THE EFFECT OF DIALYSATE TEMPERATURE ON HAEMODIALYSIS LEUCOPENIA

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Summary

We assessed the influence of dialysate temperature on intra-dialytic leucopenia. Lowering dialysate temperature from 38°C to 20.5°C caused a decrease in the dialysis associated white blood cell reduction from 82±6 per cent to 32±19 per cent. The degree of leucopenia bore a highly significant relationship with dialysate blood temperature suggesting that a further lowering of blood temperature (to about 20°C) would almost entirely prevent intra-dialytic leucopenia.

Introduction

There is increasing evidence that leucopenia occurring early during Cuprophan haemodialysis results from blood-membrane contact leading to alternative pathway complement activation, anaphylatoxin release, leucoagglutination, and pulmonary sequestration of granulocytes [1–7]. The intra-dialytic activation of complement is similar to that observed in vitro on incubating serum with zymosan [1,7]. In their original investigation Pillemar et al found that zymosan activation of the complement can be prevented if the temperature of reaction is kept at 16°C, instead of 37°C [8]. If complement activation of the alternative pathway is inhibited at low temperatures, so should the attendant leucopenia. We have, therefore, investigated whether intra-dialytic leucopenia can be prevented by lowering the temperature of blood-membrane interaction.

Materials and methods

We studied a total of 13 male patients on regular dialysis treatment during acetate haemodialysis with cuprophan hollow fibre dialysers. Patients were free of clinically manifest infections and none of them were receiving drugs known to affect white blood cell count. The mean age was 46 years (range 30–59), duration of dialysis treatment 7.8 years (range 2–10). Renal disease was chronic glomerulonephritis in five, polycystic kidneys in one, nephropathy associated with Lawrence Moon-Biedl syndrome in one, undetermined in six.
Study protocol 1. Six patients underwent three haemodialyses each, with dialysate temperature kept at 33.8±(SD) 0.3°C, 36.9±0.2°C and 38.1±0.2°C respectively.

Study protocol 2. Nine patients underwent two haemodialyses each, one with dialysate at room temperature (20.5±0.7°C), and the other at 36.8±0.5°C. In the cool procedure, before returning to the patient the blood was warmed through a serpentine inserted in the venous line and immersed in a thermostatic bath. Blood lines of similar length and conformation were employed in both procedures.

Leucocyte and differential counts were determined in duplicate by manual methods on blood drawn from the arterial line at 0, 15, 30, 60, 120 and 240 minutes of haemodialysis. Temperature was monitored by means of thermocouple needles (Ellab) placed in the blood and dialysate circuits. Dialyser urea and creatinine clearance at a mean dialysate flow of 500ml/min and blood flow of 260ml/min, were determined in duplicate.

Statistical analysis was performed by paired Student’s ‘t’ test and Spearman’s rank correlation test.

Results

Study protocol 1. After 15 minutes of haemodialysis white blood cell count fell by 59±15 per cent at a dialysate temperature of 33.8°C, 65±15 per cent

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**Figure 1.** White blood cell count at: ● 33.8±0.3°C; ○ 36.9±0.2°C; • 38.1±0.2°C; * 33.8 vs 38.1°C p<0.02; *36.9 vs 38.1 p<0.02
(SD) at the dialysate temperature of 36.9°C and 82±6 per cent at the dialysate temperature of 38°C (Figure 1). The maximal fall in white blood cell count bore a highly significant relationship with dialysate temperature (Spearman's test; r= -0.69; p<0.01). Pre- and post-dialyser blood temperature corresponding to each dialysate temperature and white blood cell count are also reported in Table 1.

