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Accuracy of fetal pulse oximetry and pitfalls in measurements

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Abstract

Pulse oximetry is a technique for estimating arterial oxygen saturation continuously and non-invasively. Reflectance pulse oximetry might become useful for monitoring the fetus during labour but it is much more susceptible to all kinds of physiological variations than the well-established transmission pulse oximetry for neonatal or adult monitoring. This review focuses on the accuracy of reflectance pulse oximetry. Results of human, animal, in vitro and theoretical models indicate that factors such as; blood volume fraction differences, haematocrit, and blood flow differences are major sources for inaccurate pulse oximetry readings in the fetal arterial oxygen saturation range of 10–80%. These factors cannot be overcome by systems using two wavelengths sensors with the 660/890 or 940 nm combination. Reported precision values (S.D. of difference between pulse oximeter and blood sample saturation) range between 2.5 and 12.9% for various 660 nm sensors. Most sensors were tested only once with a limited number of animals. A new 735/890 nm sensor (Nellcor Puritan Bennett) demonstrates a promising accuracy (precision around 5%) in two studies. Various other sensors have also been developed, but are not or scarcely evaluated. Without thorough establishment of the reliability of this technique, clinical fetal oxygen saturation data are still of limited value. © 1997 Elsevier Science Ireland Ltd.

Keywords: Accuracy; Animal; Arterial oxygen saturation; Fetal; In vitro; Pulse oximetry

1. Introduction

Accurate assessment of the fetal condition during labour is a major problem in clinical obstetrical practice. The most commonly used method of intrapartum fetal surveillance is the continuous recording of the fetal heart rate combined with the uterine activity (cardiotocogram, CTG). Unfortunately, this technique is limited and additional techniques are needed.

Pulse oximetry measures the arterial oxygen saturation (SaO₂) continuously and non-invasively, and has become a standard technique to monitor critically ill patients during anaesthesia and intensive care. With the development of a reflectance sensor this tech-

nique might be useful during labour. The first experimental reflectance sensors were built from the components of commercial transmission sensors [1–3]. Optimism rose when it appeared possible to obtain signals from the fetal scalp during labour for prolonged periods [1–3]. Since then other reflectance sensors have been developed and experiences during labour have been reported [4–7].

However, before reflectance pulse oximetry can be introduced into clinical practice, careful validation is required. In the human fetus validation is hampered because arterial blood samples cannot be obtained. The human adult is not a suitable subject because normal fetal SaO₂ values are mainly below 70% and it is unsafe to subject adults to such low saturation levels. The evaluation is therefore mostly done in animal models and in vitro models, and by simulations in theoretical models.

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The purpose of this paper is to give an overview of the accuracy of reflectance pulse oximetry for fetal use. Various factors which may influence the reliability of this technique will be discussed. The factors are divided in four groups: haemoglobin, tissue compartment, sensor-to-skin contact, and technical problems. Where possible, we will give an estimation of the magnitude of its effect for the fetal SaO_2 range (10–80%). Finally, alternative approaches in sensor design for intrapartum use will be discussed. It is beyond the scope of this survey to review all articles in which pulse oximetry is used (approx. 1000). Most articles are based on transmission pulse oximetry for an SaO_2 range of 70–100%, and have been extensively reviewed elsewhere [8–12].

2. Basic concept of reflectance pulse oximetry

Pulse oximetry relies on light absorption differences by oxyhaemoglobin (HbO_2) and deoxyhaemoglobin (Hb). Fig. 1 shows the absorption spectra of HbO_2 and Hb as measured by Zijlstra et al. [13]. In the red region of the spectrum (approx. 660 nm), Hb absorbs more light than HbO_2 , and vice versa in the infrared region (850–1000 nm). This explains why, in general, the colour of arterial blood is a more bright red than venous blood.

Reflectance pulse oximetry sensors are mostly equipped with two light emitting diodes (LEDs) which transilluminate tissue, one red and one infrared light. A photodetector receives the fluctuating back-scattered light intensities caused by the pulsating blood volume in the tissue. Pulse oximeters use a fixed empirically derived calibration curve for the relation between the SaO_2 and the ratio of the rela-

tive pulse sizes (fluctuating light intensities) for red and infrared light. As a consequence, variations in the relationship caused by differences in light propagation between subjects or locations, cannot be taken into account.

