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ACUTE CHANGES IN PLASMA FREE FATTY-ACID CONCENTRATIONS DURING HAEMODIALYSIS COMPARING HEPARIN WITH EPOPROSTENOL AS ANTICOAGULANT

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Summary

There is a sharp rise in plasma free fatty-acid (FFA) concentration following the commencement of haemodialysis using heparin as anticoagulant. This is not seen when epoprostenol is used as the sole anticoagulant, suggesting that this is an effect of heparin rather than of haemodialysis.

Introduction

Heparin is a potent activator of lipoprotein lipase [1], resulting in a rise in plasma free fatty-acid (FFA) following an intravenous bolus [2]. High plasma FFA occurs following myocardial infarction, and has been associated with an increased risk of arrhythmias [3]. Fatal arrhythmias associated with raised FFA during haemodialysis have been reported [4], and the long-term effects on lipid metabolism and the development of atheroma debated [5]. Epoprostenol (PGI_2) provides a safe alternative to heparin as an anticoagulant for use during dialysis [6], and as such offers a model for 'heparin-free' dialysis.

The aims of the present study were to demonstrate the acute changes in plasma FFA concentrations during haemodialysis, and to establish the part played in these by heparin, PGI_2 and dialysis respectively.

Patients and methods

Six patients (5 males, 1 female, aged 22–62) were studied, after obtaining their informed consent, whilst receiving routine haemodialysis using a cuprophan hollow-fibre dialysis membrane. Each patient was studied during two dialyses one week apart, which were identical in every respect excepting the anticoagulant used. Patients were fasted during dialysis and blood pressure and weight loss achieved were similar on both occasions. Anticoagulation was achieved either by giving heparin as a bolus dose (50IU/kg), followed by an infusion at 25IU/kg, or with PGI_2 infused at 5ng/kg/hr throughout the procedure.

Dialysis needles were inserted 15 minutes prior to the commencement of haemodialysis, at which time a baseline blood sample was taken and the anti-coagulant administered. Further samples were taken at 0, 5, 15, 30, 60 and 120 minutes, and analysed for non-esterified FFA [7] and triglyceride content (commercial enzymatic assay, Beckman). Results were analysed using the paired Wilcoxon rank sum test.

Results

Following the heparin bolus there was a sharp rise in the mean FFA concentration (Figure 1) from 0.20 to 1.19mEq/L ($p<0.01$) which was not seen with PGI_2, 0.15 to 0.2mEq/L (NS). There was a further rise in the FFA to a peak of 1.42mEq/L (NS) during heparin dialysis at 15 minutes, and plasma levels remained elevated throughout the period studied.

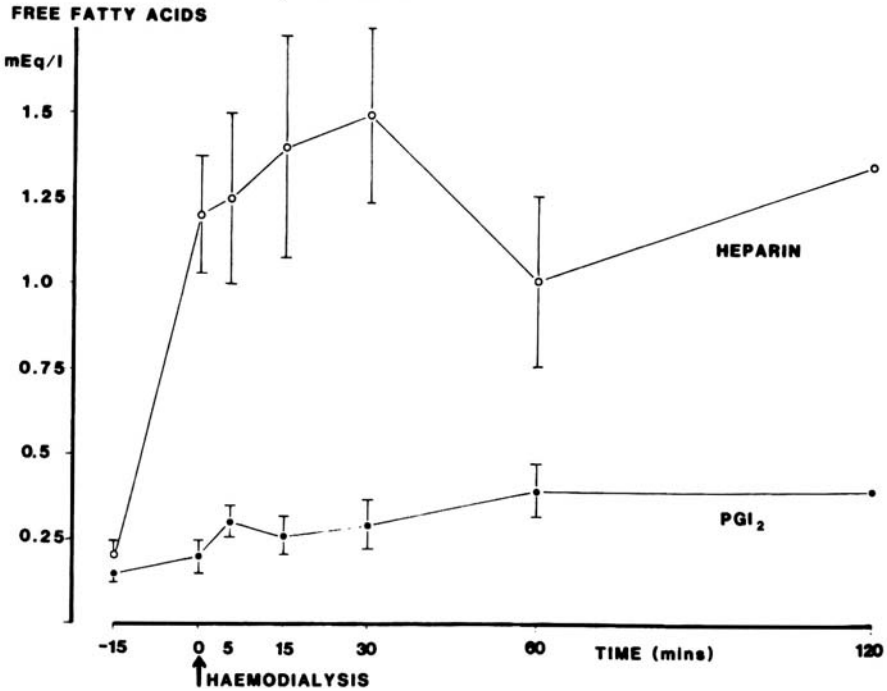

Figure 1. Acute changes in mean (±SEM) plasma free fatty-acid (FFA) concentration (mEq/L) during haemodialysis using heparin (o–o) or epoprostenol (•–•) as anticoagulant

