Comparative Evaluation of Iatrogenic Sources of Blood Loss During Maintenance Dialysis

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Introduction

The exposure of the intermittently haemodialysed patient to chronic iatrogenic blood loss has been of major concern. Figures available so far indicate that the total amount of blood lost during regular dialysis treatment may sometimes reach a maximum of 8 l per year thus contributing substantially to chronic renal anaemia (Blumberg, 1973; Koch et al, 1974; Lindsay & Kennedy, 1972; Sinn et al, 1976).

METHOD AND MATERIAL

A meticulous and at the same time acceptable new method for exactly delineating and quantifying all possible sources of blood loss during regular dialysis treatment has been developed in collaboration with the Cancer Research Centre in Heidelberg, and has been applied to the following investigation (Sinn et al, 1975). Labelling was mediated by trisbuffered acetylace tone at pH 7.6, whereby 99% of the added $^{111}$In Chloride was firmly fixed to the haemoglobin of the intact red cells (Kampfer et al, 1976). The specific activity achieved was up to 10 mCi/ml of packed red cells (Figure 1). Seven $\mu$Ci of labelled autologous red cells were given intravenously per kg body weight prior to the investigations. One hour after the injections, a 1 ml whole blood sample of the patient usually yielded approximately 5,000 counts per minute when measured in this special counting chamber. One ml whole blood was placed between two 5 x 2" sodium iodide detectors on a plate slowly rotating three times per minute. The lead shielded counting chamber was also accessible for intact dialysers, extracorporeal systems, and faecal material so that they could be counted at the same geometry and compared to the patient's 1 ml whole blood standard (Figure 1). Since counting efficiency as
WHOLE BODY COUNTER

Mean count rate: 5000 cts/ml x min

111-INDIUM (111-In) LABELLING OF RED CELLS

trisbuffer
acetylatedone
HCl + pH 7.6

111-In-Chloride

ACD blood
washed twice
in 0.9% saline

20min incubation

supernatant

111-In labelled
packed red cells

recovery 99%
activity ≤ 10 mCi/ml

Figure 1. Whole body counter and schematic representation of $^{111}$In labelling of red cells
well as geometry was excellent due to $^{111}$Indium labelling and use of a whole body counter, blood loss could be calculated with an accuracy of $\pm$ 0.1 ml (Sinn et al, 1976).

Blood volumes lost due to bleeding at puncture sites, residual blood lost in extracorporeal blood lines and in the blood compartment of the dialyser itself were simultaneously calculated in 14 patients in the paediatric age group (mean age 12.1 $\pm$ 2.3 SD).

In a second series blood loss due to laboratory samples and the contribution of intestinal haemorrhage under the conditions of regular dialysis treatment and additional administration of acetylsalicylic acid was studied in 8 patients.

The study was performed during 5 hours regular dialysis treatment thrice weekly using the Dow Cordis HFAK M 4 and M 5, the Gambro lundia nova 13.5, and the Travenol Hoeltzenbein dialyser, each at a randomised sequence over a period of two weeks. Heparinisation as well as priming of the dialyser and wash back technique were standardised throughout the series: 2,000 IU at the beginning, 1,500 IU every 2 hours during haemodialysis. Wash back was performed with 120 ml of 0.9% saline followed by air for the capillary and the Travenol Hoeltzenbein dialyser, whereas blood-air-saline-air wash back was used in the Gambro plate dialyser (Hergemöller et al, 1975).

RESULTS

Bleeding during the initial access to the vessels, estimated in 45 instances in 6 patients, accounted for 0.2 ml ranging from 0.0 to 1.3 ml, whereas leakage occurring intermittently and finally at puncture sites summed up to roughly 1 ml ranging from 0.0 to 4.6 ml, so that an average amount of 1.3 ml of whole blood was lost at puncture sites per dialysis (Table I).

TABLE I. Comparative Evaluation of Iatrogenic Sources of Blood Loss

<table>
<thead>
<tr>
<th>Sources of blood loss</th>
<th>Average ml $\pm$ SD</th>
<th>Range</th>
<th>No of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Bleeding at puncture sites</td>
<td>1.3 ml $\pm$ 1.2</td>
<td>0.0 – 4.6 ml</td>
<td>45</td>
</tr>
<tr>
<td>2 Residual in blood lines</td>
<td>1.14 ml $\pm$ 0.64</td>
<td>0.31 – 2.9 ml</td>
<td>51</td>
</tr>
<tr>
<td>3 Residual blood in dialysers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD HFAK M 5</td>
<td>12.9 ml $\pm$ 8.0</td>
<td>3.8 – 32.7 ml</td>
<td>28</td>
</tr>
<tr>
<td>CD HFAK M 4</td>
<td>9.8 ml $\pm$ 12.9</td>
<td>1.7 – 44.1 ml</td>
<td>23</td>
</tr>
<tr>
<td>Gambro lundia nova 13.5</td>
<td>2.1 ml $\pm$ 1.6</td>
<td>0.8 – 6.8 ml</td>
<td>17</td>
</tr>
<tr>
<td>Travenol Hoeltzenbein</td>
<td>2.1 ml $\pm$ 1.6</td>
<td>0.6 – 5.6 ml</td>
<td>23</td>
</tr>
<tr>
<td>4 Intestinal haemorrhage per day</td>
<td>7.9 ml $\pm$ 5.6</td>
<td>1.0 – 17.5 ml</td>
<td>33</td>
</tr>
</tbody>
</table>
Residual blood in the extracorporeal Ab Gambro blood line system ranged between 0.3 and 3.0 ml, adding an average 1.14 ml loss per dialysis.

