The goal of this study was to evaluate the effects of captopril on plasma glucose concentration. The daily profiles of the plasma glucose levels were determined in 12 non-insulin-dependent diabetic normotensive subjects, treated with or without captopril at a dose of 25 mg 3 times/day. Forearm blood flow was also measured by strain-gauge plethysmography. Administration of captopril improved the daily profile of the plasma glucose level. Postprandial forearm blood flow was also augmented 2 h after a meal. These results suggest that angiotensin-converting enzyme inhibitors may improve glucose metabolism in diabetic subjects, possibly through enhancement of blood flow to skeletal muscle. *Diabetes Care* **13**:1109–11, 1990

It is well known that diabetic subjects sometimes have associated hypertension. Although many hypotensive agents have adverse effects on glucose tolerance and lipid metabolism (1), it has been reported that angiotensin-converting enzyme inhibitors (ACEIs) do not affect the plasma glucose concentration or insulin level during the oral glucose tolerance test, even in the case of long-term administration of captopril in 12 normotensive NIDDM, excluding the hand circulation with a wrist blood pressure cuff inflated to 200 mmHg (expressed as ml · 100 ml⁻¹ · min⁻¹) (4). Vascular resistance was calculated from the equation for mean blood pressure divided by forearm blood flow (mmHg/ml · 100 ml⁻¹ · min⁻¹). In a pilot study (*n* = 4), forearm blood flow tended to decrease after breakfast through 1400. However, when captopril was administered, forearm blood flow increased significantly 2 h after breakfast and returned to basal levels before lunch with a slight but not significant increase 1 and 2 h after lunch. Hematocrit determined 2 h after lunch did not differ from control values before lunch. Based on these findings, forearm blood flow was determined before and 2 h after lunch in the remaining subjects. Plasma insulin levels were also measured in some of the subjects (*n* = 8) before and 2 h after lunch by a specific radioimmunoassay. Individual daily meals were identical during the 2 days of the study and consisted of 1300–2000 kcal containing 70–90 g protein, 50–55 g fat, and 1200–1550 ml water.

Data are expressed as means ± SE. Statistical differences were evaluated by paired Student’s *t* test or analysis of variance with repeated measurements. To evaluate changes between times, a Scheffe-type criterion was used.
RESULTS

The daily profiles of the plasma glucose levels are shown in Fig. 1. Captopril administration tended to decrease the plasma glucose level by 0.6–2.2 mM at any point. The difference was significant at 1200 and 1400. When the sum of plasma glucose levels at each time point was analyzed, captopril was found to significantly decrease the sum of plasma glucose levels from 78.2 ± 8.0 to 71.7 ± 7.1 mM (P < 0.02).

As shown in Fig. 2, postprandial forearm blood flow was decreased slightly but not significantly on the control day. On the other hand, captopril administration significantly augmented the postprandial forearm blood flow from 0.66 ± 0.08 to 1.01 ± 0.16 ml · 100 ml⁻¹ · min⁻¹ (P < 0.05) in association with a significant decrease in blood pressure. As a result, vascular resistance after a meal was also decreased after oral intake of captopril. Plasma insulin levels in response to a meal on 2 days, with or without captopril administration, were not different (10.3 ± 1.7 to 21.6 ± 4.7 vs. 10.8 ± 1.2 to 16.3 ± 2.8 μU/ml).

DISCUSSION

This study demonstrates that acute administration of ACEI exerts a marginal but beneficial effect on glucose metabolism in NIDDM, as shown by lower plasma glucose levels during captopril administration compared with untreated control subjects. Lowering of plasma glucose after captopril administration is not solely due to hemodilution. In fact, hypoglycemic episodes during captopril administration, concomitant with sulfonylureas and biguanides, have been reported in several subjects with NIDDM (5,6). Rett et al. (3) demonstrated that captopril increased both whole-body glucose elimination and the utilization rate in the forearm musculature, possibly through kinin-mediated forearm vasodilation. Recently, these findings were confirmed by another group (7). However, vasodilatory effects of ACEIs on regional blood flow distribution are not uniform in various organs. A marked increase of blood flow was observed in the kidneys and skeletal muscle, whereas hepatic blood flow was reported to be decreased by 5% in one study (8) and 25% in another (9). Food intake has been reported to increase splanchnic blood flow by 30–60% within 30–90 min.
due to increased blood flow to the splanchnic vascular beds after the meal. Note, that postprandial forearm blood flow was augmented 2 h after administration of 25 mg captopril. This could be another explanation for the improved glucose metabolism in captopril-treated NIDDM patients. However, we cannot exclude the possibility that the captopril-induced reduction of postprandial hepatic blood flow might reduce gastrointestinal glucose absorption and/or the release of hepatic glucose into the portal system. Whatever the mechanisms are, an improved glucose metabolism might add a unique advantage to ACEIs for the treatment of diabetic hyper-tension, in addition to their beneficial effect on diabetic nephropathy, possibly by ameliorating glomerular capillary hypertension.

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REFERENCES


Self-Care Predictors of Metabolic Control in NIDDM Patients

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The objective of this study was to evaluate whether the relationship between self-care behavior and metabolic control is comparable in patients with non-insulin-dependent diabetes mellitus (NIDDM) on insulin and not on insulin. We studied 84 NIDDM patients hospitalized for an elective admission in Washington University's Model Demonstration Unit. At admission, patients reported the frequency of exercise, blood glucose monitoring, and meal skipping for the previous 2 wk. Metabolic control over the previous 8–12 wk was determined from glycosylated hemoglobin assays. In cross-sectional analysis controlling for patient sociodemographic and health characteristics, glycosylated hemoglobin levels were positively related to meal skipping (P = 0.0008) and negatively related to the frequency of blood glucose monitoring (P = 0.0025). Self-care behaviors explained 26% of the variance in glycosylated hemoglobin levels in NIDDM patients. Multivariate modeling demonstrated no significant interaction effects between insulin treatment and self-care on metabolic control. In conclusion, these findings support the clinical significance of self-care activities for metabolic control in NIDDM patients, particularly meal skipping and blood glucose monitoring. Diabetes Care 13:1111–13, 1990