Serum levels of vascular endothelial growth factor in patients with duchenne muscular dystrophy

Thesis

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مستويات عامل النمو البطاني الوعائي في مرضى ضمور العضلات دوشين

رسالة

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List of Abbreviations

AAR	Area to amplitude ratio
AAV	Adenovirus vectors
ACE	Angiotensin converting enzyme
ACE	Angiotensin converting enzyme
AFOs	Ankle-foot orthoses
AMD	Age related maculer degeneration
AMI	Acute myocardial infarction
AML	Acute myeloid leukemia
ARB	Angiotensin receptor blocker
Aβ42	Amyloid beta peptide protein
bFGF	Basic fibroblast growth factor
BMD	Beckher musculer dystrophy
CD	Cluster of differentiation
CMR	Cardiovascular magnetic resonance
COPD	Chronic obstructive pulmonary disease
CPK	Creatine phosphokinase
D1	Active domain 1
D2	Active domain 2
DGC	Dystrophin-associated glycoprotein complex
DGC	Dystriphin –glycoprotein complex
DMD	Duchenne muscular dystrophy
DR	Diabetic retinopathy
EMG	Electromyography
EPC	Endothelial progenitor cell
FVC	Forced vital capacity
HDAC	Histone deacetylase
HPCs	Haemopoietic cells
HSC	Haemopoietic stem cell
MABs	Mesoangioblasts
MDs	Muscular dystrophies
MEP	Maximal expiratory pressure
MH	Malignant hyperthermia
MIP	Maximal inspiratory pressure
MLPA	Multiplex ligation-dependent probe amplification
MUP	Motor unit potential
NFG	Nerve growth factor
nNOS	Neuronal nitric oxide synthase
NO	Nitric oxide

PCR	Polymerase chain reaction
PDGF	Plateltes derived growth factor
PLGF	Placenta growth factor
PTP	Protein tyrosine phosphatases
QUS	Quantitative muscle ultrasound
rAAV	Recombinant adeno-associated viral vector
REM	Rapid eye movement
RPTPs	Receptor-like protein tyrosine phosphatases
SC	Satellite cell
Src-PTK	Src family protein tyrosine kinase
Th 2	T helper 2
TK	Tyrosine kinase
TNF-α	Tumor necrosis factor alfa
VC	Vital capacity
VEGF	Vascular endothelial growth factor
VPF	Vascular permeability factor

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Abstract

*** Background:** Muscular Dystrophies (MDs) are a heterogeneous group of degenerative disorders often characterized by progressive muscle weakness and fragility. The most common and severe form among children is Duchenne muscular dystrophy (DMD), caused by mutations in the dystrophin gene, with an average life expectancy around 25 years of age.

Vasculer endothelial growth factor (VEGF) was originally described as an endothelial cell-specific mitogen. VEGF is produced by many cell types including tumor cells, macrophages, platelets, keratinocytes, and renal mesangial cells . VEGF plays a role in normal physiological functions such as bone formation, hematopoiesis and wound healing. **VEGF** may reflect hypoxic and/or ischemic conditions in muscle tissue and have a relationship with the process of disease progression in DMD patients.

CD45 is the prototypic member of transmembrane receptor-like protein tyrosine phosphatases (RPTPs) and has essential roles in immune functions.

CD34 is a cell surface antigen of unknown function expressed in humans in hematopoietic stem cells and vascular endothelium

***Aim of the study:** Measuring serum vascular endothelial growth factor, CD34 and CD45 level in patients with Duchenne musculer dystrophy in comparison with normal

persons as a new line of diagnosis for new lines of treatment.

***Materials and methods :** This study is a cross sectional study and it was conducted on 20 patients recruited from Neurology out Patient clinic of Pediatric Hospital, Faculty of Medicine; Ain shams University.

***Results:** In the present study VEGF,CD34 and CD45 were higher in DMD patients compared to controls.

***Conclusion:** VEGF may reflect hypoxic and/or ischemic conditions in muscle tissue, and have a relationship with the process of disease progression in DMD patients.

Introduction

Muscular Dystrophies (MD's) are a heterogeneous group of degenerative disorders often characterized by progressive muscle weakness and fragility. Many of these diseases result from mutations in genes encoding proteins of the dystrophin-glycoprotein complex (DGC). The most common and severe form among children is Duchenne muscular dystrophy (DMD), caused by mutations in the dystrophin gene, with an average life expectancy around 25 years of age ***(Bengtsson et al., 2015***).

Duchenne muscular dystrophy is X-linked recessive inherited neuromuscular disorder (***Chen et al., 2014 and Falzarano et al., 2015***). The most frequent deletion spots ranged from exon45 to exon52, and exon2, exon19 were the two most frequently detected duplication spots ***(Ji et al .,2015).***

The disease results in progressive weakness and wasting of all the striated muscles including the respiratory muscles. The consequences are loss of ambulation before teen ages, cardiac involvement and breathing difficulties, the main cause of death ***(LoMauro et al.,2015).***

VEGF, also known as vascular permeability factor (VPF), was originally described as an endothelial cell-specific mitogen. VEGF is produced by many cell types including tumor cells, macrophages, platelets,

keratinocytes, and renal mesangial cells .The activities of VEGF are not limited to the vascular system; VEGF plays a role in normal physiological functions such as bone formation, hematopoiesis and wound healing (***Angela et al.,2013***).

With hypoxic stress, vascular endothelial growth factor (VEGF) is a signal protein produced by cells and further contributes to improvement of vascular functions and restoring the oxygen supply to tissues ***(Xie et al., 2014***).

In patients with muscular dystrophy, such as DMD, microcirculation abnormalities and hypoxic ischemic conditions in muscle tissues are suspected to be induced by non-symptomatic coagulation fibrinolysis abnormalities and vascular dysfunction (***Saito et al., 2009).***The authors recorded higher levels of VEGF in DMD patients compared to healthy controls .Further; the level of VEGF level of bedridden patients was significantly elevated compared with chair-bound patients. They also concluded that VEGF may reflect hypoxic and/or ischemic conditions in muscle tissue, and have a relationship with the process of disease progression in DMD patients.

CD45 is the prototypic member of transmembrane receptor-like protein tyrosine phosphatases (RPTPs) and has essential roles in immune functions. The cytoplasmic region of CD45, like many other RPTPs, contains two

homologous protein tyrosine phosphatase domains, active domain 1 (D1) and catalytically impaired domain 2 (D2).

CD45, also known as the leukocyte common antigen, is the prototype of the receptor-like PTP (RPTP) subfamily and is found in all nucleated hematopoietic cells (***Hyun-Joo et al., 2013).***

CD34 is a cell surface antigen of unknown function expressed in humans in hematopoietic stem cells and vascular endothelium . ***(Satterthwaite et al.,1992.)***

The CD34 antigen represents to date the only moleculewhose expression within the blood system is restricted to a small number of primitive progenitor cells in the bone marrow.