There was a fall in the mean plasma triglyceride concentration following heparin (Figure 2) from 283 to 243mg/100ml ($p<0.01$) which continued during dialysis reaching 207mg/100ml at 60 minutes. No such fall was seen during PGI_2 dialysis where triglyceride levels were 326 initially and 312mg/100ml at 60 minutes.

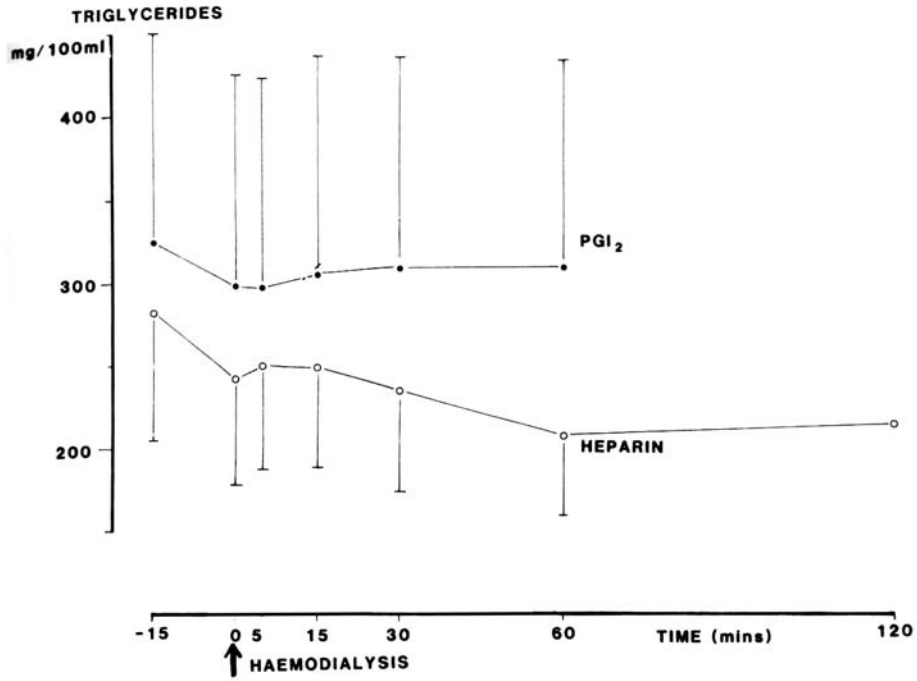

Figure 2. Acute changes in mean (±SEM) plasma triglyceride concentration (mg/100ml) during haemodialysis using heparin (o–o) or epoprostenol (•–•) as anticoagulant

There was no significant hypotension following PGI_2, but all patients experienced facial flushing and four had mild transient headaches.

Discussion

These results demonstrate that there is an acute rise in plasma FFA concentration during heparin dialysis, associated with a fall in plasma triglyceride concentration, compatible with lipoprotein lipase activation. The failure to observe similar changes during dialysis using PGI_2 as anticoagulant suggests that this is wholly a heparin effect. This conclusion is strengthened by the observation of similar abnormalities in lipid metabolism at the end of a five hour dialysis period using heparin, which were not seen in subjects given gabexate mesilate as anticoagulant [5].

FFA increases the myocardial consumption of oxygen [8], and heparin-induced elevation of plasma FFA in the ischaemic dog heart produces arrhythmias, which can be inhibited by protamine [9]. It may be that acute changes in plasma FFA increases cardiovascular instability early during haemodialysis, resulting in arrhythmias [4]. If this is the case, then for patients who are considered to have arrhythmias due to high FFA concentrations during dialysis, or are at increased risk, for example after myocardial infarction, PGI_2 offers a safer alternative to heparin as anticoagulant during haemodialysis.

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