

## **Title : Evaluation of endothelial function in patients with Type2 Diabetes Mellitus attending a tertiary care medical centre in South India**

Usharani Pingali, Chandrasekhar Nutalapati, Niranjan Koilagundla

Presenter Contact Details : Usharani Pingali, MD, DNB, FIPS, PGDipBioethics, Professor and Head; Dept of Clinical Pharmacology and Therapeutics, Nizam's Institute of Medical Sciences ( NIMS). Hyderabad. India  
Email [ushapingali@yahoo.com](mailto:ushapingali@yahoo.com); Phone: +919849574143; +91-40-23489211

Chandrasekhar Nutalapati – Senior resident, Department of Clinical Pharmacology and Therapeutics, Nizam's Institute of Medical Sciences (NIMS), Panjagutta, Hyderabad. India.

Niranjan Koilagundla

DM student Dept of Clinical Pharmacology and Therapeutics, Nizam's Institute of Medical Sciences (NIMS), Hyderabad. India.

### **Abstract:**

**Purpose:** Diabetes mellitus (DM) is associated with increased risk of cardiovascular (CV) disease. In normal healthy endothelium there is a balance between the release of vasodilatory and vasoconstrictive factors. Endothelial dysfunction(ED) is characterised by loss of endothelium dependent vasodilatation and can be considered as a major step in atherogenesis. Decreased production, increased degradation or decreased sensitivity to nitric oxide are involved in ED. Early signs of diabetic vasculopathy include impaired endothelial function and increased arterial stiffness, which are independent predictors of CV events. Testing ED noninvasively using digital pulse photoplethysmography helps in evaluation of patients with CV risk. Thus the present study was designed to evaluate the ED by endothelial dependent vascular response to salbutamol and measuring the reflection index (RI) in type2 diabetes mellitus patients at a tertiary care medical centre.

**Methods:** Drug naive type2 diabetic subjects and controls, were enrolled for evaluation after written informed consent to ethics committee approved protocol. Subjects' demography, medical history were recorded. Laboratory tests for clinical chemistry, hsCRP, lipids, HbA1c done. Endothelial function determined by endothelial dependent vascular response to salbutamol challenge; assessed by change in reflection index (RI) using photoplethysmography(PPG), non-invasive method for deriving digital pulse volume (DPV) by measuring the transmission of infrared (IR) light through the pulp of the finger (indexfinger). After overnight fast subjects rested for about half hour in temperature, humidity controlled room. Vital parameters were recorded. Baseline DPG done and three measurements of RI (Reflection index =  $b/a \times 100$ ) recorded; mean value taken. Subject then inhaled 400mcg salbutamol through spacer. Fifteen minutes later three readings of RI were noted, mean calculated. Percentage change in mean RI from baseline recorded. Endothelial dysfunction defined as  $RI \leq 6\%$  (salbutamol challenge test).

**Results:**

In the present study 152 (82M; 70F) diabetic subjects and 148 (77M; 71F) matched controls were included. BMI was significantly higher in diabetics ( $26.2 \pm 3.4$  kg/m<sup>2</sup>) than healthy controls ( $21.3 \pm 2.9$  kg/m<sup>2</sup>). Biochemical laboratory parameters were statistically highly significant compared to controls. In control group the values were within normal range but diabetic subjects had higher plasma glucose, HbA1c; total cholesterol; triglycerides; LDL and lower HDL values. The hsCRP was also higher at  $8.1 \pm 1.4$  mg/dl. Blood urea, serum creatinine and hepatic parameters were within normal range. The mean change in reflection index (RI%), is considered as a marker of endothelial function and endothelial dependent vasodilator response. The change in RI was  $-14.2 \pm 1.2\%$  (presalbutamol  $64.9 \pm 8.6$  to  $50.7 \pm 9.8$  post salbutamol) indicating normal response. In diabetic subjects however the response presalbutamol was  $60.6 \pm 9.6$  and post salbutamol was  $58.2 \pm 8.6$ ; with mean RI being  $-2.4 \pm 0.8\%$ ; indicating endothelial dysfunction.

**Conclusion:** Advances on assessment of endothelial function in last decades, mainly through the non-invasive techniques have facilitated either basic or clinical researches in cardiovascular and endocrine fields. The results of the present study highlight the importance of reflection index (RI%) in identifying vascular damage in subjects with diabetes mellitus who have high cardiovascular risk. The change in reflection index was found to be a good, sensitive, simple and reliable method for assessing subjects with increased CV risk and also serves as a non-invasive independent predictor of cardiovascular morbidity. A large number of evidences suggest that endothelial dysfunction is the main etiological factor for micro and macro vascular complications in DM. Hence identifying and correcting endothelial dysfunction helps in reducing cardiovascular morbidity. Further, long term studies in diabetic subjects to assessment reflection index for evaluation of the reversal of endothelial function with therapeutic intervention are suggested.

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