WHITE PAPER

Blood conservation with a patient dedicated arterial blood gas analyser

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Up to **90%** of patients become anaemic by the third day of ITU	Blood sampling is a significant contributor to **anaemia** and a predicator of **transfusion**	Around **40%** of patients require transfusion, increasing to **85%** of patients that stay for a week	Total costs of transfusing 2 units of blood is around **£763**	Transfusions are associated with **longer stays** and **poorer outcomes**

Proxima supports state of the art strategies for blood conservation

Strategies for blood conservation	The Proxima System
Appropriate sampling	Diminishes impact of "confidence" testing by less experienced staff, it also facilitates more frequent or faster response testing where indicated
Smaller test volumes	Entire sample is returned to the patient, resulting in zero net loss
Returning discard	Closed sampler returns all discard to the patient, avoiding line opening and blood contact

Blood conservation strategies have the potential to be of significant benefit to patients and help reduce costs of care

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RAISING THE STANDARD OF CRITICAL CARE

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Introduction

Anaemia is a frequent complication of critical care, with up to 90% of ICU (Intensive Care Unit) patients being anaemic by their third day in the ICU[1]. Anaemia is associated with poor patient outcomes, especially amongst those patients with cardiovascular disease[2 3 4 5]. The treatments of choice for anaemia are the minimisation of blood loss and the transfusion of red blood cells when necessary.

This paper explores the issues in critical care around anaemia, transfusions and blood conservation. With diagnostic testing being a significant factor in cumulative blood loss and the risk of anaemia, the use of a patient dedicated arterial blood gas analyser to minimise blood loss is described.

Anaemia in the intensive care unit

Causes

The reasons for anaemia in critically ill patients are multifactorial and include acute blood loss (e.g. from trauma, surgery or internal bleeding), iatrogenic blood loss associated with diagnostic sampling and blunted red blood cell production[6]. Of these, the blood loss associated with diagnostic testing is the factor that is most easily in the control of the intensivist.

Laboratory results are an important tool to achieve diagnosis and guide medical care, and a certain amount of blood is required to obtain this information. The gold standard for monitoring oxygenation, acid-base status and ventilation is an arterial blood gas measurement – and consequently is one of the most frequently ordered tests in the ICU[7].

Patients with indwelling central venous or arterial catheters have more frequent blood draws as blood sampling is easier[7], and relatively large volumes are drawn in comparison to that needed for the measurement itself. When sampling from an arterial line it is important to remove an adequate discard volume to ensure that a representative blood sample is obtained. If an insufficient discard volume is removed, the sample will be contaminated with saline flush solution resulting in an increased $c\mathrm{Na}^+$ and $c\mathrm{Cl}^-$ and decreased $c\mathrm{K}^+$[8]. Consequently, removal of at least three times the dead space volume is recommended[9] and the average discard volume drawn is 3.2ml[10].

Iatrogenic anaemia (also known as hospital-acquired anaemia) results from blood loss that occurs from collecting samples for laboratory testing. Blood samples may be drawn up to 24 times in a day within the ICU [6 11 12]. Therefore a series of small iatrogenic blood losses can add up, resulting in patients becoming anaemic[13].

Table 1 shows reported average phlebotomy-induced blood loss (ml/day) for various ICUs.

Reporting country	Setting	Average phlebotomy-induced blood loss (ml/day)
USA	Cardiothoracic ICU	377
USA	General surgical ICU	240
USA	Medical surgical ICU	41.5
UK	First day in ICU	85.3
UK	Following days	66.1
Europe	Medical ICUs	41.1

Table 1: Average phlebotomy-induced blood lost in critically ill patients[11]

Effects of anaemia

Oxygen delivery is determined by arterial blood oxygen content and cardiac output. Healthy individuals increase cardiac output in response to anaemia but many critically ill patients have limited capacity to generate the cardiac output required for adequate tissue oxygenation[14]. Due to the loss in oxygen carrying capacity, the consequences of anaemia in critically ill patients include reduced tissue oxygenation and eventually ischaemia of end organs.

Correlating anaemia to outcome can be complex, as the anaemia itself can be caused by underlying co-morbidities. Studies on postoperative outcomes for anaemic patients who refused transfusion on religious grounds suggested that mortality was inversely related to postoperative haemoglobin level in comparison to a control group[15]. Other data have linked the increased risk of mortality with patients with cardiovascular disease[15].

Blood transfusions within the ICU

Frequency of transfusions

Due to the prevalence of anaemia in intensive care, a large number of patients receive blood transfusions[17] in the form of packed red blood cell (PRBC) transfusions[1]. In two large multicentre cohort studies in the United States and Western Europe, 37% and 45% of intensive care patients received PRBC transfusions respectively[1 18]. Longer stays result in a higher rate of transfusion with a reported 85% of patients residing in the ICU for one week or more requiring blood transfusions[10].

