

Metabolic Effects of High Altitude Trekking in Patients With Type 2 Diabetes

PIETER DE MOL, MD¹
MARION J. FOKKERT, BAS²
SUZANNA T. DE VRIES, MD³
EELCO J.P. DE KONING, MD, PHD^{4,5}

BERT D. DIKESCHEI, PHD²
RIJNOLD O.B. GANS, MD, PHD⁶
CEES J. TACK, MD, PHD¹
HENK J.G. BILO, MD, PHD^{6,7}

OBJECTIVE—Limited information is available regarding the metabolic effects of high altitude trekking in patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS—Thirteen individuals with type 2 diabetes took part in a 12-day expedition to the summit of Mount Toubkal (altitude, 4,167 m), Morocco, after 6 months of exercise training. Energy expenditure, body weight, blood glucose, fasting insulin, lipids, and HbA_{1c} were assessed.

RESULTS—Training reduced fasting glucose (-0.7 ± 0.9 mmol/L, $P = 0.026$) and increased exercise capacity ($+0.3 \pm 0.3$ W/kg, $P = 0.005$). High altitude trekking decreased fasting insulin concentrations (-3.8 ± 3.2 μ U/L, $P = 0.04$), total cholesterol (-0.7 ± 0.8 mmol/L, $P = 0.008$), and LDL cholesterol (-0.5 ± 0.6 mmol/L, $P = 0.007$).

CONCLUSIONS—High altitude trekking preceded by exercise training is feasible for patients with type 2 diabetes. It improves blood glucose, lipids, and fasting insulin concentrations, while glucose control is maintained.

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An increasing number of people with diabetes undertake trekkings at high altitude (1,2). Exercise is associated with improved glycemic control and insulin sensitivity (3). However, the effects of exercise at sea level might differ substantially from exercise effects at high altitude.

RESEARCH DESIGN AND METHODS

Thirteen complication-free, nonsmoking subjects (8 men, 5 women) with type 2 diabetes participated in a 12-day trekking expedition to Mount Toubkal (altitude, 4,167 m), Morocco (4). Participants' characteristics were age, 48.2 ± 9.7 years; diabetes duration, 6.3 ± 3.9 years; HbA_{1c}, $6.6 \pm 0.8\%$; and BMI, 27.5 ± 4.1 kg/m². Antihyperglycemic

medication consisted of metformin ($n = 8$), a sulfonylurea derivant ($n = 4$), dipeptidyl peptidase-4 ($n = 1$), thiazolidinedione ($n = 1$), and insulin ($n = 3$).

Participants underwent a physical examination, maximal cycle ergometer testing, electrocardiography, echocardiography, and laboratory tests at baseline (day -270) and received a written training program at the start of the training period (day -180). Cycle ergometer and laboratory tests were repeated at day 0.

Participants recorded energy expenditure (SenseWear Pro Armband, Bodymedia) and fasting capillary glucose (AccuChek Compact Plus, Roche Diagnostics), and used a continuous blood glucose monitoring system (Paradigm

MiniMed, Medtronic) during 1 week every month (from day -60 onwards) at sea level and continuously at altitude.

Fasting glucose and plasma insulin were determined on days -150 , 0, 9, and 12, and homeostasis model assessment of insulin sensitivity (HOMA-IR) was calculated (5). Insulin users were excluded from HOMA-IR and fasting glucose analyses. HbA_{1c} and lipids were determined on days -270 , -150 , 0, and 12.

At altitude, acute mountain sickness (AMS) symptoms were scored daily using the Lake Louise Questionnaire.

The research protocol was approved by the Isala Clinics ethics committee, Zwolle, the Netherlands. Subjects gave written informed consent.

SPSS software (SPSS, Inc.) was used for statistical analysis. A P value of <0.05 was considered statistically significant.