The residual blood lost in 4 different dialysers comparatively studied in 91 cases in 14 patients was highest in the Dow Cordis M 5 followed by the M 4, Gambro Lundia and Travenol Hoelzenbein dialyser (Figure 2). Whereas an average of 13 ml was observed in the HFAK M 5 and 10 ml in the M 4 respectively residual blood volumes were significantly lower both in the Gambro Lundia and the Travenol Hoelzenbein dialyser, the latter demonstrating mean residual blood volumes of approximately 2 ml with consistently less variation when compared with the capillary kidneys.

Residual blood volumes in the capillary kidneys were independent of the amount of saline used for wash back. The marked residual blood volumes in the HFAK M 5 could not be reduced significantly by using wash back volumes of up to 500 ml.

Blood loss originating from blood samples drawn for laboratory investigation cannot be generally quantified, as the amount needed varies from one unit to another. Red cell loss can be substantially reduced by extracorporeal, on line, sedimentation of heparinised blood samples, if the plasma needed for laboratory analyses is gained from the supernatant (Figure 3) as recommended by other authors. Our results demonstrate that sedimentation in chronically dialysed patients is of rapid onset. Allowing 15 minutes' spontaneous sedimentation of
Figure 3. Reduction of red cell loss by sedimentation of whole blood samples

20 ml of whole blood, the red cell content of the supernatant is reduced to less than 15%. By this procedure the 8 ml of whole blood originally requested by the laboratory would contain only the equivalent of 1.2 ml of whole blood. Since

Figure 4. Daily gastrointestinal blood loss evaluated in normals, regular dialysis treatment patients (RDT) and RDT patients treated with acetylsalicylic acid (ASA)
only plasma is needed. 4 ml of the supernatant are sufficient for chemical analyses, so that the final blood loss is reduced to 0.6 ml for each full scale laboratory investigation.

Gastrointestinal bleeding was simultaneously studied in our series when first results indicated that the four above mentioned sources of blood loss fell below the figures reported on the basis of the $^{59}$Fe whole body counting method (Koch et al., 1974).

Whereas eight normal persons exhibited a daily intestinal blood loss of 1–2 ml, eight patients receiving regular dialysis treatment showed a significantly higher rate of daily blood content in their stools (Figure 4). Gastrointestinal haemorrhage was even higher in those patients receiving acetylsalicylic acid as prophylactic antithrombotic treatment.

The intestinal blood loss of regular dialysis treatment patients came up to 7.9 ml per day and increased by 100% to 16 ml when treated with acetylsalicylic acid.

**DISCUSSION**

Blood losses induced by regular dialysis treatment originating from different sources may be estimated at between 900 and 2,600 ml per year (Table II). Whereas technically unavoidable initial, intermittent, and final bleeding at puncture sites can be minimised by optimal puncturing, withdrawal of needles, and

**TABLE II.** Estimated total yearly blood loss based on $^{111}$In study in 14 patients

<table>
<thead>
<tr>
<th>TECHNICALLY UN-AVOIDABLE</th>
<th>individual range</th>
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<tbody>
<tr>
<td>puncture sites</td>
<td>200 ml</td>
</tr>
<tr>
<td>blood lines</td>
<td>180 ml</td>
</tr>
<tr>
<td>blood sampling</td>
<td>210 ml</td>
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<tr>
<td>total per year</td>
<td>590 ml</td>
</tr>
<tr>
<td></td>
<td>155 - 890 ml</td>
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<tr>
<td></td>
<td>130 - 320 ml</td>
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<tr>
<td></td>
<td>7,5 - 400 ml</td>
</tr>
<tr>
<td></td>
<td>160 - 1770 ml</td>
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<table>
<thead>
<tr>
<th>DEPENDING ON TYPE OF DIALYSER</th>
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<tbody>
<tr>
<td>CD HFAK M 5</td>
</tr>
<tr>
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<table>
<thead>
<tr>
<th>DUE TO GASTROINTESTINAL BLEEDING</th>
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</thead>
<tbody>
<tr>
<td>2,900 ml</td>
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<tr>
<td>1,300 - 4,400 ml</td>
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</table>
adequate compression of puncture sites, blood loss in the extracorporeal blood lines, to date, seems technically unavoidable. The amount of blood lost for routine laboratory analyses, however, can be essentially reduced by either restricting laboratory check-ups to a minimum or in case of vital need by using the above mentioned method of pre-analysis sedimentation and reinjection of sedimented red cells (Falda, 1971).

