



Effect of moderate-intensity aerobic exercise on glycosylated haemoglobin among elderly patients with type 2 diabetes & peripheral neuropathy

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Aerobic exercise has been known to improve glycosylated haemoglobin (HbA_{1c}) levels and insulin sensitivity in patients with type 2 diabetes mellitus (T2DM). The present study was undertaken to evaluate the effect of eight week moderate-intensity aerobic (heart rate reserve 40-60%) exercise on glycaemic control in elderly patients with T2DM and diabetic peripheral neuropathy (DPN). The participants (n=87) were randomly assigned to an eight-week programme by a computer-generated random number table to the study or control group, respectively. There were 47 participants in the control group and 40 participants in the study group after randomization. There was a significant difference in the mean values of glycated haemoglobin (HbA_{1c}) at baseline and 8th week between the two groups. Moderate-intensity aerobic exercise of eight weeks duration helped in achieving enhanced glycaemic control in the T2DM patients with DPN.

Key words Aerobic exercise - glycaemic control - HbA_{1c} - heart rate reserve - type 2 diabetes mellitus

Diabetic neuropathy is heterogeneous in its presentation. It is associated with significant morbidity and is one of the most common complications of diabetes mellitus¹. Hyperglycaemia plays an important role in the pathogenesis of diabetic neuropathy. Metabolic consequences such as advanced glycation end-products (AGE) are observed. Glycation is defined as non-enzymatic addition of glucose to proteins, and glucose forms a chemically reversible product with protein called

as Schiff base. The degree to which glycation occurs depends on blood plasma glucose concentration². AGE *in vivo* model indicates that hyperglycaemia and ageing may contribute to the pathophysiology of vascular disease in diabetes². It has been observed that in diabetic individuals, there is a proliferation of endothelial cells of the endoneural vessels due to increase in thickness of the basement membrane and there is closure of the lumen of the vessels³.

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Diabetic peripheral neuropathy (DPN) is the single leading cause for amputations in patients with type 2 diabetes mellitus (T2DM). It is associated with a poor quality of life which is reported among patients with diabetic foot ulcers in comparison with patients with T2DM and healthy individuals⁴.

Effect of aerobic exercise on metabolic control has been an important focus for glycaemic control in T2DM³. Previous studies and position statement by the American Heart Association (AHA) have reported that exercise of eight week duration leads to improvements in metabolic control, measured by glycosylated haemoglobin (HbA_{1c}), blood glucose or insulin sensitivity in patients with T2DM³. The American College of Sports Medicine and the American Diabetes Association (ADA) in their joint position statement have reported the ameliorative effect of exercise on hyperglycaemia in type 2 diabetes⁵. Benefits of aerobic exercise on diabetes management include improvement in insulin action which can be accomplished with both aerobic and resistance training. The benefits of aerobic training are associated with the management of hyperglycaemia in T1 and T2DM by minimizing the complications in type 2 diabetes^{3,5}.

Whether ameliorative effect of aerobic exercise training on hyperglycaemia can be useful in the management of DPN in elderly T2DM patients is not known. Hence, the objective of the present study was to evaluate the effect of eight weeks supervised moderate-intensity aerobic [heart rate reserve (HRR) 40-60%] exercise programme on glycaemic control (HbA_{1c}) in elderly patients with T2DM and peripheral neuropathy.

The study was conducted in the department of Physiotherapy and Medicine, School of Applied Health Sciences, Manipal University, Manipal, India, from October 2009 to December 2012. The details of methodology are given elsewhere⁶. Elderly patients above the age of 50 yr with T2DM having peripheral neuropathy were considered eligible for the study. Glycosylated haemoglobin was analysed in the hospital laboratory by high-performance liquid chromatography (HPLC). The evaluator analysing the samples was not aware of the group being analysed at baseline and at eighth week. Glycosylated haemoglobin greater than the cut-off mentioned for the Indian population 6.5 per cent was taken into account⁷. Ethical clearance for the study was obtained from the University Ethics Committee (UEC/54/2009). The trial was registered in the Clinical Trials Registry, India (CTRI/ 2011/ 07/ 001884).