Consequences

Blood transfusions are expensive, can have deleterious effects on patient outcome and can be in short supply[17].

Although the risks are very low[19], PRBC transfusions include the following adverse effects, all of which lead to significant morbidity and mortality[20 21]:

- Allergenic/anaphylactic and haemolytic transfusion reactions
- Transfusion-related acute lung injury (TRALI)
- Transfusion-associated circulatory overload (TACO)
- Acute respiratory distress syndrome (ARDS)
- Ventilator-associated pneumonia
- Nosocomial infection risk (viral, bacterial, parasitic or prion transmission) – The absolute risk for nosocomial infection was 12% among conservatively-transfused patients and 17% among liberally-transfused patients, i.e. for every 38 patients treated under a liberal transfusion strategy, another hospital-acquired infection resulted [22]

There is also a growing appreciation of the less recognised risks of transfusion relating to PRBC storage effects and to the immunomodulatory effect of PRBC transfusion[23]. Critically ill patients are likely to be more at risk of immunosuppressive and microcirculatory complications of blood cell transfusions than the general population[24].

The transfusion decision

The traditional trigger for red blood cell transfusion is a haemoglobin reading of 10g/dL or less. With the growing understanding of the side effects, there have been a number of studies carried out to compare restrictive and liberal transfusion regimes. These have demonstrated that a restrictive regime can be associated with lower rates of organ failure and mortality[3]. A recent guideline document based on a review of the available evidence concluded that a threshold of 7g/dL should be used for critical care patients unless there were specific co-morbidities or acute illness-related factors, such as sepsis, neurotrauma or ischaemic heart disease[16].

Costs associated with transfusions

Estimates of the cost of transfusions vary widely, depending on the scope of what is used in the calculation. Some or all of the following can be included:

- Acquisition, screening and storage
- Staff and hospital costs
- Management of inventory
- Pre-transfusion testing
- Management of side effects
- Follow up checks
- Overhead

A recent meta-analysis of six studies concluded that a two unit transfusion of blood in Europe cost an average of £763[25]. Taking into account the management of complications, the Mayo Clinic have estimated the true total cost of transfusion of red blood cells to be £775 for a single unit [26].

Transfusions are therefore a significant cost in critical care, and avoidance of transfusion is a worthwhile economic, as well as clinical, goal.

Blood conservation strategies

The main methods for reducing the contribution of blood tests to the incidence of iatrogenic anaemia have been identified as [27]:

- Reduction of unnecessary testing
- Drawing smaller samples
- Re-infusion of the discard volume

Appropriate testing

While there have been repeated calls in the literature to reduce the frequency of blood measurement, studies to evaluate the effect of education on the appropriate use of phlebotomy have not shown a significant change in practice[13]. Evidence shows that avoidance of excessive testing is hard to implement[24] and ICUs presently continue to take what is seen as a high number of blood draws.

Arguments for the correct frequency of testing can be retrospective in nature, determining from the test result that the patient's therapy was in control, therefore a test was not needed. This ignores whether it is readily apparent before the test that the patient was in an acceptable state, particularly given the range of experience in critical care staff.

A further issue that is rarely discussed in the literature is whether more frequent testing in some patients could be desirable in order to more rapidly detect deteriorating conditions and intervene. Introduction of continuous measurement modalities often identify that large excursions in condition occur much more frequently than is evident from intermittent measurement[28]. There are systemic factors of staff cover and blood gas analyser availability that make both rapid and frequent testing of the unstable patient difficult. This has, for example, led to difficulties in implementing protocols such as tight glycaemic control[29].

Drawing smaller samples

If collection tubes are used for blood sampling, switching from adult- to paediatric-sized tubes may reduce the diagnostic blood loss by over 40% [30]. For the majority of blood gas analysers, a typical sample volume of 150μl will provide results for blood gas, electrolytes, haemoglobin, haematocrit and blood sugar. However in a 2001 survey, O'Hare found that paediatric tubes were routinely used in only 14% of adult ICUs [10].

Whilst the use of paediatric sampling tubes reduces the volume of blood drawn from a patient, it does not address blood loss associated with the discard volume. A limited survey of current practice in the UK (Table 2) indicates that there has not been a substantial change in practice with regards to either limiting discard volume or the use of smaller draw volumes.

