

## **SECOND LEVEL PLACEBO AND LONG TERM EFFECTS OF GLUCOSE NORMALIZATION**

**M. Watve, A. Ojha**

*Biology, Indian Institute of Science Education and Research, Pune, India*

The main thrust of treatment of type 2 diabetes has been normalization of plasma glucose. It is a long held belief that glucose normalization will prevent, arrest and possibly reverse diabetic complications. However it is difficult to find evidence in support of this belief. Long term clinical trials including University Group Diabetes Program (UGDP), United Kingdom Prospective Diabetes Study (UKPDS), Normoglycemia in Intensive Care Evaluation (NICE), Action to Control Cardiovascular Risk in Diabetes (ACCORD) have addressed the question but yielded mixed or contradicting results. We point out a possible flaw in inferring the long term effects of glucose control in such trials. Diabetes treatment has a short term goal of glucose control and a long term goal comprising prevention of complications. Trials with the short term goal have a sound placebo control. However, in trials with dual goal a second level placebo effect is possible. The patient's knowledge of his sugar levels is likely to have a psychosomatic effect on the pathophysiology of complications. None of the long term clinical trials had a second level placebo control. In clinical trials for prevention of diabetic neuropathy the placebo group showed 30-40% improvements. Therefore in the absence of a second level placebo, even if a clinical trial shows reduction in complications, it is difficult to ascertain that it is an effect of glucose control. With this limitation it is necessary to re-examine the design of clinical trials as well as the main line of treatment of type 2 diabetes.