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# Review Article and Clinical Experience: DIABETES MELLITUS AND ENDOTHELIAL DYSFUNCTION: A CLINICAL APPROACH (Molecular Basis for Clinical Application)

*Abstrak :*

*SYNDROME-36 (presented in the year 2002) compiled by the Author since 1992 (SYNDROME-11) represents a cluster of 36 components (comprises Risk & Protective Factors, and Predictors), which determines the quality of Endothelial Function. The most frequent causes of Endothelial Dysfunction (ED) are Hypertension, Diabetes Mellitus, and Lipid (Dyslipidemia) which can be abbreviated as "HDL-Syndrome". In clinical practice, cigarette should be included as a major risk factor in the pathogenesis of atherosclerosis ("HDL-C Syndrome"). Four functional targets for the quality of the Endothelial Cell function are: 1. Lumen (Vasoconstrictors: ET-1, and Vasodilators: NO, Bradykinin, Hyperpolarizing Factor), 2. Growth (Stimulators: PDGF, ET, All, and Inhibitors: NO, PG12, TGF), 3. Inflammation (Proinflammatory: Adhesion Molecules, and Anti Inflammatory), and 4. Hemostasis (Prothrombotic: PAI-1, and Anti Thrombotic: PG12, tPA). The Endothelial Cell produces mediators that induce vasoconstriction, including ET (Endothelin), Prostaglandins (PGG2 and PGH2), and Angiotensin-11 (AII). The key enzyme that regulates the local generation of AII is Angiotensin Converting Enzyme (ACE). Angiotensin-II also stimulates the generation of Superoxide. Nitric Oxide (NO) is not only involved in the control of vasomotor tone, but also in vascular homeostasis and immunological functions; eleven (11) roles of NO as atheroprotector of Endothelial Dysfunction have been summarized by the author. The five principles of thetreatment of ED esp. in Diabetes Mellitus are: 1. Insulin Sensitizer (in DM: excellent glycemic control is obligatory), 2. ACEinhibitors (Tissue ACE-IS: Quinapril etc), 3. Lipid Modulators (Statins: Atorvastatin etc, and or Fibrates), 4. Antioxidants (Raxofelast 600 mg bid, Vit. C 500 mg/day, Vit. E 400-800 mg/day, Beta Carotene), and 5. Arginine Supplementation (Diet-KV, tablet Arginine 450 mg/day). Diet-KV comprises 68% cal. Cbh, 12% cal. Protein, 20% cal. Fat (Cholesterol < 300 mg/day), Fiber ± 35 g/day, Enriched with food supplements containing Arginine, Folate, Vit. B6, and Vit. B12. Several studies, fe. TREND (1996), BANFF (2000) have established that a potent tissue ACE-I (Quinapril) improves Endothelial Function in humans. Interestingly, the BANFF study showed this anti hypertensive agent from other classes has no effect on Endothelial Function. These results are strengthened by those from QUO VADIS (2000). In this study the treatment with Quinapril significantly reduced clinical ischemic events during the one-year period after coronary bypass graft surgery. The rank order of potency of several different ACE inhibitors have been determined by several investigators as follows (by sequent numbers): 1. Quinapril = Benazepril, 2. Ramipril, 3. Perindopril, 4. Lisinopril, 5. Enalapril, 6. Fosinopril, and 7. Captopril. Conclusion: Endothelial Dysfunction (ED) has been widely documented in patients with Diabetes Mellitus and more frequently in those with "HDL Syndrome". Five principles of treatment of ED are summarized. Tissue-ACE-IS (Quinapril is the most potent one) play pivotal roles in the improvement of ED and these lines of evidence are strengthened by the results of TREND, BANFF, and QUO VADIS studies.*

*Keyword :*

*diabetes mellitus, endothelium, hypertension, dyslipidemia*

*Daftar Pustaka :*

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