ABSTRACT

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Department of Biological and Medical Sciences

Title of Diploma Thesis: Effect of glipizide on the expression and function of endoglin and related biomarkers of endothelial dysfunction in type II diabetes mellitus

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Aim: The aim of this thesis was to determine how glipizide affects the expression and function of endoglin, its transcription factors and related biomarkers of endothelial dysfunction, soluble endoglin levels and monocyte adhesion to human diabetic coronary artery endothelial cells.

Methods: In this thesis we worked with human diabetic coronary artery endothelial cells. These were premedicated with glipizide at various times and concentrations. We measured protein expression of endoglin and biomarkers of endothelial dysfunction using flow cytometry. We also measured monocyte adhesion to endothelial cells using flow cytometry. We detected soluble endoglin levels by ELISA and measured mRNA expression of endoglin, its transcription factors and markers of inflammation by PCR.

Results: We demonstrated that premedication with 200µM concentration of glipizide led to a decrease in endoglin protein expression after 24 and 48 hours. The protein expression of the adhesion molecule ICAM-1 was also increased after 24 hours. After premedication with 100µM glipizide, the adhesion molecule VCAM-1 showed a decrease in protein expression after 48 hours. We also found that mRNA expression of the transcription factors Sp1, HIF-1α and the inflammation marker CCL2 was reduced after 16 hours premedication with 200µM glipizide. In contrast, under the same conditions there is an increase in mRNA expression of ICAM-1 and after 8 hours premedication there is also an increase in mRNA expression of E-selectin. At the times and concentrations examined, glipizide had no significant effect on monocyte adhesion or sEng formation.

Conclusion: In conclusion, glipizide affects the expression of endoglin and related adhesion molecules and markers that are associated with endothelial dysfunction. The reduction in endoglin expression suggests a possible therapeutic potential of glipizide in the regulation of vascular function. Further detailed in vitro and in vivo studies are required to fully understand and confirm the effect of glipizide on endoglin and other aspects of endothelial dysfunction.

Keywords: endoglin, endothelial dysfunction, diabetes mellitus, glipizide