Centre	Discard volume	Sample volume
1	10 ml*	2 ml
2	3 ml	1 ml
3	3 ml	1 ml
4	5 ml	2 ml
5	5 ml	2 ml
6	5 ml	2 ml
7	5 ml	2 ml
Average	5.1 ml	1.7 ml

** Drawn from just under the pressure transducer, estimated to contain ~ 5 ml blood.*

Table 2: Discard and sample volumes drawn in seven UK adult critical care settings

Re-infusion of the discard volume

When sampling from an arterial or venous catheter, it is important to remove an adequate amount of discard volume to ensure that a representative blood sample is obtained. One of the simplest methods to address iatrogenic blood loss is to re-infuse the discard volume once the blood sample is drawn[13]. Re-infusion of the discard volume is not without risk e.g. potential to re-infuse clot(s)/contaminated discard, potential for error including the possibility of confusing the discard syringe with the blood sample[31], infection and air embolism[10].

Closed sampler devices allow sampling of undiluted blood whilst safely storing the discard volume in a reservoir within the line's circuit. This allows for return of the discard volume to the circulation whilst maintaining a closed system. A recent review article of the relatively limited clinical literature[24] concludes that use of closed blood samplers:

- Reduces the amount of blood drawn
- Does not have a detrimental effect on the rate of catheter related infections
- Has promising evidence for the reduction of anaemia and transfusions

The strongest evidence for the latter was a 250 patient study that found the use of a blood conservation device was independently associated with lower RBC transfusions (control group 0.13 units vs. active group 0.068 units RBC/patient/day)[17]. The study had broad inclusion criteria, and it is likely that patient groups requiring higher rates of testing and therefore more at risk of anaemia are likely to have benefitted more than this averaged figure.

Patient dedicated analysers and blood conservation

The Proxima System is a patient dedicated blood gas analyser (Figure 1). The Proxima Sensor is integrated into the patient's arterial line operating as a closed system to minimise blood handling and infection risk. During the sample measurement procedure, the user draws blood into the Proxima Sensor using a closed sampler device. Once the sample has been analysed, all blood is returned to the patient. Results are displayed on the bedside monitor.

Table 3 presents the design features of the Proxima System and how common effective blood conservation strategies are addressed within this new medical device.

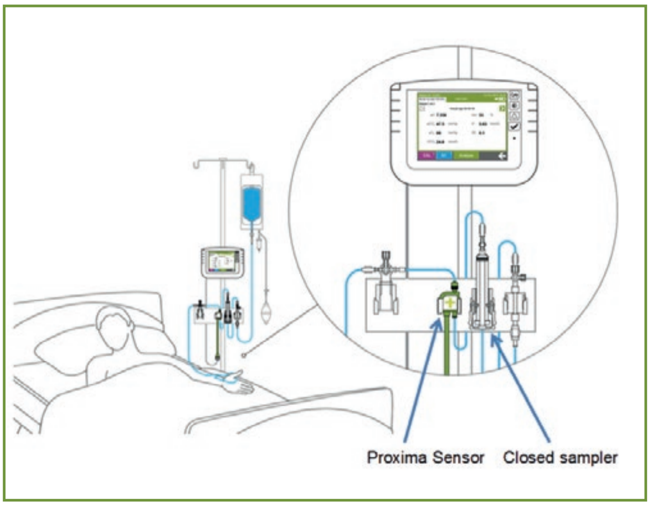

Figure 1: The Proxima System designed for on-demand bedside blood gas analysis

Blood conservation strategy	How a patient dedicated system helps
Appropriate sampling	• By substantially changing the constraints around blood loss, incremental cost and staff impact, a patient dedicated blood gas analyser **redefines the boundaries** of what is appropriate testing frequency. • As well as diminishing any impact of the more frequent "confidence" testing by less experienced staff, it also **facilitates more frequent or faster response testing** where indicated.
Smaller test volumes	• By **integration of the blood gas analyser** into the arterial pressure monitoring set, the analysed blood **sample is retained within the set during the measurement process.** • After analysis, the **entire withdrawn sample is returned to the patient**, resulting in **zero net loss**.
Returning discard	• The system incorporates the use of **a closed sampler device** within the design. • As well as allowing all **discard to be returned safely to the patient**, there is no need to open the line to withdraw a sample, thereby **reducing the risks** of introducing an infection or handling potentially infectious blood.

Table 3: Design features of the Proxima System that address blood conservation strategies

Conclusions

- **Medical personnel can cause substantial blood losses in their patients – phlebotomy is an extensively studied example. Diagnostic blood loss is a major determinant of anaemia in ICUs, accounting for substantial amounts of transfused blood. Within the ICU setting, the total amount of diagnostic blood loss is a significant predicator of allogeneic transfusion**
- **Transfusions are associated with poorer outcomes and longer stays**
- **Transfusions and delayed discharge both cost money**
- **Blood conservation strategies have the potential to be of significant benefit to patients and will help reduce costs of care. Proxima embodies a device that supports state of the art strategies for blood conservation while allowing more frequent blood gas measurement if appropriate**

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