

The DIGAMI (Diabetes Mellitus, Insulin–Glucose Infusion in Acute Myocardial Infarction) study



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The combination of intravenous glucose, insulin and potassium has been used by cardiologists and cardiac surgeons for many years to improve cardiac metabolism and function following myocardial infarction and during cardiac surgery. Prior to the publications of the DCCT (Diabetes Control and Complications Trial) and UKPDS (United Kingdom Prospective Diabetes Study), however, there was little evidence that intensive treatment of hyperglycaemia in people with diabetes reduced risk of poor microvascular or macrovascular outcomes. It was the DIGAMI (Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction) Study Group, based in the Karolinska Hospital, Sweden, who had the audacity to combine these different approaches in an attempt to reduce the mortality of people with diabetes following myocardial infarction (Malmberg et al, 1995). The DIGAMI study was based on the hypothesis that intensive intravenous insulin, followed by intensive, multi-dose subcutaneous insulin, would reduce total mortality following acute myocardial infarction in individuals with diabetes.

To recruit participants, the investigators did not worry about the World Health Organization nuances about the diagnosis of diabetes, and instead adopted a pragmatic approach and defined diabetes as either known diabetes or a blood glucose concentration above 11 mmol/L. The DIGAMI study was performed in 19 Swedish coronary-care units, and recruited 620 individuals who were randomised in an open fashion to either conventional or intensive treatment. After 1 year of follow-up, a highly significant reduction in total mortality was observed. The results were presented at European cardiology meetings, and published in cardiology journals (Malmberg et al, 1996; 1997).

An editorial in the *British Medical Journal (BMJ)* publicised the results, and hypothesised that people with glucose intolerance may also benefit (Davey and McKeigue, 1996). My own personal response to the results was less enthusiastic, and, in retrospect, this was heavily influenced by the fact that only 620 of 1240 eligible patients had been included, and the other half had been excluded for a variety of reasons, including inability or unwillingness to manage multi-dose insulin. I felt that it would be difficult to translate this complex study in routine clinical practice, and recorded my reservations in a letter to the *BMJ* (Fisher, 1996). The following year the longer-term results were published in the *BMJ*, showing a mortality benefit at a mean of 3 years follow-up (Malmberg, 1997). This was accompanied by a supportive editorial that endorsed this more aggressive approach (Nattrass, 1997), and I again expressed my reservations in a letter (Fisher, 1997).

Prompted by the long-term results, several cardiologists and diabetologists in Scotland proposed a multi-centre trial focusing on the intensive intravenous insulin, but despite detailed discussions, a clear protocol for the intervention did not emerge. During these discussion we learned that the DIGAMI group were undertaking a second study, and I was delegated to contact them to find out details of their study. They replied that the DIGAMI 2 study, which had three treatment arms, was having difficulty in recruiting participants in Sweden, and suggested that Scottish centres could help recruitment by joining, along with other interested colleagues in Norway, Holland and England.

I represented Scotland and the North of England on the steering committee, and became closely acquainted with several European cardiologists and diabetologists. Apart from the friendships forged during this time, I personally learned a large amount about the design and running of complex, multi-centre trials. Unfortunately, despite strenuous efforts from the investigators and steering committee the study was underpowered for its primary outcome, and the negative results were perhaps not unexpected.

Finally, on a personal note, Ken MacLeod represented South West England on the DIGAMI 2 steering committee and I was saddened by his recent sudden and premature death. He will be a great loss to his family, friends, patients and the wider diabetes community.

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