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Effects of Anemia on Pulse Oximetry and Continuous Mixed Venous Hemoglobin Saturation Monitoring in Dogs

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The accuracy of pulse oximetry (for pulse hemoglobin oxygen saturation [Sp_{O_2}]) and mixed venous oximetry (for mixed venous hemoglobin oxygen saturation [$S\bar{v}_{O_2}$]) was assessed during progressive normovolemic anemia in dogs. Splenectomized mongrel dogs under general anesthesia were monitored with a three-wavelength pulmonary artery oximeter catheter (10 dogs) and a pulse oximeter (11 dogs). Data were collected while fractional inspired oxygen concentration (FI_{O_2}) was varied from 1.00 to 0.05 in seven steps. The dogs then underwent isovolemic hemodilution, and the FI_{O_2} was again varied. This sequence continued until data no longer could be obtained. The accuracy of each device was assessed by determining the bias (the average difference between the continuous monitor oximeter and the bench oximeter) and the precision (the standard deviation of the difference). For the three-wavelength Oximetrix catheter (for hemoglobin oxygen saturation denoted here Sox_{O_2}), the overall bias ($Sox_{O_2} - S\bar{v}_{O_2}$) and precision were $-0.7 \pm 8.6\%$ for the 193 data points. The accuracy as assessed by bias and precision for Sox_{O_2} was similar for hematocrits of 40–15%. (Bias ± precision was $2.1 \pm 5.7\%$ for hematocrits greater than 40%, and $-1.1 \pm 7.5\%$ for hematocrits of 15% to 19%). At hematocrits between 10 and 14%, the precision worsened to 12%, and for hematocrits less than 10% the bias ± precision was $-11.5 \pm 11.8\%$. The overall Sp_{O_2} accuracy was $0.2 \pm 7.6\%$ for 178 points. The pulse oximeter's accuracy was similar, down to hematocrits of 10%. Below 10%, the bias and precision worsened to $-5.4 \pm 18.8\%$. In some instances, a reliable pulse oximeter reading was not obtained, as evidenced by pulse oximeter pulse rate in disagreement with ECG heart rate. The frequency of these failures increased with decreasing hematocrit, especially at hematocrits less than 10%. We found that both of the continuous saturation monitoring techniques maintained acceptable accuracy at hematocrits as low as 10–15%. For both techniques, accuracy became unacceptable when the hematocrit was less than 10%. (Key words: Blood, hemoglobin: saturation; anemia. Monitoring: oximetry.)

OVER THE PAST DECADE techniques have been developed for continuous monitoring of arterial (Sa_{O_2}) and mixed venous hemoglobin oxygen saturation ($S\bar{v}_{O_2}$). $S\bar{v}_{O_2}$ is monitored by analyzing a reflected light signal transmitted through fiberoptic bundles incorporated into a pulmonary artery catheter (for hemoglobin oxygen saturation denoted here Sox_{O_2}). Sa_{O_2} has become a standard for intraoperative monitoring since the development of pulse oximetry (for hemoglobin oxygen saturation denoted here Sp_{O_2}) in the early 1980s. The same time period has seen an increased awareness of the infectious risks of blood products, resulting in a tendency to withhold blood transfusion until absolutely necessary. Thus, arterial and venous *in vivo* oximetry will be used with increasing frequency on patients with hematocrits less than normal. Theoretically, there should be a hemoglobin level below which the oximeter does not have sufficient signal to determine the hemoglobin saturation. However, few data have been published on the possible effects of decreasing hemoglobin concentrations on the accuracy of these monitors.[1,2],§ The purpose of this study was to determine the accuracy in dogs of two different types of *in vivo* oximeters, the noninvasive transmission pulse oximeter and the invasive reflectance pulmonary artery oximeter, under the conditions of normovolemic anemia.

Materials and Methods

This study was approved by the University Animal Research Committee. Eleven mongrel dogs weighing 10–20 kg received 0.3 mg/kg intramuscular acepromazine, and intravenous access was established in a forelimb vein. Anesthesia was induced and maintained by intermittent boluses of pentobarbital 10–20 mg/kg. Pancuronium 0.1 mg/kg was given only if shivering occurred. After induction of anesthesia and tracheal intubation, the animal's lungs were mechanically ventilated to produce normocapnia. A femoral cutdown established access for a 16-G arterial catheter and an 8.5-Fr venous introducer. The 7.5-Fr Oximetrix P7110 Shaw Opticath pulmonary artery catheter (Abbott Laboratories, Mountain View, CA) was calibrated *in vitro* as recommended by the manufacturer and then inserted to a wedge position by observing the pressure waveform. Oximetrix catheters were inserted in 10 of the 11 dogs. A disposable Nellcor finger probe (model D25) was applied to the tongue and secured with a towel clamp. The sensor was connected to the N-100 pulse oximeter (Nellcor, Hayward, CA). Each data set

