study, the intervention patients who received a written action plan significantly improved their ACQ results than routine care group who did not receive a plan (p<0.0001). The intervention also reduced reliever medication use and the frequency of night-time awakenings due to asthma. Inhalation technique and adherence to controller medication were significantly better in the intervention group.

Conclusion:

The present study results provide supportive evidence concerning pharmacists' favorable effects on asthma patient care and support clinical pharmacists as key members of the health care team.

Keywords: Asthma Control Questionnaire; Asthma Action Plan; Patient education; Adherence; Inhalation Technique.

ACKNOWLEDGEMENT

I wish to express my deepest thanks and respect to Prof. Mamdouh Ahmed Zaki, Prof. Taher El-Naggar and Prof. Manal El-Hamamsy for their continuous advice, close supervision and kind support all through this study.

I wish to express my thanks and respect to Dr. Mohsen Fathallah, executive manager of Genuine Research Center, for statistical advice.

I would like to thank Dr. Ahmed Galal, Department of Chest Diseases, Faculty of Medicine, Ain Shams University, as well as all staff members and allied health team for their help complete this study as appropriate.

I wish to express my gratitude to staff members from the Department of Hypersensitivity and Immunology, Faculty of Medicine, Ain Shams University, for their co-operation.

LIST OF CONTENTS

| ABSTRACT | i |
|--|-----|
| ACKNOWLEDGEMENT | iii |
| LIST OF CONTENTS | iv |
| LIST OF TABLES | vii |
| LIST OF ILLUSTRATIONS | ix |
| LIST OF ABBREVIATIONS | xii |
| INTRODUCTION | 1 |
| 1. Definition and Pathogenesis | 1 |
| 2. Factors influencing the development of asthma | 15 |
| 3. Signs, Symptoms& Diagnosis | 25 |
| Reversibility Testing: | 35 |
| Differential Diagnosis: | 37 |
| 4. Management of Asthma | 43 |
| Corticosteroids | 50 |
| Beta2 – adrenoreceptor Agonists | 59 |
| Anticholinergics | 65 |
| Leukotriene Modifiers | 66 |
| Methylxanthines | 69 |
| Immunomodulators | 71 |
| Complementary Therapy | 73 |

| Bronchial Thermoplasty | 75 |
|---|-----|
| New Drugs for Asthma | 76 |
| 5. Role of Clinical Pharmacist | 79 |
| Asthma Triggers Avoidance | 79 |
| Proper Inhaler Use | 80 |
| Choosing the appropriate inhalation device | 83 |
| Educating the patient about proper inhaler use | 84 |
| Maintaining proper inhaler technique | 85 |
| Changing inhalers and patient preferences | 85 |
| Adherence | 86 |
| Written Action Plans and Asthma Self-management | 87 |
| Shared Decision Making | 87 |
| AIM OF THE WORK | 88 |
| PATIENTS & METHODS | 89 |
| Patients | 89 |
| Methods | 90 |
| Setting | 90 |
| Study Design | 90 |
| Materials | 93 |
| Tools of the Study | 94 |
| Outcome Measures | 111 |
| Statistical Analysis | 112 |

| RESULTS | |
|------------------------------------|--|
| Asthma Control: | |
| Adherence to Controller Medication | |
| Inhalation Technique 122 | |
| DISCUSSION | |
| Conclusion | |
| Study Limitations | |
| Recommendations | |
| APPENDIX | |
| REFERENCES | |
| أ الملخص العربي | |