Residual blood volumes in dialysers also contribute crucially to the annual iatrogenic blood loss (Lindsay et al., 1973). Our data support the finding that the individual case the capillary kidney retains a higher residual blood content often underestimated, even though priming and wash back may be carried out under optimal conditions (Möhring et al., 1972; Lindsay et al., 1973).

The degree of gastrointestinal haemorrhage found in our series was somewhat unexpected. Methodological errors could be ruled out, both by experimental clinical observations. In normals we found that gastrointestinal blood loss was the same order of 1–2 ml per day as found by the $^{51}$ Chromium labelling method (Uthgenannt & Timm, 1976). On the other hand, daily red cell loss by the gastrointestinal tract would explain the reported difference between annual total blood loss calculated to be 6–8 l on the basis of $^{59}$ Iron total body counting; our own findings that iatrogenic blood loss at puncture sites, in blood lines, from diagnostic samples, and residual blood in dialysers summed up to only 2,600 per year. This discrepancy is explained by our data that gastrointestinal bleeds adds up to an average of 3 l per year so that the total annual blood loss estimated by our method reaches the same order of 6–8 l per year estimated by the $^{59}$ I method (Koch et al., 1974).

The final conclusion can be drawn from our data that additional exposure to drugs which have been proven to increase gastrointestinal bleeding in normals should be undertaken with caution in patients receiving regular dialysis treatments.

CONCLUSIONS

Whereas a healthy person capable of compensating for even gross bleeding is usually well aware of accidentally occurring minor blood loss, the chronic dialysis patient carries the risk of exposure to iatrogenic blood loss with the additional drawback of markedly impaired intrinsic red cell production (Blumberg, 1971). Iatrogenic chronic blood loss, often underestimated in degree, can very easily exceed the patient's compensatory capacity. Dialysis personnel should be well aware of the accidental haemorrhage they may induce by regular dialysis treatment, thus minimising the need for transfusions with the inherent risks of hepatitis and formation of antibodies which might lead to early transplant rejection (Brunner et al., 1972).
References

Blumberg, A (1973) Therapeutische Umschau, 30, 772
Lindsay, RM, Burton, JA, King, P, Davidson, JF, Boddy, C and Kennedy, AC (1973) Clinical Nephrology, 1, 24
Lindsay, RM, Burton, JA, Edward, N, Dargie, HJ, Prentice, CRM and Kennedy, AC (1973) Clinical Nephrology, 1, 29

Open Discussion

KRAITINGER (Karlsruhe) When did you inject your labelled tracer substance: before you start dialysis or during? If you injected it before, have you measured the amount which remains in the liver, in the RES system?

MOHRING We injected the labelled red cells 60 minutes prior to the first dialysis. We performed animal experimentation, including whole body counting, which showed that the labelled red cells were stable in vivo and that there was no immediate turnover to the RES.

KENNEDY (Glasgow) I think the figure you gave for the blood loss in normal controls was 1–2 ml/day. Did you observe the effect in these individuals of acetyl salicylic acid?

MOHRING We did not personally investigate that, but I checked the literature. All antirheumatic drugs, particularly acetyl salicylic acid, lead to a drastic increase
in intestinal blood loss. In normal individuals on acetyl salicylic acid intestinal
blood loss increases to double, and in patients on regular dialysis treatment it
might increase from 5–10 ml to 15–30 ml.

KENNEDY What is the safest analgesic to give to our regular dialysis patients
in respect to blood loss?

MOHRING We do not give acetyl salicylic acid as an analgesic. We thought of
using it years ago as an antithrombotic drug in case of impending shunt com-
plications or secondary to an AV fistula operation, as it might decrease the incid-
ence of shunt or fistula clotting, but now we totally avoid that drug. We did not
especially check on use of analgesic drugs.

ANDREUCCI (Naples) I apologise for repeating the question I asked yesterday.
You have shown the blood loss in the lines and the filters. Now when we send
home patients who are Australia antigen positive what happens to these dis-
posable materials once they have been used? I asked some colleagues and most
of them do not care much. I am afraid that when we send patients to home
dialysis and they are HBs Ag positive and we do not care about the waste mate-
then we are spreading hepatitis in the community.

MOHRING I am certainly not an expert on hepatitis. But I think it is essentia-
to keep blood loss to a minimum and this has to be taken into consideration.