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§ Tremper KK, Hufstedler SM, Barker SJ, Adams AL, Wong DH, Zaccari J, Benik K, Lemons V: Accuracy of a pulse oximeter in the critically ill adult: Effects of temperature and hemodynamics (abtract). ANESTHESIOLOGY 63:A175, 1985.

included heart rate, respiratory rate, core and rectal temperatures, systemic and pulmonary arterial pressures, cardiac output by thermodilution, inspired oxygen fraction (FI_{O_2}), end-tidal carbon dioxide, Sa_{O_2}, $S\bar{v}_{O_2}$, and arterial and mixed venous hemoglobin saturation by the N-100 (Sp_{O_2}) and Opticath (Sox_{O_2}), respectively. The N-100 was considered to give a valid reading if the heart rate was within 5 beats per min of the ECG value. Arterial and mixed venous blood samples were obtained anaerobically for immediate analysis by an IL-282 co-oximeter set for canine hemoglobin (Instrumentation Laboratories, Lexington, MA) and an ABL-2 blood gas machine (Radiometer, Copenhagen, Denmark). Both bench instruments were calibrated daily. Hematocrit was determined for each data point as the mean of three samples by spun capillary tube.

To test the response of the oximeters, the fractional inspired oxygen concentration (FI_{O_2}) was varied in steps from 1.00 to 0.05 (1.00, 0.40, 0.24, 0.18, 0.14, 0.10, and 0.05) using nitrogen. The lower limit of FI_{O_2} was increased at lower hematocrits if the dog was hemodynamically unstable. Fifteen minutes was allowed to attain equilibrium at each FI_{O_2} before data were sampled. Following measurements at the lowest FI_{O_2}, the FI_{O_2} was increased to 1.0 prior to isovolemic hemodilution. Hemodilution was accomplished by removing 20–30 ml/kg of blood and replacing it 3:1 with crystalloid or 1:1 with colloid. Pulmonary artery pressures were maintained near baseline values. Sampling was then continued by varying FI_{O_2} at the newly established hematocrit. The cycle of varying FI_{O_2} and stepwise hemodilution was continued until data were no longer obtainable. Normothermia was maintained with a heating blanket, warmed intravenous fluids, and hot water bottles placed on the thorax and abdomen.

It became apparent after the first three dogs were studied that their spleens are very effective in autotransfusion. The hematocrit gradually increased as the FI_{O_2} was decreased at hematocrits less than 20%, necessitating further hemodilution for each sampling point. This problem led us to perform splenectomies upon the remaining dogs before any data were collected.

The accuracy of the two *in vivo* oximeters was determined by comparison with the IL-282 co-oximeter using the method described by Bland and Altman.[3,4] The bias or systematic error is defined as the mean difference between the *in vivo* oximeter reading and the IL-282 co-oximeter. Precision or random error is defined as the standard deviation of those differences.[3,4] Actually, as originally described by Bland and Altman, the bias is defined as the "gold standard" minus the "new method."[3,4] For the current study, the bias therefore was the mean of the IL-282 co-oximeter minus the *in vivo* monitor's reading. Therefore, if the new method underestimates the standard method, the bias will be positive. Unfortunately, this procedure is not consistent with the presentation of data in the United States literature. It also seems more intuitive if a negative bias means an underestimation by the new method and a positive bias means an overestimation by the new method. For that reason, we have defined bias in the current study as the mean of the "new method" minus the "gold standard."

Percent hemoglobin oxygen saturation from the IL-282 co-oximeter represents fractional saturation defined as $100\% \times Hb_{O_2}/(Hb_{O_2} + Hb + Hb_{CO} + Hb_{met})$, where Hb_{O_2}, Hb, Hb_{CO}, and Hb_{met} represent oxyhemoglobin, reduced hemoglobin, carboxyhemoglobin, and methemoglobin, respectively. All blood samples in this study contained less than 1% Hb_{met} or Hb_{CO}.