LIST of TABLES

| Table Page |
|---|
| Table 1.Key inflammatory mediators in the pathogenesis of asthmatic inflammation |
| Table 2.Asthma Susceptibility Genes Selected Examples |
| Table 3. Clinical features in adults that influence the probability of asthma |
| Table 4. Lung Volumes and Capacities- Explanatory Table34 |
| Table 5. Differential diagnosis for asthma in adults |
| Table 6. Asthma Control |
| Table 7. Classification of Asthma Severity in Adults and Adolescents 12 Years and Older |
| Table 8. Assessment of Overall Asthma Control in Adults47 |
| Table 9. Effect of glucocorticoids on transcription of genes related to asthma |
| Table 10. Possible adverse effects of oral corticosteroid therapy 56 |
| Table 11. Estimated equipotent daily doses of ICS (μg) for adults 59 |
| Table 12. Different types of inhalation devices available for asthma |
| Table 13. Inhaler selection algorithm. 84 |
| Table 14. Pharmaceutical Products Used in the Study94 |
| Table 15. Asthma Control Questionnaire |
| Table 16. Overview of Patient Education Intervention |
| Table 17. Demographic Characteristics for Patients Participating in the Study |

| e |
|-----|
| 115 |
| |
| |
| 116 |
| • |

LIST OF ILLUSTRATIONS

| Figure Page |
|---|
| Figure 1. Cycle of chronic inflammation in patients with asthma5 |
| Figure 2. Pathogenesis of allergic asthmatic inflammation |
| Figure 3. Viral Infections and Asthma Susceptibility |
| Figure 4. Barrel Chest in asthma |
| Figure 5. The mechanics of breathing and the respiratory muscles 31 |
| Figure 6. Atopic skin conditions associated with asthma |
| Figure 7. A schematic illustration of lung volumes and capacities .34 |
| Figure 8. A spirogram comparing FEV1 values in asthmatic and healthy subjects |
| Figure 9. Reversibility testing |
| Figure 10. Goals of Asthma Management |
| Figure 11. Stepwise management approach for asthma46 |
| Figure 12. Chronic Inflammation in asthma and potential therapeutic targets |
| Figure 13. Gene regulation by histone acetylation |
| Figure 14. Acetylation of Glucocorticoid Receptor (GR) |
| Figure 15. Cellular and structural effects of glucorticosteroids 54 |
| Figure 16. Schematic representations of the disposition of inhaled drugs |
| Figure 17. Mechanism of action of β 2-agonists |
| Figure 18. Actions of β_2 -agonists in airways |

| Figure 19. Complementary actions of LABAs and corticosteroids in the pathophysiology of asthma |
|--|
| Figure 20. The molecular interaction between corticosteroids and β2-agonists |
| Figure 21. Diagram of Leukotriene Formation |
| Figure 22. Omalizumabo (Xolair®) Mechanism of Action72 |
| Figure 23. Flow of Participants in the Study |
| Figure 24. Patient Data Record |
| Figure 25. Flowmate Plus 2500. |
| Figure 26. Asthma Action Plan (English Version) |
| Figure 27. Asthma Action Plan (Arabic Version) |
| Figure 28. Pathogenesis of Asthma |
| Figure 29. Patient Education Card-1 Asthma Triggers |
| Figure 30. Patient Education Card-2 Proper Use of MDI (Metered-Dose Inhalers) |
| Figure 31. Proper Inhaler Technique Checklist for Metered Dose Inhaler (MDI) |
| Figure 32. Proper Inhaler Technique Checklist for Discus Dry Powder Inhaler |
| Figure 33. Study Flow Diagram |
| Figure 34. ACQ-scores after a 2-month Follow-up |
| Figure 35. dC-FEV1% after a 2-month Follow-up |
| Figure 36.ER-Visits and Hospitalization related to asthma 119 |
| Figure 37.Short-Acting β2-Agonist use after a 2-month follow-up119 |

| Figure 38.Inhaled Corticosteroid Use after a 2-month follow-up 120 |
|--|
| Figure 39.Number of Courses of Systemic Steroid Used during a 2-month follow-up |
| Figure 40. % Patients achieved asthma control at the end of the study |
| Figure 41. Patient Adherence to Therapy |
| Figure 42. %Patients Achieved Correct Steps Inhalation Technique at Baseline |
| Figure 43. %Patients Achieved Correct Steps Inhalation Technique at the End of the Study |