2.1. Haemoglobin

Human fetal (HbF) and human adult haemoglobin (HbA) differ slightly in their spectra in the visible range [13]. Since most commercial pulse oximeters are programmed with a calibration curve derived from studies in healthy adults, this curve might not be applicable to the fetus with high concentrations of HbF. Based on the Lambert–Beer model Zijlstra et al. [13] concluded that these differences in spectra do not affect the accuracy of pulse oximetry in the SaO_2 range of 70–100%. They used the extinction coefficients at 660 nm and 940 nm in their model [13]. An evaluation in neonates, in which arterial values were compared to pulse oximetry saturation readings (SpO_2) over a range of 80–100%, revealed similar results [14]. However, at an SaO_2 level of 25%, Nijland et al. [15] calculated that such commercial pulse oximeters will underestimate the SaO_2 by 5%. These calculations were made with the same wavelengths as Zijlstra et al. [13], using the Lambert–Beer model as well as a more complex model as described by Schmitt [15,16].

Being a two-wavelength device, a pulse oximeter can only measure the ratio of concentrations of HbO_2 and Hb, which makes it specifically sensitive to changes in SaO_2 . However, other haemoglobin derivatives, like carboxyhaemoglobin (COHb) and methaemoglobin (MetHb) also absorb light in the visible