Results

The bias and precision data are presented in table 1 for the two monitors for hematocrits ranging from >40 to <10%. The results are illustrated in figures 1 and 2 for the pulse oximeter and the oximeter catheter, respectively. In these figures bias values are plotted as a function of hematocrit, and the vertical hash marks represent ± 1 precision (standard deviation of the bias). For the pulse oximeter, an overall bias of 0.2 ± 7.6% was obtained. The bias and precision values were relatively constant over the entire range until the hematocrit decreased to <10%. Because the dogs could not tolerate the combined insults of severe anemia and arterial hemoglobin desaturation, there were fewer data in the lowest hematocrit range. As noted in table 1, one of the seven data

TABLE 1. Bias and Precision of Nellcor and Oximetrix Oximeters at Various Hematocrits

Hematocrit (%)	Bias (%)	Precision (%)	Number of Data Points
Nellcor N-100			
<10	−5.4 (1.7)	18.8 (2.4)	7 (6)
10–14	0.8	3.7	28
15–19	−0.9	5.9	32
20–24	−0.5	6.9	39
25–29	0.3	7.8	23
30–34	1.2	6.8	28
35–39	5.5 (3.8)	7.4 (5.3)	11 (10)
≥40	−0.4 (3)	11.5 (4.3)	10 (9)
All	0.2	7.6	178
Oximetrix Opticath			
<10	−11.5	11.8	12
10–14	2.5	12	36
15–19	−1.1	7.5	33
20–24	1	7.3	39
25–29	2.4	5.5	25
30–34	2.9	3.9	27*
35–39	1.5	3.4	11
≥40	2.1	5.7	193

Data in parentheses exclude conspicuous outlier data points.
* Mixed venous blood sample error.

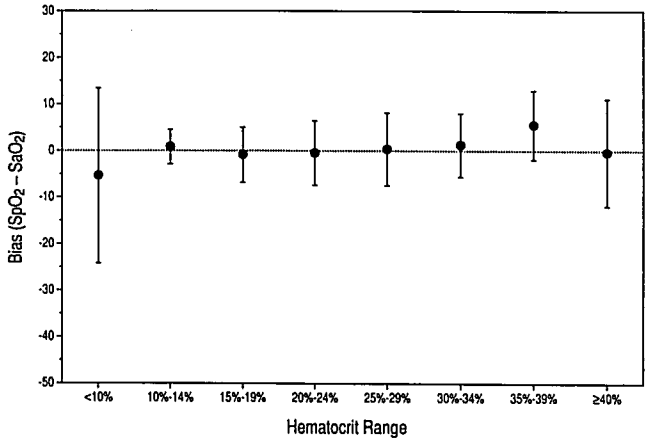

FIG. 1. Pulse oximeter bias and precision data *versus* hematocrit range. The vertical bars represent positive or negative precision (standard deviation). The bias values in each hematocrit range are pooled data from 11 dogs while FI_{O_2} was varied from 1.00 to 0.05. This range of FI_{O_2} resulted in Sa_{O_2} values from 100 to 12%.

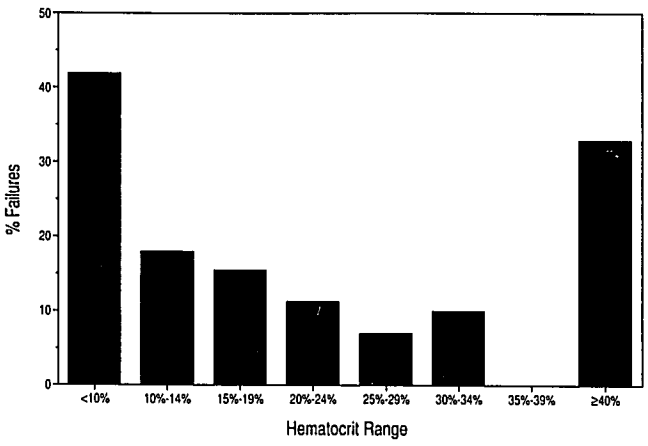

FIG. 3. The frequency of pulse oximeter failures *versus* hematocrit. A failure was defined as complete loss of signal by the pulse oximeter or a pulse oximeter pulse rate that differed from the ECG, heart rate, and arterial pulse rate by greater than 5 beats per min.

points in the lowest hematocrit range was a significant outlier. When this point was removed from the calculations, the bias and precision for this range demonstrate the same accuracy as in the other ranges of hematocrit. This also occurred at the higher hematocrit range (table 1). Although the accuracy of the pulse oximeter did not appear to be substantially affected by hematocrit, the signal failure rate was affected by it. (A pulse oximeter failure was defined by either the inability to detect a signal or by a difference between pulse rate and heart rate of greater than 5 beats per min.) Figure 3 illustrates that the pulse oximeter failure rate increased with decreasing hematocrit. Curiously, the data with hematocrits >40% also had a high failure rate.