Eighty seven T2DM patients with DPN were evaluated in the study. After randomization, there were 40 participants in the study group and 47 in the control group. There were 30 males and 17 females in the control group and 23 males and 17 females in the study group at baseline. The control (standard care) group had a mean age of 59.45±1.16 yr, and the study group had a mean age of 54.40±1.24 yr. The mean duration of T2DM (months) for control group was 82.10±1.66 and that for study group was 65.49±1.96.

The comparison of the mean values of study and control groups for HbA_{1c}, post-prandial blood sugar (PPBS) and fasting blood sugar (FBS) at baseline and eighth weeks is presented in the Table. On comparison of the two groups, the results of RANOVA indicated

Table. Comparison of glycosylated haemoglobin, fasting blood sugar and post-prandial blood sugar at baseline and 8th week in the study and control groups

Blood parameters	Control group Mean±SD, CI (n=47)	Study group Mean±SD, CI (n=40)
Baseline		
HbA _{1c}	8.02±1.47, 8.44-7.6	8.37±1.92, 7.77-8.97
FBS	137.17±41.14, 125.41-148.93	145.42±48.51, 130.39-160.45
PPBS	217.12±92.58, 190.65-243.59	214.82±73.73, 191.97-237.67
Eighth week		
	n=37	n=29
HbA _{1c}	8.03±1.46, 7.56-8.5	7.58±1.4, 7.07-8.09***
FBS	141.58±44.46, 127.25-155.91	116.41±23.71, 107.78-125.04
PPBS	202±75.13, 117.79-226.21	149.22±41.26, 134.20-164.24

****P*<0.001 compared to control group. HbA_{1c}, glycosylated haemoglobin; FBS, fasting blood sugar; PPBS, post-prandial blood sugar; SD, standard deviation; CI, confidence interval

that there was a significant difference in the mean value of HbA_{1c} at baseline and eighth week between the two groups ($P < 0.001$). The mean value of glycosylated haemoglobin showed a mean reduction of 0.79 per cent in the study group whereas PPBS and FBS of the two groups had no significant difference.

Linear regression analysis was done for glycosylated haemoglobin and predictor variables such as PPBS, FBS were included in the model where PPBS and duration of diabetes appeared the most important predictors in the model using stepwise method that revealed an adjusted R² value of 0.53. Further, PPBS had a beta value of 0.65 which indicated that a change of one standard deviation in the predictor variable would result in a change of 0.65 standard deviations in the criterion variable. This indicates that the higher the beta value, the greater will be the impact of the predictor variable on the criterion variable.

Benefits of exercise on glycaemic control are enormous⁸. HbA_{1c} is considered a gold standard for glycaemic control in diabetes as it accurately reflects glycaemic control over a period of time⁹. In a clinical setting, T2DM usually presents with poor glycaemic control which increases the morbidity and mortality risk in the population. High HbA_{1c} concentrations are associated with an increased risk of developing DPN and may also impose risks of developing diabetic retinopathy and nephropathy in due course of time¹⁰.

In the present study, aerobic exercise with standard care had an anti-glycation effect which resulted in a mean reduction of HbA_{1c} levels in the study group by 0.79 per cent. The United Kingdom Prospective Diabetes Study (UKPDS)-35, a prospective observational study which aimed at finding an association of glycaemia with macrovascular and microvascular complications in T2DM, demonstrated a 14 per cent reduction in the incidence of acute myocardial infarctions, 21 per cent reduction in diabetes-related deaths, with every one per cent reduction in the HbA_{1c} levels in T2DM¹⁰.

Increase in HbA_{1c} is also associated with risks of lower extremity amputation in type 2 diabetes¹¹. With every one per cent increase in HbA_{1c} levels, there is a substantial increase in risk of lower extremity amputation¹². A prospective study of 10 year duration found that peripheral neuropathy was an independent indicator of lower extremity amputation in type 2 diabetes¹².

With increased use of intensive therapy (multiple injections of insulin) there is a chance for hypoglycaemia-related fear, limiting the ability of current diabetes medications to achieve and maintain optimal levels of glycaemic control¹³⁻¹⁵. On the contrary, more prudent use of exercise with standard care as a therapy may lower the risk of hypoglycaemia, may also help patients achieve improved glucose control for longer periods and thus reduce the risk of complications in T2DM.

The findings of the current research shows that moderate-intensity aerobic exercise of eight week duration may be an imperative line of therapy for achieving glycaemic control for elderly T2DM patients with DPN.

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Conflicts of Interest: None.

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