LIST OF ABBREVIATIONS

5-LO inhibitor 5- Lipooxygenase inhibitor

AC Adenylyl Cyclase

ACQ Asthma Control Questionnaire

ACT Asthma Control Test
ASM Asthma Self-Management

ATS/ERS American Thoracic Society/ European Respiratory

Society

BA-pMDI Breath-actuated pressurised Metered-Dose Inhaler
BREATHE Better Respiratory Education and Asthma Treatment

in Hinton and Edson

BT Bronchial Thermoplasty

CAM Complementary and Alternative Medicine

c-AMP cyclic- Adenosine monophosphate

CCL5 Chemokine Ligand 5 CCR3 Chemokine Receptor 3

CD4 Cluster of Differentiation type 4

COPD Chronic Obstructive Pulmonary Disease

CSS Churg-Strauss Syndrome
CYP Cytochrome p450 enzyme
Cys-LTs Cysteinyl Leukotrienes
DNA Deoxy Ribonucleic Acid
DPI Dry Powder Inhaler

ER visits Emergency Room visits related to asthma
EXCELS The Epidemiologic Study of Xolair: Evaluating
study Clinical Effectiveness and Long-term Safety in

Patients with Moderate-to-Severe Asthma (EXCELS)

FCeRI high-affinity receptor for the Fc region of

immunoglobulin E

FDA Food and Drug Administration FE_{NO} Fractional Exhaled Nitric Oxide

FEV1 Forced Expiratory Volume in one second

FVC Forced Vital Capacity

GINA Global Initiative for Asthma

GM-CSF Granulocyte-Macrophage Colony-Stimulating Factor

GR Glucocorticoid Receptor GWA Genome-Wide Association HDAC2 Histone deacetylase type 2 HLA Human Leukocyte Antigen

HRV Human Rhinovirus

IBM Corp. International Business Machine Corporation

ICS Inhaled corticosteroid
IgE Immunogloulin E
IL-4 Interleukin-4

LABA Long-acting beta2 agonist

LAMA Long-acting muscarinic antagonist
LRI Lower Respiratort Infections
LTRA Leukotriene Receptor Antagonist
m-RNA messenger- Ribonucleic acid

NCCAM National Center for Complementary and Alternative

Medicine

NNT Number needed to treat

PC₂₀ Provocation Concentration of methcoline required to

cause a 20% fall in FEV1

PCAP Pharmacy Asthma Care Program

PDE Phosphdiestrase
PEF Peak Expiratory Flow
PKA Protein Kinase A

p-MDI pressurised Metered-Dose Inhaler RSV Respiratory Syncytial Virus SABA Short-acting beta2 agonist

SFC Salmeterol/Fluticasone Combination
SPSS Statistical Package for the Social Sciences

Th2
 T-lymphocyte helper cell type 2
 TNF-α
 Tumer Necrosis Factor-alpha
 TSLP
 Thymic Stromal Lymphopoietin

VCD Vocal Cord Dysfunction
VHC Valved holding chamber
WAAP Writen Asthma Action Plan
WHO World Health Organization

INTRODUCTION

Asthma is a common chronic disorder with increased prevalence worldwide. World Health Organization (WHO) estimates that 300 million people are affected with asthma (Anandan, et al., 2010).

Asthma is characterized by paroxysmal or persistent symptoms such as dyspnea, chest tightness, wheezing, sputum production and cough, associated with variable airflow limitation and a variable degree of airways hyper-responsiveness to endogenous or exogenous stimuli (Lougheed, et al., 2010). Although good asthma control can be achieved in clinical trials, it is more difficult to achieve in real-life situation studies (Rabe, et al., 2004). Despite advances in asthma management, a large number of patients are still "insufficiently controlled", putting them at risk for asthma-related morbidity and mortality (Mehuys, et al., 2008).

Salama and his colleagues reported that health care delivery was inadequate in Egypt as irrational prescribing and practices were generally widespread and misconceptions were commonly encountered, both among the public and health professionals. Therefore, minimum standards of health care for individuals with asthma must be identified (Salama, et al., 2010).

In an attempt to improve asthma control, the Global Initiative for Asthma (GINA) updated its asthma management guidelines