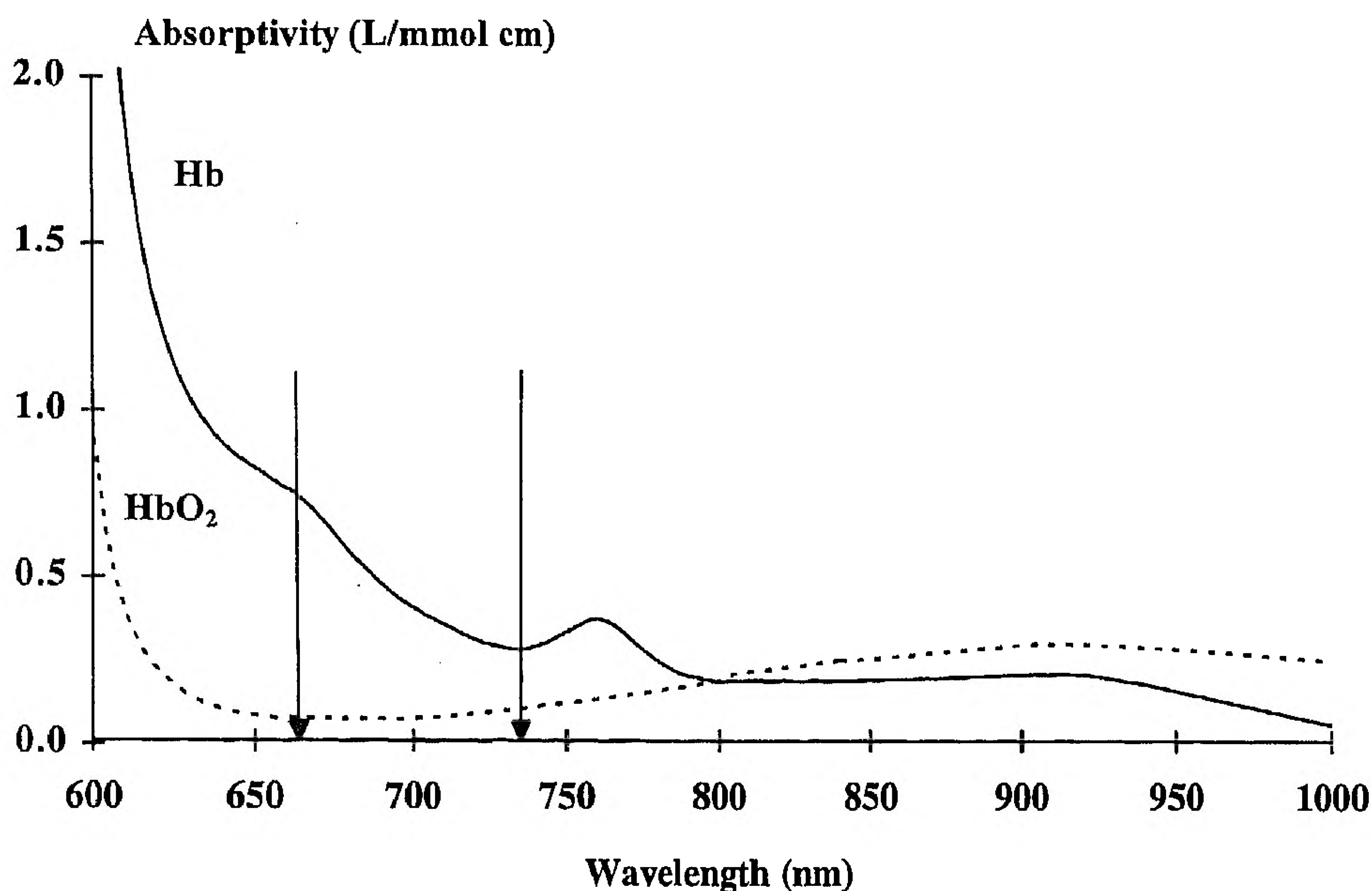


Fig. 1. Absorbance spectrum, HbO_2 : oxyhaemoglobin, Hb: deoxyhaemoglobin. Arrows indicate 660 nm and 735 nm wavelengths.

range and might therefore lead to errors in the SpO_2 . The error caused by the presence of 10% COHb appeared to be insubstantial over the whole SaO_2 range, for the wavelengths 660 nm and 940 nm, based on calculations with the Lambert–Beer model [13,15]. Barker et al. [17] and Reynolds et al. [18] reported that pulse oximeters provided erroneous readings in the presence of high levels of COHb. However, this was based on a misunderstanding of pulse oximetry, comparing the SpO_2 with the fraction of oxyhaemoglobin instead of the oxygen saturation [19]. In the presence of 10% MetHb, the Lambert–Beer model predicts an underestimation at $>70\%$ and an overestimation at $<70\%$ SaO_2 [13,15]. Similar findings were also reported by Reynolds et al. [18] using an in vitro model and by Barker et al. in dogs [20]. However, concentrations of 10% COHb and 10% MetHb are not expected in the human fetus during labour. In non-smoking pregnant women and their newborns, COHb concentrations are reported to be $<0.5\%$. COHb concentrations in blood of newborns of cigarette smoking mothers were 1.9% (S.D. 1.2%) [21].

The calibration of reflectance pulse oximetry for fetal use is more complicated than the calibration of transmission pulse oximetry for adult or neonatal use, as sample SaO_2 values cannot be obtained in the human fetus. In critically ill neonates, SaO_2 values may become as low as 60% [22], an SaO_2 value still not low enough for a fetal calibration. Therefore, animal models are used to calibrate reflectance pulse oximetry. Differences in the light absorption characteristics of haemoglobin of other species in the spectral range might lead to a different calibration line for the human fetus. Although, no differences were found at 660 nm and 940 nm for dogs and rabbits [23,24]. Presumably, haemoglobin light absorption characteristics of other mammals will not differ substantially from humans.

2.2. Tissue compartment

The attenuation of the light received at the photodetector is not only caused by absorption, but by scattering of light in tissue. The scattering of light by erythrocytes (e.g. velocity, size and shape) is of special importance, because it causes most of the fundamental problems in pulse oximetry at low saturation values. The scattering is largely determined by the haematocrit, blood flow conditions, and blood volume changes. Erythrocyte differences between human subjects and between animals might have an effect on the accuracy of pulse oximetry but this factor has not been studied yet.

The effect of various levels of haematocrit (Ht), using 660/940 or 950 nm transmission pulse oximetry,

