Influence of Different Dialysis Membrane Types on Cardiac-Specific Troponin T Levels

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Introduction

Mortality of patients with end-stage-renal-failure (ESRD) remains still high, exceeding 20%, compared to the general population, as the US renal data system 1997 annual report revealed. In the aging patient (>75 years) it averages 45.5 per 100 patients per year (1). Several factors, such as age, gender, primary kidney disease, co morbid conditions (diabetes mellitus, peripheral and cerebral vascular disease, the presence of neoplasia, heart failure) influence hemodialysis patients survival. Cardiovascular diseases still remain the main cause of death in ESRD patients, accounting for almost fifty percent of the total (2).

Cardiac troponin T (cTnT) is a subunit of the cardiac actin-myosin complex with molecular weight 33kDa that leaks into the circulation due to myocardial damage (3). It is used as a sensitive marker to detect patients with myocardial infarction despite the fact that its presence is associated with increased mortality even in the absence of a myocardial infarction as in cases of unstable angina. Therefore cTnT is considered a useful tool for risk stratification in patients with coronary heart disease (4).

In patients with renal failure the diagnostic value of cTnT is not clearly established, since elevation of cTnT is observed in uremic patients without suspected cardiac ischemia. According to one study, up to 73% of patients on renal replacement therapy (RRT) might present elevation of cTnT. Other investigators have found that 71% of patients on hemodialysis, 57% of patients on peritoneal dialysis and 30% of patients with renal failure not yet on RRT had cTnT abnormal levels (5).

The cause of the unexpected increase of cTnT in hemodialysed patients is not clear. A possible explanation may be the different effects of dialysis on cTnT and the use of serum samples drawn before and after dialysis for comparison (6).

Aim of the Study

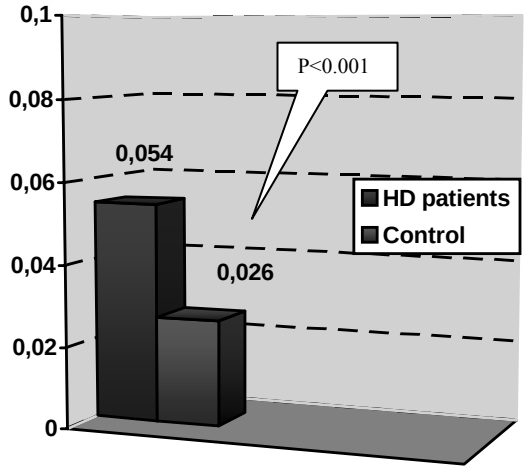
As the use of high-flux membranes with higher clearances for molecules of similar weight to cTnT (33kDa) became more common during the last years, the aim of our study was to investigate, whether serum cTnT levels are influenced by the use of different membrane types during HD and thus if cTnT is a reliable marker for cardiovascular events in HD patients.

Materials and Methods

We studied cTnT levels of 23 patients, 9 males and 14 females with mean age 68.3 ± 12.5 on haemodialysis, from 123 to 6 months. Samples to determine cTnT levels were drawn before and after dialysis treatment in two consecutive sessions. In the first session classic cellulosynthetic membrane (Hemophan LF) and in the second high flux synthetic membrane Polysulfone (HF) was used. Moreover, baseline cTnT values of the haemodialysis patients were compared (Wilkoxon test) to cTnT levels of healthy subjects of similar age and sex. Patients with peripheral vascular disease, diabetes, active infections, peripheral neuropathy or retinopathy were excluded from our study.

Results 1

Baseline cTnT levels of the haemodialysis patients compared to cTnT levels of healthy subjects



Discussion

In various studies, serum cTnT increase is correlated not only to cardiac ischemia but also to other parameters such as age, gender, CRP levels. Furthermore, elevated levels are found in diabetes mellitus, peripheral vascular disease, neuropathy, systemic infections and renal failure (7).

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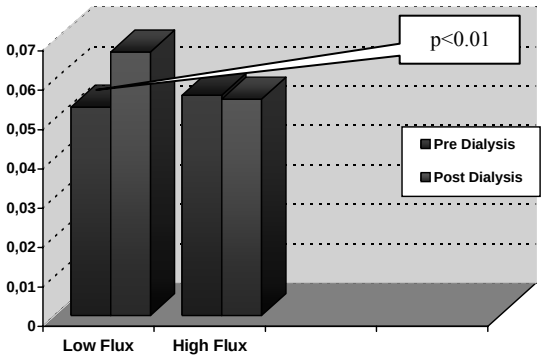
Results 2. cTnT (µg/L) changes during hemodialysis session



	pre	post	p
Low Flux	0,053 ± 0,033	0,067 ± 0,047	<0.01
High Flux	0,056 ± 0,036	0,055 ± 0,034	N.S.

The reason of increased cTnT in renal patients is not clear. By some investigators cTnT expression in uremic muscles, leading to cross reaction with muscle proteins has been suggested but not yet proved. According to others it simply expresses the high incidence of coronary insufficiency and/or arteriosclerosis in renal patients (8).

In our study, significantly higher baseline levels of cTnT in hemodialysis patients were found. Although coronary disease is common in these patients, there is no clinical evidence to support ischemic heart disease as the basis of this observation. The practical consideration should be that clinicians using this assay should recognise the high incidence of increased values in hemodialyzed patients without overt acute coronary disease. Probably raising the cutoff value to 0.2 µg/L or higher will improve specificity of the test with little compromise in sensitivity for the diagnosis of acute myocardial infarction, because cTnT concentrations in the latter are usually much higher.

Many factors may provoke cTnT elevation during the hemodialysis session. Hyperfibrinogenemia, use of heparin, retention of middle molecular weight substances or just hemoconcentration have been considered as single factors or in combination. On the other hand, no correlation to urea and creatinine level, time in the hemodialysis program or adequacy of dialysis was found (9).

Because several different dialysis membranes are used in HD, we were wondering if various dialysis membranes types can achieve different clearances of cTnT. In clinical practise, two types of clearance (diffuse clearance and convective clearance) and two types of membranes (high-flux and low-flux membranes) can be altered. With high-flux membranes, diffuse clearance removes molecules up to 15 kDa, whereas with low-flux membranes, only molecules up to 5 kDa are removed. Convective clearance removes high molecular weight substances when high-flux membranes are used, but only molecules up to 9 kDa with low-flux membranes (10, 11).

In our study, a high-flux (Polysulfon) and a low-flux (Hemophan) membrane were used. We observed significant difference in cTnT removal attributable to the membrane type. Thus we found significant higher levels of cTnT only after dialysis with low-flux membrane while the cTnT levels at the end of dialysis with high-flux membranes were practically unchanged. Therefore, clearance should be the reason for the relatively reduced cTnT concentrations after dialysis with high flux membranes. As a conclusion, to achieve reliable values for clinical decision, it is necessary to take blood samples before dialysis. Only then can a correct comparison be carried out.

Conclusions

Hemodialysis patients reveal significant higher cTnT levels compared to healthy subjects. As different membrane types are found to influence cTnT levels, to achieve reliable values for clinical diagnosis, it is necessary to take blood samples before dialysis session.

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