Evaluation of Role of intestinal microflora on Phagocytic Function of Leucocytes in Diabetic Patients

Thesis

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By

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AAT	= α1-antitrypsin
AAD	= antibiotic-associated diarrhea
AC	= acarbose
AGEs	= advanced glycated end products
AKt	= associated kinase t
ATP	= adenosine triphosphate
BMI	= body mass index
CBC	= Complete blood count
CD	= Crohn's Disease
CFU	= Colony forming unit
Cox	= cyclo-oxygenase
CTLA-4	= cytotoxic T-lymphocyte-associated protein-4
DCs	= Dendritic cells
DM	Diabetes mellitus
DNA	= Deoxy riboneuclic acid
EHEC	= enterohemorrhagic E. coli
FBS	= fasting blood sugar
FFA	= free fatty acids
FIAF	= fasting-induced adipocyte factor
G6PD	= glucose 6 phosphate dehydrogenase
GALT	= Gut-associated lymphoid tissue
GI	= gastrointestinal

GLP-2	glucagon-like peptide-2
GLUT	= glucose transporter
HbA1c	=glycated hemoglobin
HCAs	= heterocyclic amines
HF-OFS	= high-fat oligofructose
H.Pylori	= Helicobacter Pylori
IBD	= inflammatory bowel diseases
IBS	= irritable bowel syndrome
ICAM-1	= intercellular adhesion molecule-1
IDDM	= insulin dependant diabetes mellitus
sIgA	= secretory Immunoglobulin A
IgE	= Immunoglobulin E
IGF1	= insulin growth factor 1
IgG	= Immunoglobulin G
IkB	= inhibitory kB
IL	= interleukin
La	= Lactobacillus acidophilus
LAB	= Lactic Acid Bacteria
LcS	= Lactobacillus casei strain Shirota
LF	= lactoferrin
LPS	= lipopolysaccharide
MAP	= mitogen-activated protein
MRS agar	= de man rogosa sharp agar
NAD	= nicotinamide adenine dinuclotide

NADPH	= nicotinamide adenine dinuclotide diphosphate
NF-kB	= nuclear factor-kappa-B
NK	= natural killer cells
NO	= Nitric oxide
NOD mice	= non obese diabetic mice
OVA	= ova-albumin
PBMCs	= peripheral blood mononuclear cells
PDX-1	= Pancreatic duodenal homeobox-1
PKC	= protein kinase C
PMNs	= polymorphonuclear leucocytes
PPBS	= postprandial blood sugar
PRR	= pattern recognition receptors
RAGE	= The receptors for AGE
ROS	= Reactive Oxygen Species
SCFAs	= short chain fatty acids
SPP	= Species
T1D	= Type1 diabetes
T2D	= type 2 diabetes
TAG	= triacylglycerol
TGFβ	= transforming growth factor β
Th1	=T helper1
Th2	= T helper2
TLC	= total leukocytic counts
TLR	= Toll-like receptors

TNF	= tumor necrosis factor
Treg	= regulatory T-cell
Tr1	= regulatory T-cell1
UC	= ulcerative colitis
Vs.	= versus

Introduction

Diabetes is a chronic global health problem; about 246 million peoples worldwide are currently estimated to have diabetes, a global prevalence of 5.9% ***(IDF, 2006).***

The diabetes is expected to cause 3.8 million deaths among adults 20 years of age and older, approximately 6% of total world mortality. Over two third of these death occur in developing countries ***(IDF, 2006).***

Type 2 diabetes is the most common form of diabetes and accounts for 85%-95% of all diabetes in developed countries and higher proportion in developing countries ***(Essue et al., 2007).***

Infection is an important cause of morbidity and mortality in diabetic patient. Infection is responsible for 6.0% of diabetic deaths; chronic hyperglycemia impairs host defense mechanism, such as polymorphonuclear leucocytes (PMNL) function including chemotaxis, adherence and phagocytosis ***(Bhattacharya et al., 2007).***

Several studies work upon the intestinal microflora and their capacity to interact with the immune system of the host showing the following results. The intestinal microflora keep normal physiological and immunological intestinal barrier by secretion of antimicrobial substances, stimulation of expression of protective molecules including Toll Like Receptors family (TLRs) that signal the presence of specific microorganism to the host to initiate specific intracellular immune response ***(Corthésy et al., 2007)*.**

Lactobacillus acidophilus increase the phagocytic capacity of murine peritoneal macrophages in addition ,it was demonstrated that L-acidophilus La1 increase the phagocytic capacity of leucocytes (mononuclear and polymorphonuclear) isolated from the blood of humans who had consumed probiotics, a further study showed that a milk product containing L-rhamnosus GG up-regulate the expression of important phagocytosis receptors ***(Delecenserie et al., 2008)*.**

Lactobacillus increases the cytotoxic activity of natural killer cells ***(Corthésy et al., 2007)*.**

Furthermore, it seems that the positive effects of probiotics on phagocytosis and NK cell function may be greater in immune

deficient elderly persons. Thus consumption of probiotics may favour innate immune defences in immune deficient individuals ***(Delecenserie et al., 2008)*.**

Lactobacilli keep Th1\Th2 balance via stimulation of T regulatory cell ***(Yeun et al., 2007)*.**