Subcutaneous insulin therapy fails to protect against oxidative stress and inflammation

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Subcutaneous insulin infusion (CSII) is the gold standard for type 1 diabetic patient therapy. Less physiological than intraperitoneal administration, the subcutaneous route may induce glycemic variability in some patients, a powerful enhancer of reactive oxygen species (ROS) production. While this oxidative stress is recognized to play a role in diabetes and its complications, its characterization has not been fully achieved, especially in the liver, the target organ for insulin sensitivity. Under physiological conditions, an endogenous antioxidant system ensures the oxidative balance. Host survival depends upon the ability of cells and tissues to adapt to or resist the stress and repair or remove damaged molecules and cells.

Sigrist and colleagues at the European Center of Diabetes Study (CEED, Strasbourg, France) have reported in the January 2016 issue of *Experimental Biology and Medicine* that, in a diabetic rat model, a rapid increase of hepatic oxidative stress and inflammation biomarkers were observed, which is associated with drastic decrease of glycogen storage and protein synthesis. Continuous administration of insulin subcutaneously, using an osmotic mini-pump (CSII), rapidly decreased oxidative stress in liver and plasma, but failed after longer diabetes status. Moreover, hepatic and systemic inflammation was not prevented and a high variability of glycogen content was observed. In fact, CSII was not able to preserve the balance of anti- and pro-oxidant species. "Favoring a more physiological pathway for insulin administration would be a real advantage for better glycemic control, preserving organs from glucotoxicity-induced disorders and oxidative stress" stated Stéphanie

DAL. These data support, for the first time, that targeting oxidative stress and inflammation could be a new therapeutic approach since conventional insulin therapy does not allow protection of the liver from chronic diabetes effects.

Dr Steven R. Goodman, Editor-in-Chief of *Experimental Biology and Medicine* said "Dal et al have demonstrated the need for consideration of combining insulin with therapeutics directed towards inflammation and oxidative stress for diabetics".

More information: S. Dal et al. Featured Article: Oxidative stress status and liver tissue defenses in diabetic rats during intensive subcutaneous insulin therapy, *Experimental Biology and Medicine* (2015). DOI: 10.1177/1535370215603837