Online measurement of haemoglobin concentration

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Abstract

Background. Regular monitoring of haemoglobin in chronic haemodialysis patients is essential to ensure that targets for anaemia management are consistently achieved. Repeated blood sampling can be time consuming, invasive and, for pragmatic reasons, only infrequently performed, often delaying therapeutic change. On-line optical continuous monitoring of the haemoglobin concentration would allow non-invasive assessment of haemoglobin, and immediate therapeutic changes could be implemented, thereby improving the efficiency of anaemia management. This study aimed to evaluate the use of on-line haemoglobin concentration measurement.

Methods. Eleven dialysis monitors (Integra®/C213 Hospal) were calibrated using at least five haemoglobin samples spread over at least 4 g/dl. Optical measurement of haemoglobin concentration is already incorporated into the dialysis monitor to allow the study of relative blood volume. Fifteen patients were studied with paired haemoglobin measurements (i.e. dialysis monitor value and conventional laboratory assessment) taken at intervals over 7 months (mean 11.0±0.28 g/dl, range 7.5–14.8).

Results. Haemoglobin measured by Hemoscan® correlated well with the laboratory measurements ($r^2=0.83$, $P<0.0001$), indicating that the machine values are broadly comparable with laboratory figures. There was a mean underestimate of haemoglobin by Hemoscan® of 0.34%. There was no significant deterioration in the quality of this correlation over the study period ($r^2>0.8$).

Conclusion. The ability of the dialysis monitor to measure the optical concentration of haemoglobin compared with conventional laboratory assessment is both precise and accurate. Regular on-line assessment of haemoglobin may allow more proactive micromanagement of renal anaemia, with a reduction in the time taken to achieve clinically important targets and give early warning of suboptimal response to treatment.

Keywords: haemoglobin concentration; on-line monitoring

Introduction

The measurement of haemoglobin (Hb) concentration is of great importance in the haemodialysis (HD) population [1], with considerable resources of time, effort and finance being expended to ensure that the patients gain the greatest benefit from maintenance of their Hb at normal or near normal levels [2,3]. Hb measurements are not routinely measured at <4 weekly intervals, as this is the NKF-K/DOQI recommended frequency for checking $Kt/V$ [4]. This inevitably introduces a delay between any change in the patient’s Hb concentration and institution of an appropriate therapeutic response. The greatest individual component of this delay is likely to be the time between the change in Hb occurring and the next routine blood round, but other components are also involved. These include the time between taking the blood sample and processing it, the time between the result being available and the appropriate physician being aware of it, and the time from then until the appropriate therapeutic response is actioned. All of these factors impair the efficient detection and correction of anaemia in HD patients.

Potentially, more frequent venesection could help to improve this situation. There would, however, be a significantly increased cost in laboratory consumables, and inconvenience to nursing staff and patients. Furthermore, increased numbers of blood tests can result in worsening anaemia if a sufficient volume of blood is withdrawn [5]. Optical measurement of Hb ($H_{opt}$) would avoid these problems.

Although optical monitoring of relative change in Hb concentration has been integrated into many
dialysis monitors for some time, this has not generally been used to monitor absolute Hb concentrations [6,7]. The Hemoscan® (Hospal, Mirandola, Italy) system allows calibration of Hbopt against local laboratory-based measurement. If Hemoscan® is to be used for Hb monitoring in the clinical arena, it is important to assess its accuracy and reliability. As Hb concentration changes over the course of a dialysis session, it would also be important to check that the initial measurement of Hbopt correlates closely with the pre-dialysis Hb measured in the laboratory on a sample taken at the initiation of dialysis.

The accuracy and reliability of Hemoscan® have not been tested in routine clinical use. The aim of this study was to make an initial assessment of the clinical utility of on-line measurement of Hbopt.