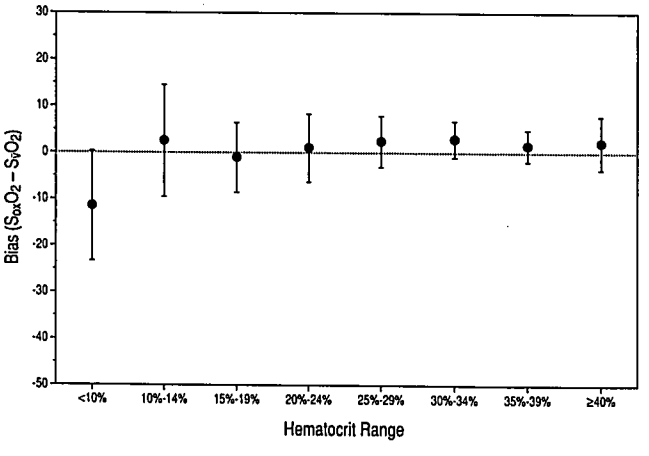

FIG. 2. Bias and precision for the Oximetrix catheter (Sox_{O_2}) *versus* hematocrit range. The vertical bars represent positive or negative precision (standard deviation). The bias and precision data are calculated from pooled data in each range collected from 10 dogs while the FI_{O_2} was varied from 1.00 to 0.05. This range in FI_{O_2} resulted in a $S\bar{v}_{O_2}$ range of 96 to 10%.

The oximeter catheter also demonstrated relatively consistent accuracy over a wide range of hematocrit (table 1 and fig. 2). An overall bias of 0.7 ± 8.6% was obtained from 193 data points. The accuracy deteriorated significantly when the hematocrit decreased to <10%. There were no "signal failures" with the Oximetrix catheter, but one mixed venous blood sample was erroneous (table 1).

Although the bias values for both of these monitors over much of the hematocrit range were close to zero, the precision values demonstrate significant random error. The limits of agreement have been defined as the bias ± 2 precision values. This is the range over which 95% of the data will lie.[3,4] For most of the data this implied a range of greater than ± 10% (table 1).

Discussion

Theoretically, severe anemia is expected to affect the accuracy of oximeter monitors.[5] Both the pulse oximeter and the mixed venous oximeter estimate relative concentrations of oxyhemoglobin by measuring the ratios of either reflected or transmitted light intensity. Hemoglobin in the reduced and oxidized forms has different absorbance and reflectance coefficients at the light frequencies used by these monitors. This difference produces a change in the intensity of the light signal relative to incident light as the proportions of oxidized and reduced hemoglobin change. In either case, in the absence of hemoglobin there should be no change in signal with changes in oxygenation. With very small concentrations of hemoglobin, this signal is expected to be small relative to the background noise.

A small signal-to-noise ratio usually leads to a less accurate measurement.

Early studies evaluating the accuracy of oximeters have used linear regression analysis to assess accuracy.[1,6-10] The scatterplot presented in these reports and later studies that presented bias and precision show ranges of "accuracy" similar to those found in this study.[11-15] Previous studies have also validated the application of data obtained from dogs to humans with respect to the absorption spectra of the two species' hemoglobins.[1,13] The data from our study with dogs indicates that the accuracy of both oximeter monitoring devices is relatively independent of hematocrit, down to a range of 10–14%. Below this hematocrit accuracy deteriorates. From the size of the precision values, one might also conclude that there is significant random error throughout the entire range of hematocrit when either device is used in dogs. Gettinger *et al.* compared the accuracy of two $S\bar{v}_{O_2}$ catheters during induced normovolemic anemia in dogs.[1] They concluded that the catheter that uses two wavelengths of light (American Edwards) was less accurate than the Oximetrix catheter, which uses three wavelengths of light. Their study produced hemoglobin values down to a range of "less than 10 mg/dl" (hematocrit ~30%). They did not report the actual values. They also did not report bias or precision data but performed regression analysis with correlation coefficients. Despite the high correlation coefficient they reported for the Oximetrix catheter (r = 0.99), their scatterplot plot showed significant random error.[1] The current study confirms and extends the findings of Gettinger *et al.* that the Oximetrix catheter provides $S\bar{v}_{O_2}$ data that are relatively independent of hematocrit down to the hematocrit range of 10 to 15%.

