

Influence of reduced glutathione infusion on glucose metabolism in patients with non-insulin-dependent diabetes mellitus.

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To evaluate the relationship between oxidative stress and glucose metabolism, insulin sensitivity and intraerythrocytic reduced glutathione (GSH)/oxidized glutathione (GSSG) ratio were measured in 10 non-insulin-dependent diabetes mellitus (NIDDM) patients and 10 healthy subjects before and after the intravenous administration of GSH. In particular, after baseline insulin sensitivity was assessed by a 2-hour euglycemic hyperinsulinemic clamp, either glutathione ($1.35 \text{ g} \times \text{m}^2 \times \text{min}^{-1}$) or placebo (saline) were infused over a period of 1 hour. The same protocol was repeated at a 1-week interval, in cross-over, according to a randomized, single-blind design. In healthy subjects, baseline intraerythrocytic GSH/GSSG ratio ($P < .0005$) and total glucose uptake ($P < .005$) were significantly higher than in NIDDM patients. In the same subjects, GSH infusion significantly increased total glucose uptake (from $37.1 \pm 6.7 \text{ micromol kg}^{-1} \times \text{min}^{-1}$) to $39.5 \pm 7.7 \text{ micromol} \times \text{kg}^{-1} \times \text{min}^{-1}$, $P < .05$), whereas saline infusion was completely ineffective. In addition, the mean intraerythrocytic GSH/GSSG ratio significantly increased after GSH infusion (from 21.0 ± 0.9 to 24.7 ± 1.3 , $P < .05$). Similar findings were found in diabetic patients, in whom GSH infusion significantly increased both total glucose uptake (from $25.3 \pm 9.0 \text{ micromol} \times \text{kg}^{-1} \times \text{min}^{-1}$) to $31.4 \pm 10.0 \text{ micromol} \times \text{kg}^{-1} \times \text{min}^{-1}$, $P < .001$) and intraerythrocytic GSH/GSSG ratio (from 14.8 ± 4.1 to 21.7 ± 6.7 , $P < .01$). Pooling diabetic patients and controls, significant correlations were found between intraerythrocytic GSH/GSSG ratio and total glucose uptake ($r = .425$, $P < .05$), as well as between increments of the same variables after GSH infusion ($r = .518$, $P < .05$). In conclusion, our data support the hypothesis that abnormal intracellular GSH redox status plays an important role in reducing insulin sensitivity in NIDDM patients. Accordingly, intravenous GSH infusion significantly increased both intraerythrocytic GSH/GSSG ratio and total glucose uptake in the same patients.

