OBSERVATIONS

Fatigue in Hemodialysis Patients With and Without Diabetes: Results From a Randomized Controlled Trial of Two Glucose-Containing Dialysates

In hemodialysis (HD), dialysate glucose concentrations differ worldwide between 0 and 200 mg/dl and can, if above the serum glucose levels, lead to diffusive glucose shifts into the patient (1). The effects of glucose (2) and insulin (3) on the autonomic nervous system, as well as during HD with different glucose concentrations, (4) have been reported. However the effect of dialysate glucose on fatigue has not been studied. This study investigated fatigue in chronic HD subjects treated with 100 mg/dl (G100) versus 200 mg/dl dialysate glucose (G200).

In this randomized, crossover, multicenter study (www.clinicaltrials.gov, NCT00618033), diabetic and nondiabetic patients were enrolled in a 1:1 fashion. Diabetes was defined as either requiring oral antidiabetic medication or insulin or having random blood glucose levels above 200 mg/dl during the preceding 12 months. The study protocol was approved by the Beth Israel Medical Center Institutional Review Board and was conducted in full accordance with the Declaration of Helsinki.

Subjects were randomized to receive either G100 or G200 with a crossover after 3 weeks. Dialysis regimen and medication remained unchanged during the study.

At the end of each period, the patient's perception of fatigue was assessed by the nine items on the Fatigue Severity Scale (FSS) (5). FSS scores range from one to seven with lower scores indicating less fatigue. The FSS comprises nine items grouped in six domains: *1*) motivation, *2*) exercise, *3*) physical functioning (two items), *4*) duties and responsibilities, *5*) social life, and *6*) subjective perception of fatigue (three items). Internal test consistency was assessed by Cronbach's α. Paired *t* test was employed to compare FSS scores between G100 and G200, and unpaired *t* test was used for comparison between diabetic and nondiabetic subjects. Data are means ± SD.

Thirty chronic HD patients (age 54 ± 13 years, 13 males, 13 blacks, 13 diabetic patients) were enrolled. One subject was withdrawn prior to any study intervention, and two failed to complete both questionnaires. Internal consistency of the FSS was high (Cronbach's α 0.9). FSS scores were significantly higher with G200 as compared with G100 in diabetic subjects (G200: 5.0 ± 1.0; G100: 4.2 ± 1.1; $P < 0.05$) (supplemental Fig. 1, available in an online appendix at http://care.diabetesjournals.org/cgi/content/full/dc10-1043/DC1) but not in nondiabetic subjects (G200: 3.5 ± 1.9; G100: 3.0 ± 1.6; $P = 0.234$) (supplemental Fig. 1). In cross-sectional analysis, the FSS was higher in diabetic patients (G200: +1.3 ± 0.6, $P < 0.05$; G100: +1.2 ± 0.5, $P < 0.05$) (supplemental Fig. 1).

In conclusion, postdialytic fatigue is more pronounced in diabetic than in nondiabetic patients and is significantly increased with the use of G200. G100 decreased fatigue in diabetic patients to a level observed in healthy subjects (5). Why diabetic subjects experience more postdialytic fatigue remains to be determined; the effects of glucose on the autonomic nervous system may be relevant (4). Based on these results, G100 offers advantages over G200 in diabetic HD patients.

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References

1. Schneditz D, Hafner-Giessauf H, Holzer H, Thomaseth K. Intracorporeal glucose disposal during hemodialysis after a standardized glucose load. ASAIO J 2010;56:204–209
2. Kanaley JA, Baynard T, Franklin RM, Weinstock RS, Goulopoulou S, Carhart R Jr, Ploutz-Snyder R, Figueroa A, Fernhall B. The effects of a glucose load and sympathetic challenge on autonomic function in obese women with and without type 2 diabetes mellitus. Metabolism 2007;56:778–785
3. Paolisso G, Manzella D, Rizzo MR, Barbieri M, Varricchio G, Gambardella A, Varricchio M. Effects of insulin on the cardiac autonomic nervous system in insulin-resistant states. Clin Sci 2000 (Lond);98:129–136
4. Ferrario M, Raimann J, Signorini MG, Kruse A, Thijssen S, Kotanko P, Levin NW, Cerutti S. Heart rate variability and autonomic responses in diabetic and nondiabetic subjects during dialysis with different dialysate dextrose concentrations (Abstract). Blood Purif 2010;29:231
5. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The fatigue severity scale: application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46:1121–1123