The accuracy of the Nellcor pulse oximeter also appears to be relatively constant down to a hematocrit range of 10–15% (table 1 and fig. 1). At the extremes of hematocrit, the pulse oximeter failure rate increased (fig. 3). During severe anemia one expects the signal failure rate to increase because the pulse amplitude of absorbance decreases. It is not clear why the pulse oximeter failure rate increased when the hematocrit was >40%. There were only 10 data points in this range, and all were collected from three dogs. After the induction of anesthesia and splenectomy in the other dogs, the first blood samples obtained all had hematocrits of 39% or less. It is possible that this relative "polycythemia" in these dogs represented chronic disease that resulted in a diminished pulse as detected by the oximeter. These three dogs had twice the overall pulse oximeter failure rate compared to the other eight dogs. There may also have been problems associated with the attachment of the oximeter probe to the dog's tongue. All of these failures occurred during desaturation.

Few clinical data are available on the accuracy of Sp_{O_2} measurement in anemic patients. Severinghaus and Koh have presented accuracy data in adult volunteers during severe desaturation.[2] Several of their subjects were mildly anemic (hemoglobin in the range of 10–12 g/dl), and one subject had a hemoglobin concentration of 8 g/dl. Multiple pulse oximeters were placed on these subjects as their Sa_{O_2} was reduced in a rapid fashion to approximately 50%. Their results demonstrated an increasingly negative bias with desaturation in the anemic subjects. In the most anemic subject, the mean pulse oximeter bias was −15% at a saturation of 54%.[2] Figure 4 presents our animal data for the low saturation points, mean Sa_{O_2} = 53.9% ± 12.2%. The bias showed a negative trend, from +15% in the hematocrit range of 35–39% to −6% in the hematocrit range of 25–29%. The bias remained slightly negative down to severe anemia (hematocrit <10%), where the bias decreased further to −14%. Because the dogs could not tolerate a saturation of 50% with a hematocrit of only 10%, there were only three data points during these combined insults.

These results demonstrate a trend similar to that found by Severinghaus and Koh[2] but with quantitative differences. Our bias starts positive and decreases to −6% over the same hematocrit range, whereas their data start with a slightly negative bias and decrease to −15%. Furthermore, these two studies differ dramatically in methods. Our animal study was conducted with the pulse oximeter of one manufacturer (Nellcor) on 11 dogs. Severinghaus and Koh collected data with 13 different pulse oximeters on a few mildly anemic human subjects. Our data were collected during steady state (15-min equilibrium), whereas their data were collected during a rapid, brief desaturation event. Despite these differences, the data from both studies demonstrate that anemia produces a

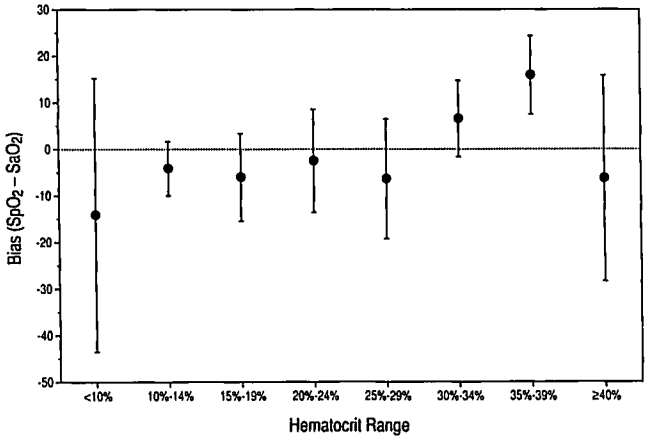

FIG. 4. Bias and precision pulse oximeter data *versus* hematocrit range for $Sa_{O_2} \leq 75\%$ only. The vertical bars represent positive or negative precision (standard deviation). The data in each range are pooled data from 11 dogs when the Sa_{O_2} was ≤ 75%; mean Sa_{O_2} = 53.9 ± 12.2%. Note that the bias trends negatively for these data as the dogs become more anemic.

negative bias during desaturation. Clinically this may be protective, for it will make desaturation events appear more severe in anemic patients. There may also be a physiologic reason for these results. Presumably the tissues and capillaries of anemic subjects desaturate more quickly as Sa_{O_2} decreases. The pulse oximeter may be detecting a portion of its signal from the blood in the desaturating microcirculation.

Both the invasive and the noninvasive oximeter monitors demonstrate surprisingly consistent accuracy over a wide range of hematocrit. The accuracy of both devices deteriorates as hematocrit decreases to <15% and becomes unacceptable at hematocrits of <10%. Although the bias values are small for both devices when hematocrits are >15%, the precision values demonstrate significant random error. It should therefore be kept in mind that individual data points may show significant error despite the overall accuracy of these devices.

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