

Clinical Significance of Multidrug Resistant 1 Gene Polymorphism C3435T in Ulcerative Colitis

Thesis

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List of Contents

Title	PageNo.
List of Tables	i
List of Figures	iv
List of Abbreviations	vii
Introductio.....	
Aim of the Work.....	
Review of Literature	
▪ Chapter (I): Ulcerative Colitis	1
a. Definition.....	1
b. Epidemiology	1
c. Risk Factors	3
d. Pathophysiology of UC	
e. Diagnosis of UC	11
f. Classification	18
g-Prognosis.....	20
h-Treatment	21
▪ Chapter (II):Multi Drug Resistance (MDR1)	
Gene.....	23
a. Location of multidrug resistance (MDR1) Gene	
.....	23

b. Mechanism of Action of P-glycoprotein Transport System.....	23
c. Site of Action of P-glycoprotein	24
d. MDR1 Gene Polymorphisms and Related Disorders	25
e. Methods of Assay of MDR1 Gene.....	28
Subjects and Methods.....	37
Results.....	46
Discussion.....	70
SummaryandConclusion	76
Recommendations.....	79
References	
Arabic Summary	

List of Abbreviations

Abb.	Meaning
5-ASA	5-Aminosalicylic Acid
6-MP	6-Mercaptopurine
ABCB1	ATP-Binding Cassette Subfamily B Member 1
ASCA	Anti - Saccharomyces Cererisiae Antibodies
ATP	Adenosine Triphosphate
AZA	Azathioprine
CAPS	Cleaved Amplified Polymorphic Sequence
CBC	Complete Blood Count
CD	Crohn's Disease
CI	Confidence Interval
CRP	C-Reactive Protein
CT	Computed Tomography
DNA	Deoxyribonucleic Acid
dNTP	Deoxynucleotide
EDTA	Ethylenediaminetetraacetic acid
ESR	Erythrocyte Sedimentation Rate
χ^2	Chi Square
GC	Glucocorticoid
IBD	Inflammatory Bowel Disease
IL-1	Interleukin-1
WBCs	White Blood Cells

List of Abbreviations

Abb.	Meaning
IL-6	Interleukin-6
IL-8	Interleukin-8
MCH	Mean Corpuscular Hemoglobin
MCV	Mean Corpuscular Volume
MDR1	Multi Drug Resistance Gene
MRI	Magnetic Resonance Imaging
MUC2	Mucin 2
NF-k.B	Nuclear Factor-Kb
NSAIDS	Non-Steroidal Anti-Inflammatory Drugs
OR	Odds Ratio
P value	Probability Value
p-ANCA	Perinuclear Antineutrophil Cytoplasmic Antibodies
PCR	Polymerase Chain Reaction
PCR-RFLP	PCR-Restriction Fragment Length Polymorphism
P-gp	Permeability Glycoprotein
IV	Intra Venous
RNA	Ribonucleic acid
SD	Standard Deviation
SE	Standard Error of Population
SNP	Single Nucleotide Polymorphism
SPSS	Statistical Package for the Social Sciences

List of Abbreviations

Abb.	Meaning
Th-2	T Helper-2
TLC	Total Leucocytic Count
TNF- α	Tumour Necrosis Factor- α
U/S	Ultrasound
UC	Ulcerative Colitis
<i>E.coli</i>	<i>Escherichia Coli</i>
ELISA	Enzyme-linked Immunosorbent Assay
MHC	Major Histocompatibility Complex
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
KDa	Kilo Dalton
Rs	Reference SNP
FCGR2A	Fc Fragment of IgG Receptor
p	Short Arm of Chromosome
q	Long Arm of Chromosome

List of Tables

TableNo.Title	PageNo.
Table (1): Diagnostic Features of UC.....	17
Table (2): Classification of Disease Severity in UC patients	19
Table (3): Mayo Activity Scoring Index for UC	19
Table (4): Characteristics of UC Patients.....	51
Table(5): Descriptive and Comparative Statistics of General Laboratory Parameters in UC patients and Healthy Controls	52
Table (6): Descriptive and Comparative Statistics of Genotype Frequencies of MDR1(C3435T) Gene Polymorphism in UC Patients and Healthy Controls	53
Table (7): Statistical Comparison of the Frequency of Genotypes of MDR1 (C3435T) Gene Polymorphism in UC Patients and Healthy Controls	54
Table (8): Descriptive and Comparative Statistics of Allele Frequencies of MDR1 (C3435T)Gene Polymorphism in UC Patients and Healthy Controls	56
Table (9): Descriptive and Comparative Statistics of Genotype Frequencies of MDR1 (C3435T)Gene Polymorphism in Male and Female UC Patients	
Table (10): Descriptive and Comparative Statistics of Allele Frequencies of MDR1 (C3435T) Gene Polymorphism in Male and Female UC Patients	