RESULTS—During the training period, the dose of antihyperglycemic medication (insulin or tablets) was stopped in two subjects (one sulfonylurea derivant and one thiazolidinedione) and reduced in five subjects. Energy expenditure increased from $2,997 \pm 386$ to $3,361 \pm 358$ kcal/day (day -180 vs. -60 , $P = 0.01$; Fig. 1). Fasting glucose decreased from 7.6 ± 1.5 to 6.9 ± 1.2 mmol/L ($P = 0.026$), whereas maximal workload increased from 2.6 ± 0.8 to 2.9 ± 0.8 W/kg (day -180 vs. 3, $P = 0.003$).

Fasting plasma triglycerides decreased from 2.2 ± 0.9 to 1.6 ± 0.6 mmol/L (day -270 vs. day 0, $P = 0.025$), whereas LDL (2.3 ± 1.0 mmol/L), HDL (1.4 ± 0.6 mmol/L), and total cholesterol (4.6 ± 1.1 mmol/L) did not change. HbA_{1c}, HOMA-IR, and body weight remained unchanged ($P = 0.27$; day -180 vs. day 0).

All participants summited Mount Toubkal (altitude, 4,167 m), and AMS scores remained low (Fig. 1). During the expedition, mean fasting glucose was lower in the second half compared with the first half at altitude (7.1 ± 1.2 vs. 6.6 ± 0.9 mmol/L, $P = 0.022$) but did not differ from sea level (6.9 ± 1.2 mmol/L; Fig. 1).

The area under the curve for glucose and the time (median \pm interquartile range) at sea level versus altitude in

From the ¹Department of Internal Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands; the ²Department of Clinical Chemistry, Isala Clinics, Zwolle, the Netherlands; the ³Department of Cardiology, Tjongerschans Hospital, Heerenveen, the Netherlands; the ⁴Department of Endocrinology, University Medical Center, Leiden, the Netherlands; the ⁵Department of Nephrology, University Medical Center, Leiden, the Netherlands; the ⁶Department of Internal Medicine, University Medical Centre, Groningen, the Netherlands; and the ⁷Department of Internal Medicine, Isala Clinics, Zwolle, the Netherlands.

Corresponding author: Pieter de Mol, p.demol@aig.umcn.nl.

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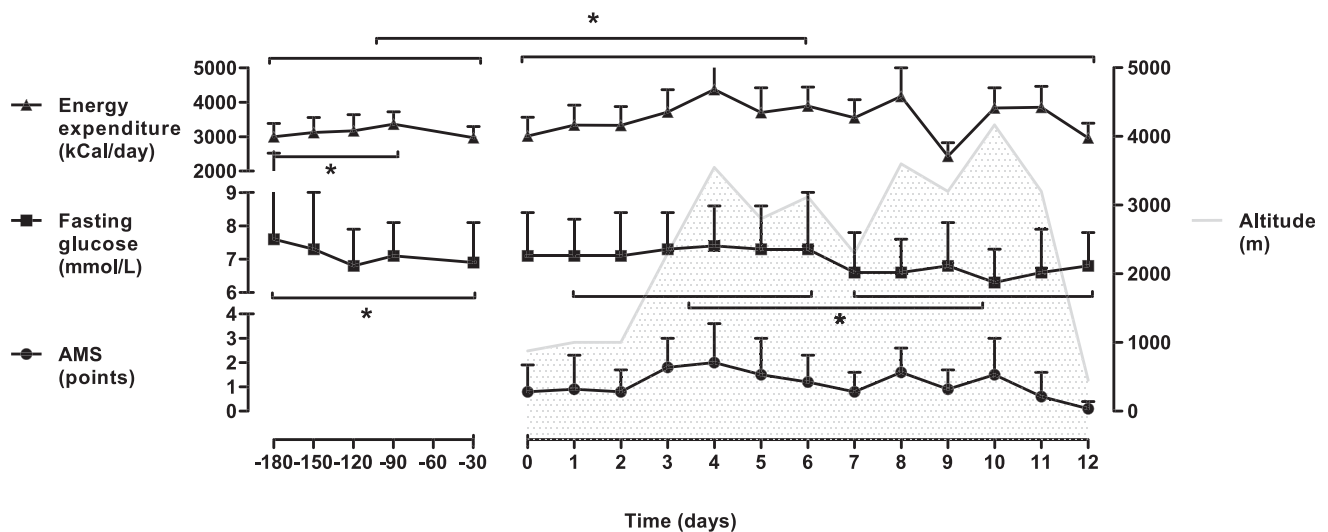