Methods

Eleven Integra® (Hospal, Mirandola, Italy) dialysis machines were assessed. Relative blood volume (RBV) monitoring by Hemoscan® is fitted as standard to these machines. This module allows continuous monitoring of RBV, the display of signals in numerical and graphical mode, off-line data retrieval and periodic on-board alignment to the laboratory Hb values, thereby accounting for any relative drift between the two devices. Alignment with the local laboratory involves the simultaneous measurement of Hb by both Hemoscan® and standard laboratory assessment, and consists of three parts. First, the Hemoscan® module collects data during a dialysis session, laboratory data are then inserted and finally standard linear regression is performed. Five separate pairs of samples are required to align the machines correctly (not necessarily from the same patients). Sufficient spread between the results is also required (at least 4 g/dl between the maximum and minimum recorded values). All blood samples were taken directly from the arterial line while a useable Hemoscan® trace was available. Hb was subsequently measured by the hospital laboratory Sysmex XE 2100® analyser (Sysmex, Kobe, Japan), which uses the sodium lauryl sulfate-haemoglobin method, and has a coefficient of variation of <1% for all red blood cell (RBC) parameters [8]. The coefficient of variation is higher at lower Hb levels, rising to 3.9% for samples with a mean Hb of 6.9 ± 0.27 g/dl. Once sufficient numbers and spread of samples are available, the Integra® monitor internally aligns Hbopt against the laboratory samples with standard linear regression. After it has been performed, the displayed values of Hbopt and blood volume are computed by applying the regression coefficients. Hemoscan® has a range of measurement from 7 to 14 g/dl, an accuracy of ±0.5 g/dl if aligned and a resolution of ±0.1 g/dl.

In the first phase of the study, further paired measurements were made from a range of dialysis patients, using all 11 machines, at regular intervals over the course of 7 months, in order to ascertain the accuracy and reliability of the Hemoscan®. Blood samples for laboratory analysis were taken mid-dialysis while a useable Hemoscan® trace was available, and a simultaneous note of Hb opt was made. Ten further paired observations were taken in the middle of the study.

In the second phase of the study, 16 blood samples were taken at dialysis initiation for laboratory analysis, as per routine clinical blood sampling guidelines. The laboratory values obtained were then compared with Hbopt recorded by Dialmaster® (Hospal, Mirandola, Italy) at the start of dialysis. Dialmaster® is a central computer system with the facility to record data from dialysis monitors linked to the system. Patients are identified by a card system, allowing for subsequent off-line analysis and interpretation of a large number of monitored variables. In this instance, a record of Hbopt was studied, and the initial value was taken from the first Hbopt recorded after dialysis initiation.

A total of 46 data points were collected (11 at initial alignment of the dialysis monitors, 10 from the middle of the study, nine at completion at the study and 16 from a comparison of recorded data with pre-dialysis samples). Autocalibration sufficient to analyse RBV is performed prior to every dialysis session. There are no manufacturer’s guidelines as to the frequency with which further laboratory alignment should be performed.

Patients

Fifteen patients were recruited from our chronic HD population, mean age 65 years. All patients were undergoing standard HD. Patients were dialysed using bicarbonate buffering, a dialysate sodium concentration of 140 mmol/l and a dialysate flow rate of 500 ml/min. HD used either low-flux haemophan polycarbonate membranes (Hospal HG 500–700) or mid-flux cellulose diacetate membranes (Hospal Diacepal 20); no dialysers were reused, and a linearly decreasing ultrafiltration profile was used throughout. Those known to have haemoglobinemia or myoglobinemia or those prescribed rifampicin were excluded. These substances absorb light at the same wavelength as Hb and can interfere with the accurate measurement of Hbopt.

Appropriate ethical approval was obtained from the local research ethics committee.

Statistical analysis

All data were analysed using GraphPad Prism version 3.00 for Windows (GraphPad Software, San Diego CA, www.graphpad.com). Data are expressed as mean ± SD unless otherwise stated. Bland–Altman plots were created by plotting the difference between Hbopt and laboratory-measured Hb, expressed as a percentage of the mean of the two measurements, against the mean of the two measurements.

Results

Hb measured by Hemoscan® shows a strong correlation with that measured by Sysmex® analyser (r² = 0.89, Figure 1) and is accurate as demonstrated in the Bland–Altman plot (Figure 2). Mean overestimate of Hb by Hemoscan® was 1.3 ± 2.4%.