Table (11):	Descriptive and Comparative Statistics of MDR1 (C3435T) Gene Polymorphism in UC Patients Regarding Disease Severity
Table (12):	Statistical Comparison of the Frequency of Different Genotypes of MDR1 (C3435T) Gene Polymorphism in Mild, Moderate and Severe UC Patients
Table (13):	Descriptive and Comparative Statistics of Allele Frequencies of MDR1 (C3435T) Gene Polymorphism in Mild, Moderate and Severe UC Patients
Table (14):	Descriptive and Comparative Statistics of MDR1 (C3435T) Gene Polymorphism in GC Responders and GC Non-responders
Table (15):	Statistical Comparison of the Frequency of Genotypes of MDR1 (C3435T) Gene Polymorphism among GC Responders and GC Non-responders
Table (16):	Descriptive and Comparative Statistics of Allele Frequencies of MDR1 (C3435T) Gene Polymorphism in GC Responders and GC Non-responders.....

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Gross features of UC	8
Figure (2):	Microscopic features suggestive for diagnosis of UC	9
Figure (3):	Pathophysiology and therapeutic approaches of UC.....	11
Figure(4):	The therapeutic pyramid for ulcerative colitis	21
Figure (5):	Algorithm for treatment of UC.....	23
Figure (6):	Cytogenetic localization of MDR1	23
Figure (7):	Structure of P-glycoprotein	25
Figure (8):	Site of action of P-glycoprotein.....	27
Figure (9):	The localization of P-gp at the Blood Brain Barrier	28
Figure (10):	MDR1 gene organization pattern.....	29
Figure (11):	The steps involved in the first few rounds of a PCR	31
Figure (12):	Steps of real-time PCR	36
Figure (13):	Band patterns of Sau3AI restriction site(C3435T) of MDR1 gene	43
Figure (14):	Frequency of MDR1 (C3435T) genotypes in group I and group II	
Figure (15):	Frequency of MDR1 alleles (C and T) in UC patients and healthy controls	
Figure (16):	Frequency distribution of MDR1 (C3435T) genotypes in mild, moderate and severe UC patients	

Figure (17): Frequency distribution of MDR1 (C3435T) genotypes in GC responders and GC non-responders

Introduction

Ulcerative colitis (UC) is one of the inflammatory bowel diseases (IBD) which affects the colon and rectum. It is characterized by recurrent episodes of inflammation restricted to the mucosa only (*Bodor & Kelly, 2005 and Molodecky et al., 2012*). The pathogenesis of UC is thought to rely on defective mucosal barrier and dysregulated immune response to a host's microbiota in genetically susceptible individuals (*Hisamatsu et al., 2013*).

Among the genes regulating innate immunity is a member of adenosine triphosphate - binding cassette superfamily which is also known as multidrug resistance 1 (MDR1). The encoded product of the MDR1 gene is P-glycoprotein 170 (P-gp). The latter is expressed on epithelial cells of kidney, liver, pancreas, small intestine and colon. Due to its expression on epithelial surfaces of enterocytes and colon, it plays an important role in the secretion of toxic compounds from the intracellular area to extracellular area with its ATP-dependent efflux transporter pump function. It is thought that the physiologic role of intestinal P-gp might prevent entry of bacterial toxins into the intestinal wall mucosa and prevent intestinal inflammation. Thus, alteration of P-gp expression and function may contribute to pathogenesis of IBD (*Tahara et al., 2009*).

Several drugs routinely used in UC therapy including corticosteroids and immunosuppressants are substrates for P-gp. However, some patients are resistant to these drugs and require surgery. Many studies have suggested that single nucleotide polymorphisms (SNPs) of MDR1 gene changes the level of expression of P-gp and might be associated with corticosteroid resistance, failure of medical treatment, increasing disease severity and therefore the need for surgery in IBD (***Brambila-Tapia,2013 and Yanju et al.,2015***).

One of the MDR1 gene polymorphism is C3435T which is the matter of many researches (***Bodor and Kelly,2005, Onnie et al.,2006 and Yanju et al.,2015***).