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Brief Report

The effect of haemodialysis on transcutaneous oxygen tension in patients with diabetes—a pilot study

Robert J. Hinchliffe[1], Bernie Kirk[1], Dipankar Bhattacharjee[2], Simon Roe[2], William Jeffcoate[1] and Fran Game[1]

[1]Foot Ulcer Trials Unit, Department of Diabetes and Endocrinology and [2]Department of Renal Medicine, City Hospital, Nottingham NG5 1PB, UK

Abstract

Background. Established renal failure in diabetes is associated with a high incidence of foot ulcers and gangrene, and these are major causes of morbidity and mortality. It has been suggested that this problem is particularly associated with the onset of renal replacement therapy, and since there is evidence that haemodialysis causes hypoxaemia, we have undertaken a pilot study to determine the effect of haemodialysis on lower limb transcutaneous oxygen tension ($TcpO_2$).
Methods. $TcpO_2$ was measured on the dorsum of the foot through a single dialysis treatment and over the succeeding 4 h using a transcutaneous monitor (TCM400/3, Radiometer Ltd, Copenhagen, Denmark).
Results. The median age (range) of the 10 (7 male) participants was 73 (58–83) years. The median duration of diabetes was 16.5 (7–30) years and that of dialysis treatment 29 (10–88) months. The median (range) baseline $TcpO_2$ on the dorsum of the foot was 54.5 (51–77) mmHg and 54.0 (24–87) at the end of dialysis. Median $TcpO_2$ at 1, 2 and 4 h after the end of dialysis was 50.0 (33–81), 49.0 (24–78) and 47.0 (20–78) mmHg. Analysis by ANOVA suggested a trend towards a difference between median $TcpO_2$ concentrations at different time points ($F_{(1.752, 15.765)} = 3.359$, $P = 0.066$).
Conclusions. The data identified a trend towards a fall in lower limb $TcpO_2$, and that this fall continued for at least 4 h after the end of treatment. Dialysis-associated lower limb hypoxia may be a factor leading to the increased incidence of critical limb ischaemia in this group and further work is needed to define its cause and implications for clinical care.

Keywords: amputation; diabetes; dialysis; foot ulcer; gangrene; renal failure

Introduction

Diabetes is the commonest single cause of established renal failure (ERF) [1], and is associated with a relatively poor prognosis [2,3]. Survival for 3 years with diabetes may be as low as 28% [4], while survival for 5 years in non-diabetics ranges from 58 to 72% [2]. The presence of peripheral arterial disease is strongly associated with reduced survival in diabetes [5] and the incidence of critical limb ischaemia and amputation is approximately 10 times higher [6]. It has recently been suggested that this increase in incidence is a feature more of dialysis than of renal failure itself [7], and that major amputation is especially likely in the first 12 months after starting renal replacement therapy [8,9].

Many factors may contribute to the association between ERF and limb-threatening disease, and these have been reviewed elsewhere [10]. These factors include the effect of associated complications of diabetes (e.g. poor vision, peripheral neuropathy), with increased risk of trauma. Tissue oxygenation may be worsened by anaemia and by tissue oedema. Additional factors include arterial calcification, associated coronary artery disease, autonomic neuropathy with disordered vasomotor regulation and reduced resistance to infection. None of these, however, would explain any tendency for an increase in the incidence of new foot ulcers and amputation around the commencement of dialysis treatment. The purpose of this study was to determine whether the process of haemodialysis itself may be associated with reduced oxygenation of peripheral tissues in patients with diabetes.

Subjects and methods

All patients who were diagnosed with diabetes mellitus and undergoing maintenance haemodialysis at the City Hospital, Nottingham, were invited to participate in a study which

Correspondence and offprint requests to: Fran Game, Department of Diabetes and Endocrinology, City Hospital, Nottingham, NG5 1PB. Email: fgame@futu.co.uk

involved measurement on a single occasion of lower limb transcutaneous oxygen monitoring ($TcpO_2$) through the course of dialysis treatment and for 4 hours afterwards. Those with a history of limb ulceration or previous amputation were excluded. Ten agreed to participate in the study which involved continual measurement of $TcpO_2$ through haemodialysis and 4 hours after, using a transcutaneous monitor (TCM400/3, Radiometer Ltd, Copenhagen, Denmark). The pressure of workload on the dialysis unit was such that it was not always possible to apply the sensor and allow it to equilibrate for 10 min prior to the start of the dialysis, and so it was applied while the treatment was being set up. The sensor was applied to the dorsum of the foot and it remained in the same position throughout dialysis. The manufacturer recommends that it should not be used continuously at a single site for more than 4 h, it was repositioned for the period of observation after dialysis. The extent of any macrovascular disease was assessed on a subsequent day by an expert technician blind to the results of the earlier study, using ankle: brachial pressure indices (ABPI) and lower-limb arterial duplex scanning. The study received approval from the local research ethics committee and the participants gave informed written consent.

