

# Quality Control, Intervention and Management of Patients with Diabetes Mellitus

Arnon Blum\*

Bar Ilan University, Israel

\*Corresponding author: Arnon Blum, Bar Ilan University, Israel, Tel: 2129063900; E-mail: navablum@hotmail.com

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## Editorial

Many patients with Diabetes Mellitus (DM) do not maintain their disease well and thus can't properly manage DM and its cardiovascular complications. There are multiple reasons for this poor management including lack of patients' knowledge and understanding, lack of proper intervention by the medical community, and inability of the medical authorities to cooperate or to work in harmony with different medical disciplines that are involved with diabetic patient care and long-term management.

We believe that the main issue here is the basic concept of vascular complications that is somehow neglected in diabetic patients. Physicians who are dedicated to treat patients with diabetes focus on sugar level, Hemoglobin A1C%, but not on end organ damage/complications.

We believe that diabetes mellitus is a very complicated multi systemic disease, and the main issue in diabetes is the vascular complications-that involve all organs in the body, starting from vascular complications of the retinal arteries causing blindness, vascular complications of the kidneys, causing end stage renal failure, and general atherosclerosis (accelerated atherosclerosis) causing peripheral artery disease, coronary artery disease, cerebrovascular disease and cognitive impairment.

Our belief is that we should study the present status of patients' management, including patients' education, pharmacological management and monitoring, educational interventions, and the multidisciplinary combined approach of management, and to change the goals of management of this chronic disease, focusing on the vascular complications and the end organ damage and less on sugar level as the main goal of treatment.

We believe that evaluating endothelial function and measuring the ability to grow colonies of endothelial progenitor stem cells could be a sensitive biomarker for vascular complications of diabetes mellitus that will lead eventually to organ failure.

In order to explore these aspects of diabetes we should check the Hemoglobin A1C% (HgA1C%), protein urea (as a bio marker of kidney function), but to focus on vascular

inflammatory markers like C reactive protein (CRP), vascular endothelial growth factor (VEGF), intercellular adhesion molecule (ICAM-1), vascular cellular adhesion molecule (VCAM-1), and vascular endothelial function (that will be measured non-invasively by the brachial artery method), to focus on genetic vascular traits like the ability to grow endothelial progenitor stem cells-colony forming units (EPC-CFU) in culture.

Our goal is to achieve a better understanding of vascular responsiveness (that will be evaluated by non invasive methods like the endothelial function measurement) and stem cells' stimulation and function (EPC-CFUs growth), the inflammatory profile (CRP level and other inflammatory markers) [1-5].

## The Non Invasive Methods of Vascular Measurements and Evaluation

### Flow Mediated Diameter percent change (FMD %)

All measurements of brachial artery diameter and FMD will be done early in the morning, in a quiet and dark room and at controlled ambient temperatures between 20°C and 26°C. Studies will be conducted after an over night fast of at least 10 hours (water permitted), with the subjects supine and after 10 minutes of rest.

The subject's right arm will be comfortably immobilized in the extended position, allowing for ultrasound scanning of the brachial artery 5-10 cm above the antecubital fossa. In each examination, recording of vessel images will be followed by inflation of a cuff to supra-systolic pressure (40 to 50 mmHg above systolic pressure) for 5 minutes. Then the cuff will be deflated and the brachial artery diameter will be imaged and recorded for 3 minutes. FMD% more than 10% is considered a normal response.

Lower than 10% FMD% reflects endothelial dysfunction, which means a high likelihood to develop a cardiovascular event in the future. Subjects with negative FMD% results (the

artery is constricted after stress and not dilated as was expected) have the worst prognosis.

### Isolation of endothelial progenitor cells from peripheral blood

The investigator who will perform the laboratory experiments will be blinded to the patients' clinical data. Venous blood samples will be drawn from an antecubital vein into ethylenediaminetetraacetic acid-containing tubes. Forty milliliters of blood will be processed; peripheral blood mononuclear cells will be isolated by Ficoll density-gradient centrifugation, washed twice in phosphate-buffered saline with 5% fetal bovine serum, and re-suspended in media-EndoCult basal media with supplements (Stem Cell Technologies, Vancouver, BC, Canada)-for endothelial progenitor cell colony forming assay [6].

### Assay of colony forming units

Cells will be plated on human fibronectin-coated plates (BIOCOAT; Becton Dickinson Labware, Bedford, Mass) at a density of  $5 \times 10^6$  cells/well and incubated at 37°C in humidified 5% CO<sub>2</sub>. After 48 hours, the non-adherent cells will be re-plated onto fibronectin-coated 24-well plates at a density of  $1 \times 10^6$  cells/well. After 5 days colony forming units (defined as a central core of rounded cells surrounded by elongated and spindle-shaped cells) will be counted manually in 8 wells of a 24-well plate. The average number of colony forming units per well is represented [7].

### Summary

Measuring vascular parameters and vascular genetic traits (like endothelial stem cells in the peripheral blood) will give a

better opportunity to understand the development of vascular complications in patients with diabetes. It will open a new approach in the management of diabetic patients and may prevent future cardio-vascular complications and will guide timely interventions.

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