Seven months later, precision and accuracy appear undiminished (Figures 3 and 4) (r² = 0.97, P < 0.0001). At this stage, there is a mean underestimate by Hemoscan® of 1.0 ± 1.5%. Two machines had had adjustment of their software or other problems, and were no longer aligned. These monitors were removed from further analysis.
Hemoscan® was also accurate in the second phase of the study. Laboratory Hb measured in the standard pre-dialysis manner was comparable with the value for Hbopt recorded by Dialmaster® at the start of dialysis (Figure 5). In this case, Hemoscan® underestimated Hb by a mean of 0.7 ± 4.1% compared with the Sysmex® analyser, though precision was slightly reduced ($r^2 = 0.75$, compared with $r^2 = 0.90$ for all paired samples).

Finally, in an overall analysis ($n = 46$), Hemoscan® shows good precision and accuracy (Figure 6). Mean overestimate by Hemoscan® was 0.1 ± 3.3%. This is despite combining results from alignment, the middle and the end of the study, or from the comparison of initial Dialmaster records of Hbopt, for blood samples and Hemoscan® results taken simultaneously.

**Discussion**

Initial results immediately post-alignment comparing Hbopt and Hb measured by the Sysmex® XE 2100 analyser show good precision and accuracy. This precision and accuracy are maintained in at least the medium term (over the 7 month period of this study). Overall results suggest that precision is increased for higher values. Some of the scatter seen is due to inherent variability within the Sysmex XE 2100® analyser used as a comparator. While there appears to be less agreement between the two methods at lower Hb levels, the documented precision of the Sysmex® analyser is also reduced for these concentrations [8]. Therefore, the scatter seen at lower Hb concentrations may be due to the Sysmex® analyser...
rather than the Hemoscan® module alone. In either case, the magnitude of the fluctuations is sufficiently small that they would have little impact on clinical decision making.

Results from the comparison of off-line analysis of the Hemoscan® results with pre-dialysis blood samples demonstrated slightly reduced precision and accuracy compared with the initial alignment samples ($r^2 = 0.75$, as compared with $r^2 = 0.90$). This is still sufficiently reliable for the vast majority of clinical situations, and is further supported by the ability of Hemoscan® to measure Hbopt at every dialysis session. Any inaccuracy would be automatically re-checked after 2 or 3 days, and there will be less urgency to respond to single results if trends in Hb can be observed. Recorded Hemoscan® results by Dialmaster are suitably comparable with pre-dialysis Hb results measured in the conventional manner.

Our data suggest that while some precision is lost, this is still a clinically useful measure of Hb. Therefore, off-line results will be available at the physician’s convenience.

Measurement of Hbopt may also lead to further refinement of anaemia management. Measurement of Hbopt at every dialysis session would lead to early detection of anaemia, and therefore should reduce the response time prior to appropriate clinical therapeutic action. This in turn should lead to an overall increase in the total time that a patient spends with a satisfactory Hb. Secondly, when considering the response to changes in Hb and erythropoietin doses, currently available algorithms [9] depend on considering both the absolute Hb concentration and the rate of change of Hb concentration. Similar algorithms could be constructed responding to smaller rates of change in Hbopt, potentially delivering a much more individually tailored and more efficient erythropoietin regimen.

The full value of anaemia management using Hbopt compared with monthly laboratory-based measurement would require evaluation by further study.

It is important to note that optical measurement of Hb does have some limitations. Its use is restricted in situations where substances that absorb light at the same wavelength as Hb may be present. These include treatment with rifampicin, myoglobinaemia and haemoglobinemia. Our data would indicate that repeated alignment of the Hemoscan® module with the local laboratory should perhaps be performed every 3 months to ensure that drift does not occur.

Overall, this study suggests that Hemoscan® is a reliable system for producing an accurate measure not only of RBV, but also of absolute Hb concentration. This has the potential to be a useful tool with which to adjust erythropoietin dosages, enabling a more rapid response to any change in Hb, and hence more efficient use of a scarce resource.

Conflict of interest statement. C.W.M. has received an unrestricted educational grant from Gambro Hospal. No other authors have any conflict of interest to declare.

References


Received for publication: 14.12.04
Accepted in revised form: 4.5.05