Figure 1—Daily energy expenditure (upper panel, ▲), fasting glucose ($n = 10$ [insulin users excluded]; middle panel, ■), and AMS score (lower panel, ●) during the training period and the 12-day expedition. The altitude presented (right y-axis, shaded gray area) refers to the highest altitude reached that specific day. Data are presented as mean \pm SD. * $P < 0.05$. Note: Days 0, 9, and 12 represent resting days. Energy expenditure and fasting glucose monitoring were unavailable during the fifth month (day -60 to day -30) of the training period. A diagnosis of AMS is based on the presence of a headache, at least one other symptom (gastrointestinal symptoms, dizziness or being light headed, difficulty sleeping, fatigue or weakness) and a total score of ≥ 4 .

hyperglycemia (74 ± 251 vs. 147 ± 388 min/day, $P = 0.20$) and hypoglycemia (0 ± 29 vs. 0 ± 66 , $P = 0.43$) remained unchanged.

HOMA-IR at 3,200-m altitude (day 9: 1.9 ± 0.8) was decreased compared with lower altitudes (day 12: 2.7 ± 1.2 , $P = 0.024$; day 0: 3.8 ± 1.8 , $P = 0.013$).

High altitude trekking led to decreased cholesterol (4.5 ± 1.3 vs. 3.8 ± 1.8 ; $P = 0.008$) and LDL cholesterol (2.5 ± 1.0 vs. 1.9 ± 0.7 mmol/L; $P = 0.007$) on day 0 vs. day 12; triglycerides and HDL remained unchanged.

Energy expenditure increased at altitude and peaked on days of largest altitude gain (Fig. 1). Body weight remained stable.

CONCLUSIONS—Our study indicates that patients with complication-free type 2 diabetes can safely take part in high altitude trekking after adequate preparation.

The results of the training period showed reductions in triglycerides and fasting glucose, while workload capacity increased and body weight remained stable. These effects are generally in line with previous studies (6–8) and most likely associated with the increase in physical activity, as reflected by the energy expenditure. That HbA_{1c} did not change is probably explained by the already low values at inclusion and the reduction in medication. These facts and the small sample size might also explain the unchanged HOMA-IR at sea level.

During the expedition, HOMA-IR and lipids decreased, while body weight, blood glucose, and food intake (data not shown) remained stable.

Exposure to high altitude can initially lead to higher levels of insulin, glucose, and counter-regulatory hormones, possibly related to AMS (9–11), which typically occurs at altitudes above 3,000 m (12,13). In our study, mean glucose and time in hyper- and hypoglycemia remained stable, consistent with absent glycemic deregulation at altitude. The gradual ascent, and the fact that we only resided at altitudes above 3,000 m on days 8–11, could explain the stable glucose profiles and low AMS scores.

The lower HOMA-IR at 3,200 m was driven by a drop in fasting insulin. Because insulin users were excluded from analyses and antihyperglycemic medication and dietary intake remained unchanged, the most likely explanation is increased exercise-stimulated glucose uptake. However, in the absence of a direct measure of insulin sensitivity, increased insulin- or hypoxia-stimulated glucose uptake cannot be excluded (14).

Our study implies that there are no objections for subjects with complication-free type 2 diabetes and normal results on cardiac exercise tests to participate in high altitude trekking. Regarding glycemic control, we would consider any subject with type 2 diabetes capable of safely exercising at high altitude, irrespective of the type of hypoglycemic medication.