was studied by De Kock and Tarassenko [25], and Vegfors et al. [26] with in vitro models, and by Lee et al. [27] in dogs. De Kock and Tarassenko found that the pulse oximeter was not affected by Ht differences (20, 39 and 60%) at SaO_2 levels $>50\%$, while $SaO_2 <50\%$ higher Ht levels resulted in lower red/infrared ratio's and thus in higher SpO_2 values [25]. However, Vegfors et al. found no correlation between SpO_2 readings and blood sample SaO_2 values over an SaO_2 range of 60–100% at Ht levels of 41–44%. Only after hemodilution to Ht levels of 10–11% a good agreement was found between pulse oximetry readings and sample SaO_2 values [26]. The contrasting results are probably caused by differences between the in vitro models. Lee et al. found that Ht changes did not seriously influence the accuracy of pulse oximetry when diluting the blood from 40 to 10% Ht. Below 10% Ht, pulse oximetry became inaccurate [27]. Fetal Ht levels in major blood vessels are mostly $>40\%$. In rabbit muscle capillaries Ht levels were found to be 10–15% [28]. The vascular distribution and which vascular tissue contributes to the received light is not known. It remains therefore to be seen how important Ht differences are for fetal reflectance pulse oximetry.

The effect of blood flow differences was studied with in vitro models, by De Kock and Tarassenko [25], and Lindberg et al. [29]. Above 40% SaO_2 , no effects were found on 660/950 nm transmission pulse oximetry values with different flow rates by De Kock and Tarassenko. Below 40% SaO_2 , lower flow rates resulted in lower red/infrared ratio's and higher SpO_2 values [25]. In contrast with these results, Lindberg et al. found lower SpO_2 values at low blood flow conditions at an SaO_2 of around 99%, with 660/940 nm transmission pulse oximetry [29]. It is not known how accurately the in vitro models represent the human fetal responses at low SaO_2 values.

The effect of blood volume fraction differences was studied with theoretical models [16,30] and in vitro models [25]. The theoretical models predicted that the influence of blood volume is of minor importance for the accuracy of 660/940 nm reflectance pulse oximetry if the $SaO_2 >70\%$ [16,30]. However, at an SaO_2 of 25% an overestimation of around 25% is predicted, when the blood volume was changed from 1 to 5% [16,30]. By changing the depth of the blood film in their in vitro model, De Kock and Tarassenko found similar results for 660/950 transmission pulse oximetry using an in vitro model [25]. By placing a prototype 660/890 nm reflectance sensor with the photodetector above the superficial temporal artery, Nijland et al. observed an underestimation with 5.8% for adults and 7.5% for neonates compared to the forehead location [31]. Placing the sensor with the LEDs over the artery did result in larger plethysmographic sig-

nals, but no difference in the SpO₂ values were observed [31]. An underestimation was also observed, when the same sensor was placed with the photodetector above a subcutaneous vein on the fetal lamb head [32]. The underestimation ranged from –16 to –28% in four fetal lambs, at an SaO₂ range of 20–50%. After coagulation of the vein, the difference between the intravascular SaO₂ and the SpO₂ was abolished [32]. The underestimation is in contradiction with the theoretical models [16,30] which predicted an overestimation as a result of increased blood volume. However, one must consider that in those models homogenous media of absorbers and scatters were used, which may not be applicable for the heterogeneity of in vivo tissue. Administration of adrenaline resulted in a vasoconstriction, and in an overestimation of 6–37% in five fetal lambs, at an SaO₂ range of 20–50% [32].

Using transmission pulse oximetry, venous pulsations are reported to give an underestimation of the SaO₂, for normal adult SaO₂ values [33].

2.3. Sensor-to-skin contact

Scattering of light occurs in all situations whenever there are variations of the refractive index i.e. at cross-sections of different tissue layers, at the boundaries of blood vessels and even within the cells themselves (e.g. by the mitochondria). It is therefore likely that differences in skin structure between animals and humans will influence the calibration of reflectance pulse oximetry. For none of the animal models the magnitude of this effect is known. The piglet has histologically a skin structure most alike to humans [34].

Several circumstances at the level of sensor-to-skin contact may lead to a reduced accuracy. Johnson et al. showed that meconium stained skin caused an inaccurate oxygen saturation reading in a neonate. Their explanation for this inaccuracy was that red light was more absorbed by meconium than infrared light [35]. Optical shunting through hair is also mentioned as a possible cause for inaccuracy. However, Nijland [36] did not observe differences between measurements on wet hair or shaved skin in three fetal lambs, with a prototype 660/890 nm Nellcor sensor. Gardosi et al. [37] showed that improper contact of the sensor to the skin can lead to erroneous pulse oximeter readings, if the light is directly shunted towards the photodetector.