| TABLE I. Dialysate temperature, blood temperature and white blood cell count in the two studies |
|---|---|---|---|---|
| n | Dialysate temperature °C | Pre-dialyser blood temperature °C | Post-dialyser blood temperature °C | White blood cell x 10^3 mm^-3 pre-HD at max.fall |
| 1st study | 6 | 38.1±0.2 | 36.0±0.4 | 36.4±0.5 | 6.9±1.7 | 1.28±0.48 |
| | 6 | 36.9±0.2 | 36.2±0.5 | 35.5±0.7 | 6.2±1.2 | 1.87±0.58 |
| | 6 | 33.8±0.3 | 35.6±0.7 | 33.0±0.3 | 6.2±1.9 | 2.34±0.45 |
| 2nd study | 9 | 36.8±0.5 | 35.7±0.4 | 35.1±0.4 | 8.2±2.6 | 1.97±0.57 |
| | 9 | 20.5±0.7 | 34.9±0.6 | 20.6±0.9 | 8.2±4.2 | 5.15±2.7 |

HD=haemodialysis

Figure 2. White blood cell fall at dialysate temperature of 36.8±0.5°C (○) and 20.5±0.7°C (●). *p<0.01
Study protocol 2. Use of dialysate kept at room temperature (20°C) caused a 15°C fall in blood temperature along the dialyser (Table I). At this temperature the fall in white blood cell count was less than half that occurring in the control procedure, i.e. 32±19 per cent versus 73±17 per cent (p<0.01) (Figure 2). Leucopenia was sustained primarily by the fall in total neutrophils, which averaged 94 per cent in the control procedure, and was reduced to 43 per cent in the dialysis at room temperature (Figure 3) (p<0.001).

Figure 3. Effect of dialysate temperature on the percentage maximal fall of neutrophils and lymphocytes. Dialysate temperature: open column: 20.5±0.7°C; stippled column: 36.8±0.5°C

Figure 4. Relationship between Δ temperature and maximal percentual fall in white blood cell count
Analysing together all the studies performed in the two protocols, the relationship between dialysate temperature and maximal white blood cell fall remained highly significant (Figure 4) (Spearman’s test; \( r = -0.76; p<0.001 \)). A highly significant relationship was also observed between blood temperature (average of pre- and post-dialyser blood temperature) and maximal white blood cell count fall (\( r = -0.77; p<0.001 \)).

Lowering the dialysate temperature caused only minor decrease in dialysis efficiency. In fact in the cooler procedure (20.5°C) the dialyser clearance for small solutes diminished by less than 10 per cent, the urea clearance from 186±27ml/min to 172±23ml/min, the creatinine clearance from 146±22 to 135±22ml/min.

**Discussion**

Our studies show that lowering the dialysate temperature to 20°C markedly lessens the degree of intra-dialytic leucopenia. This effect can be obtained at the expense of only a slight decrease in small molecule clearance.

A likely explanation of our findings is that cooling of blood in contact with the dialyser membrane causes a lesser degree of complement activation than in standard dialysis. The lesser degree of complement activation would in turn produce a lesser degree of leucopenia.

We conclude that intra-dialytic leucopenia is a temperature dependent phenomenon. Basing ourselves on the regression line between blood temperature and maximal fall in white blood cells, we predict that further decreasing blood temperature to 20°C or less would almost entirely prevent complement activation with its attendant leucopenia.

**Acknowledgments**

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**References**

7. Jacob HS. *Q J Med* 1983; 207: 289
Open Discussion

UNKNOWN (Antwerp) Do you think this temperature phenomenon could be the explanation of the different results in the human study? Could it be that in the human study there was no hypoxaemia or increase in vascular resistance because there was no or lesser complement activation?

ENIA I don’t know if we can explain the differences on the basis of complement activation and we found that at this level of blood cooling complement activation decreased, so it is a possibility.

RITZ (Heidelberg) Are you suggesting that your present findings are an explanation for the improved vascular stability you saw during low temperature dialysis?

ENIA There are some benefits of lowering dialysate temperature down to 34°C, but I don’t know if at 34°C there is a lesser degree of complement activation. We studied activation only at extreme conditions and we are now going to study complement activation at 34°C.