This study has limitations. Because of the uncontrolled study design, it is not clear whether the improved fasting glucose and HOMA-IR were due to the increased energy expenditure, to the hypoxic conditions at altitude, or to other factors. HOMA-IR is validated for studies with large samples (15), so these results should be interpreted with caution. The research setting precluded the use of direct measures of insulin sensitivity and limited the number of patients.

In conclusion, high altitude trekking is feasible for subjects with type 2 diabetes after a preparatory training phase. Beyond the objective improvement in blood glucose, lipids, and fasting insulin, the successful accomplishment of a summit may have substantial beneficial psychological effects.

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P.d.M. wrote the study protocol, researched the data, and wrote the manuscript. M.J.F. and S.T.d.V. contributed to the study design and data collection, researched the data, and reviewed the manuscript. E.J.P.d.K. and H.J.G.B. contributed to the study design and reviewed and edited the manuscript. B.D.D. contributed to the study design, researched the data, and reviewed and edited the manuscript.

R.O.B.G. contributed to the study design and reviewed and edited the manuscript. C.J.T. contributed to, reviewed, and edited the manuscript. P.d.M. is the guarantor of this work and, as such, had full access to all data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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References

1. Brubaker PL. Adventure travel and type 1 diabetes: the complicating effects of high altitude. *Diabetes Care* 2005;28:2563–2572
2. Panofsky D. Handling type 1 diabetes in the mountains: considerations for the diabetic climber. In *Health and Height. Proceedings of the Vth World Congress of Mountain Medicine and High Altitude Physiology*. 1st ed. Viscor G. Ed. Barcelona, Edicions Universitat Barcelona, 2003, p. 237–246
3. Meex RC, Schrauwen-Hinderling VB, Moonen-Kornips E, et al. Restoration of muscle mitochondrial function and metabolic flexibility in type 2 diabetes by exercise training is paralleled by increased myocellular fat storage and improved insulin sensitivity. *Diabetes* 2010;59:572–579
4. Bas van de Goor Foundation Atlas Diabetes Challenge [article online], 2011. Available from <http://www.bvdgf.org/atlaschallenge>. Accessed 14 June 2012
5. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;28:412–419
6. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C. Physical activity/exercise and type 2 diabetes. *Diabetes Care* 2004;27:2518–2539
7. Thomas DE, Elliott EJ, Naughton GA. Exercise for type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2006;3:CD002968
8. Mourier A, Gautier JF, De Kerviler E, et al. Mobilization of visceral adipose tissue related to the improvement in insulin sensitivity in response to physical training in NIDDM. Effects of branched-chain amino acid supplements. *Diabetes Care* 1997;20:385–391
9. Larsen JJ, Hansen JM, Olsen NV, Galbo H, Dela F. The effect of altitude hypoxia on glucose homeostasis in men. *J Physiol* 1997;504:241–249
10. Sawhney RC, Malhotra AS, Singh T, Rai RM, Sinha KC. Insulin secretion at high altitude in man. *Int J Biometeorol* 1986;30:231–238
11. de Mol P, de Vries ST, de Koning EJ, Gans RO, Tack CJ, Bilo HJ. Increased insulin requirements during exercise at very high altitude in type 1 diabetes mellitus. *Diabetes Care* 2011;34:592–595
12. Mairer K, Wille M, Burtscher M. The prevalence of and risk factors for acute mountain sickness in the Eastern and Western Alps. *High Alt Med Biol* 2010;11:343–348
13. West JB, Milledge JS, Schoene RB. Acute mountain sickness. In *High Altitude Medicine and Physiology*. 4th ed. Shaw P, Ed. London, Hodder Arnold, 2007, p. 253
14. Azevedo JL Jr, Carey JO, Pories WJ, Morris PG, Dohm GL. Hypoxia stimulates glucose transport in insulin-resistant human skeletal muscle. *Diabetes* 1995;44:695–698
15. Muniyappa R, Lee S, Chen H, Quon MJ. Current approaches for assessing insulin sensitivity and resistance in vivo: advantages, limitations, and appropriate usage. *Am J Physiol Endocrinol Metab* 2008;294:E15–E26