Results

Ten patients enrolled in the study (but one subsequently declined to return for vascular assessment). The median (range) age was 73 (58–83) years, and seven were male. Nine had type 2 diabetes (of whom three were insulin-treated). The median duration of diabetes was 16.5 (7–30) years and that of dialysis treatment 29 (10–88) months. Eight had diabetic retinopathy, nine had ischaemic heart disease, three had previous transient ischaemic attack or stroke and six were ex-smokers. Medication included aspirin ($n = 5$), clopidogrel (3), lipid-lowering therapy (5) and β-blockers (4). Three patients had a history of peripheral vascular disease: arterial bypass surgery (1) and claudication (2). In three of the nine patients who returned for vascular assessment, the calculation of ABPI was not possible because the arteries in the calf were incompressible. The median ABPI in the remaining six was 0.8 (0.7–0.9). Two patients had significant arterial occlusive disease in the femoro-popliteal segment detected by Duplex ultrasonography. The median pre-dialysis weight was 82.4 (63.0–122.1) kg and dialysis resulted in a median weight loss of 1.7 (0.8–4.3) kg on the day of study. The median (range) systolic and diastolic blood pressures were 158 (103–219) and 82 (61–98) mmHg before dialysis, and 152 (105–214) and 70 (56–102) mmHg at the end of the treatment period. The blood pressure was not recorded in the post-dialysis period. The median (range) baseline $TcpO_2$ on the dorsum of the foot was 54.5 (51–77) mmHg and 54.0 (24–87) at the end of dialysis. The median $TcpO_2$ at 1, 2 and 4 h after the end of dialysis was 50.0 (33–81), 49.0 (24–78) and 47.0 (20–78) mmHg, and analysis by ANOVA suggested that there was a trend towards a difference between the groups ($F_{(1.752, 15.765)} = 3.359$, $P = 0.066$) (Figure 1). There was no obvious relationship between the magnitude of the fall in $TcpO_2$ and extent of macrovascular disease documented at the later vascular assessment (data not shown).
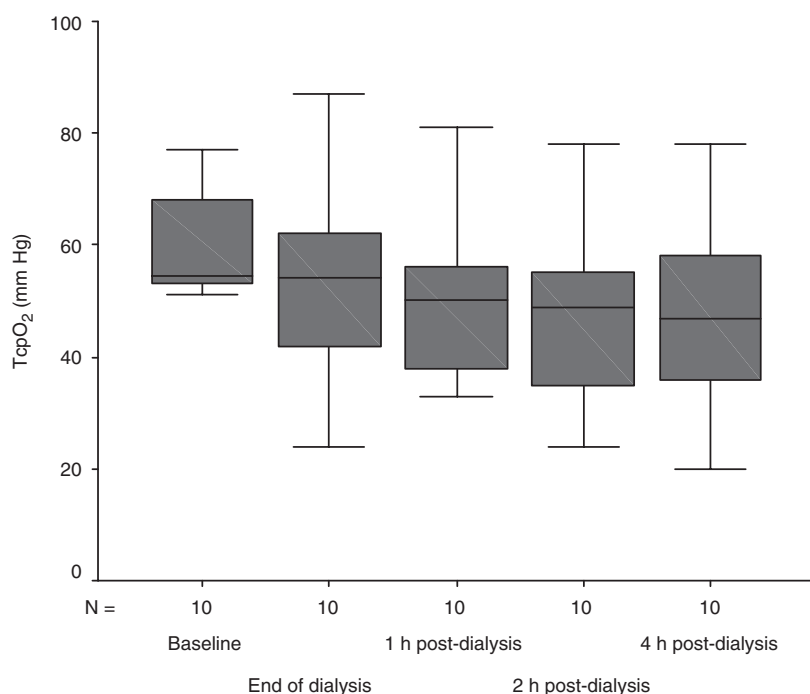
Fig. 1. Median, interquartile and total ranges for $TcpO_2$ measured on the dorsum of the foot in 10 patients undergoing dialysis and for a period of 4 h afterward.

Discussion

In this small cohort, there was a trend towards a fall in tissue oxygenation during and after haemodialysis. Any such tendency might be more clearly demonstrated in a larger series, especially in those with more severe macrovascular disease. Moreover, it could be argued that this group was selected in the sense that they had not had a previous ulcer or amputation despite being treated with dialysis for a median 29 months, and as such might differ from those in whom there may be a closer association between the onset of dialysis and the development of critical limb ischaemia.

The demonstration of the trend to a fall in tissue oxygenation confirms earlier observations that haemodialysis is associated with systemic hypoxaemia (determined by both pulse oximetry and arterial sampling), which persists into the post-treatment period [11–13]. It has been concluded that this systemic hypoxaemia might result from a number of factors, including pulmonary microatelectasis, a change in pH of the dialysate and a change in the oxygen dissociation curve, the use of acetate dialysis buffers, or activation of complement [14,15]. However, it is also possible that a fall in circulating arterial pO$_2$ is made worse in the periphery by the fluid shifts inherent in the process of dialysis, hypotension and any associated haemodynamic response which reduces peripheral flow in an attempt to conserve central circulation. The effect is likely to be most marked in diabetes because of the high prevalence of distal arterial disease, combined with autonomic neuropathy and microvascular disease.

If these observations are confirmed, they are of potentially great clinical significance. They would highlight the need to adopt therapeutic measures which might help offset any tendency for tissue oxygen to fall. There may be a case for considering more widespread use of lipid lowering agents in maximal doses and/or pre-emptive vascular reconstruction. However, such interventions should be part of a comprehensive strategy to reduce the incidence of foot ulceration, and amputation, in this very high risk group. There is evidence that a programme of multidisciplinary care may reduce the incidence of foot disease and amputation [16], and that this benefit may be even greater in groups at particular risk [17,18]. Urgent consideration should be given to adopting similar approaches in every dialysis unit.

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