



HOPE FOR REDUCING SA'S TRAUMA DEATHS?



Professor Ken Boffard.

A so-called 'blood substitute' that can give physicians up to 19 hours of respite in time-critical blood transfusions is being used for the first time in a clinical setting for acute trauma patients, making South Africa the only country in the world to do so.

If the trial proves successful and increased production lowers costs, the drug could help South Africa shrug off the unwelcome mantle of being a world leader in all-cause trauma mortality.

The product is licensed for exclusive use in acute anaemia. Called Hemopure, it improves oxygen transportation without toxicity dangers, but is still far from being a blood substitute – one of the ultimate goals of its developers.

The theory is that it might be better than blood for perfusing certain hypoperfusion states like shock and that it will improve oxygen levels in the tissues after a surgical procedure. However, this is as yet unproven and in the Johannesburg Hospital the most far-reaching trial is about to begin – testing its use in clinical trauma situations.

Says Dr Charl van Loggerenberg, General Manager of Biopure South Africa: 'If this type of study helps bring an oxygen-carrying fluid closer to the point of need then it has the potential to save many lives.'

The Medicines Control Council has so far only registered it (in 2001) for treating adult surgical patients who are

acutely anaemic and for delaying the need for a predictable blood transfusion in these patients.

Principal investigator for the local leg of the multinational trials, Professor Ken Boffard, head of surgery at Johannesburg General Hospital, described Hemopure as a haemoglobin-based oxygen carrier (HBOC) or an 'oxygen bridge' between cell and tissue.

Hemopure (created using haemoglobin polymer synthesised from bovine haemoglobin) and another similar product, Polyheme (derived from human haemoglobin), has been under evaluation in the trauma setting for about a year, with the latter in trial use by paramedics in non-hospital settings in Denver, Colorado. Both drugs are fully accepted by Jehovah's Witnesses, who have long prompted ethical controversy by refusing potentially life-saving blood transfusions. The drugs have been in veterinary use for about 5 years.

Its chief known benefits include being stable at room temperature, having a shelf life of 3 years, being easy to store and eliminating blood cross-matching problems.

Boffard and his colleagues, who are working intimately with the Federal Drug Administration (FDA) and the local Medicines Control Council (MCC), secured the ethics go-ahead for the trauma trial in February this year after a strict 5-month vetting process.

They will use 50 volunteers, each of whom requires some 40 hours of assessment over and above normal medical care. Other clinicians associated with the team will set up an 'absolutely consistent' laboratory.

Boffard expects to see the first results in about a year when he sits down with the statisticians, independent assessors

and the MCC. He says local vascular surgeons are already using Hemopure extensively. Its chief known benefits include being stable at room temperature, having a shelf life of 3 years, being easy to store and eliminating blood cross-matching problems.

He cautioned surgeons to take haemoglobin measurements from patients before administering Hemopure, saying machine readings could otherwise be difficult to interpret.

Van Loggerenberg says his company trains all hospital laboratory staff before the product is introduced but agreed that were this not the case, 'you could have a problem result'.

Both men dismiss 'Mad Cow' or any other disease being potentially transmissible, emphasising that it is a synthetic product using haemoglobin chains derived from bovine haemoglobin. All possible infectious diseases are 'eradicated in the manufacturing process'.

'It's so far removed from the original haemoglobin that it's safe to call it a synthetic product – which is why the Jehovah's Witnesses allow it,' said van Loggerenberg.

The product drew controversy when described as 'cow's blood' in the lay media in Johannesburg, alarming several people potentially enrolled into the trials who had yet to go through the strict informed educational consent process.

Boffard emphasised that Hemopure was 'not a substitute for anything else we do. All the patients get normal treatment but half of them get this as well at no extra cost'. Both men confirmed that the reportage in the *Citizen* newspaper had resulted in a worried call from the national Department of Health. The DOH was reassured that no unauthorised 'experimentation' was underway.

Dr Robert Crookes, medical director of the South African National Blood



Service (SANBS), says that while a potential life-saver, Hemopure does not, in the vast majority of patients, replace the need for red cells, platelets or clotting factors that were found in fresh frozen plasma. It would not impact on the country's current blood needs nor was it a viable routine alternative to blood.

'Its risks and side-effects have to be carefully evaluated and then compared with those of ordinary blood – it's no use substituting an alternative therapy for one that might have an increased risk,' he adds. Crookes says that the SANBS has put in place highly effective measures to manage the risk of transfusion-transmissible diseases via blood.

Van Loggerenberg and Boffard agreed, adding that South Africa had an enviable reputation for safe blood in spite of a 26% HIV prevalence in the general population. 'We have some of the safest blood in the world – it's far more aggressively screened than most other places and it's a superb service,' adds Boffard.

Asked how long it would be before an artificial blood product became a reality, he said he believed this would come within 5 years.

Crookes says the reported HIV incidence in the SANBS's latest annual haemo-vigilance report is one in 390 000 transfusions. The actual calculated risk (taking into account the window period of HIV infection and the HIV seroprevalence of donors) is currently approximately one in 100 000. There were five HIV transfusion 'breakthroughs' in the over 4 million blood products transfused in the past 5 years (881 000 transfusions last year).

Dr Theresa Nel, a lead consultant with the SANBS, told the *SAMJ* that 66% of all transfusion reactions are the result of the patient receiving the wrong unit of blood and the ensuing reactions are mainly attributable to human error. A full 59% of these occurred at the bedside. Last year just three 'probable cases' of disease transmission by blood transfusion were reported, one a bacterial infection and the other two HIV window period transmissions.

'What happens is people don't declare high-risk behaviour – we've learnt that more stringent donor education is needed to secure self-exclusion. It's difficult because they don't think they've been risky.'

Nel said she saw the current application of Hemopure as being mainly where there was a specific

indication such as bypass surgery and acute transfusion needs. Where there was a marginal need for blood, Hemopure was not indicated while the clinical condition of the patient needed careful evaluation before a blood transfusion was considered.

'Even where there's an acute blood loss situation and you need a rapid blood volume expander, you do not necessarily need cells or blood products that carry oxygen as first-line therapy. These are not volume expanders. The clinician must evaluate whether the patient needs the oxygen-carrying products or volume replacement as first-line therapy. There will always be arguments for and against.'

Synthetic oxygen carriers have their research origins in the United States military in the 1950s and have obvious applications anywhere that refrigeration and blood are in short supply.

The SANBS cannot afford to remain anything but hyper-vigilant. A recent mortuary survey of young males between 15 and 40 years who died of trauma in KwaZulu Natal hospitals and in the Johannesburg Hospital revealed that 40 - 50% of them were HIV-positive, said Boffard.

Chris Bateman

The main reason for major reactions and deaths in patients from 2000 to 2003 – SANBS