Two studies have addressed the point of pressure to the back of the sensor [38,39]. Köning et al. [38] showed that pulsatility improved markedly at the forehead of adults if pressure was increased, but no consistent effect was observed in neonates. Dassel et al. [39] showed that red/infrared variability decreased with pressures between 80 and 120 mmHg applied on

the back of the sensor, at the forehead of adults. Increasing the pressure on the sensor probably decreases the venous blood in the tissue [39]. However, a lower pressure on the 660/940 nm sensor gave inconsistent results in the red/infrared ratio. The red/infrared ratio decreased or increased to a stable level or remained unchanged [39]. The effect of most of the factors mentioned in this paragraph have not been studied in the fetal SaO₂ range.

2.4. Technical problems

Certain technical situations may interfere with a reliable estimation of the SaO₂. Some problems related to the use of fetal reflectance pulse oximetry will be discussed in this paragraph: i.e. small pulses and signal analysis, the choice of the LED wavelengths, and motion artifacts.

The fetal plethysmographic signals obtained with reflectance pulse oximetry are typically one-tenth of the adult transmission pulse oximetry signals. The amplitude of the pulsatile component of the signal is often below 0.2% of the total signal, which is at the lower limit of signal acceptance for some commercial transmission pulse oximeters [8,40]. These small pulses lead to a lower signal to noise ratio and as a consequence a less accurate device. To optimize signal quality, fetal plethysmographic signals should be maximized while the noise is minimized. Pulse oximeters use several ways to enhance the signal processing. The fetal electrocardiogram is used to cardiosynchronize the red and infrared pulses. A high pass filter is used to detect the red and infrared peak and trough and the pulse oximeter verifies if the red and infrared peak and trough are in phase with each other. A weighted moving average of red to infrared ratio's is calculated over several heart beats [41] and the average value is converted into an SpO₂ value. If the red and infrared pulses are not properly synchronized to the fetal electrocardiogram or not in phase with each other, inaccurate SaO₂ estimations may be the result [42]. Such phase shifts of the red and infrared pulses with the heart rate was observed by placing a 660/940 sensor on a caput succedaneum [42].

The LEDs used in commercial transmission sensors are not ideal light sources. The LEDs emit light in a narrow spectral range. However, the center wavelength of the emitted light varies between diodes of the same type of sensor, by up to 15 nm [43]. A shift in the wavelength results in a different extinction coefficient (Fig. 1) and hence in an error in the estimated SaO₂. The effect of variation in the center wavelength will be greater for the red (660 nm) than for the infrared wavelength because its absorption spectrum shows a steeper slope. This problem can be solved in two ways. First, LEDs with center wavelengths which fall outside a specified range may be

rejected. Second, the pulse oximeter may be programmed to accept several ranges of LED center wavelength for both the red and infrared, and to correct for these different wavelengths internally [8].

Another problem related to the 660 nm LED is that a small amount of light in the infrared region is often emitted in addition to the center wavelength [43]. Although this so called 'secondary emission' does not influence the accuracy at high SaO_2 values, it might influence the accuracy at low fetal SaO_2 values.

3. Accuracy studies

For a proper evaluation of the accuracy of reflectance pulse oximetry, several issues should be considered. SpO_2 values should be compared to a reliable standard which measures the intra-arterial oxygen saturation. In general, arterial blood sample saturation values measured by multi-wavelength photometers are used. According to the manuals of these devices, the accuracy of various multi-wavelength photometers is $\pm 1\%$ absolute over the total oxygen saturation range of 0–100%. Sufficient subjects should be used and exclusion criteria for data should be specified beforehand. SpO_2 values should be obtained over the total fetal SaO_2 range, preferably for all subjects.

For the comparison of two methods measuring the same quantity, it is recommended that the mean difference and standard deviation of differences is calculated [44]. The mean difference is called the bias and may show a systematic over- or underestimation of a method relative to the standard method. The standard deviation of differences is called the precision and represents the random 'variability' of the system. Another measure for the random 'variability' of the system can be obtained by calculating the standard deviation of residuals with linear regression analysis. The standard deviation of residuals and the precision will be equal if the bias is zero. The correlation coefficient is not a sufficient measure of accuracy. If the accuracy of a reflectance pulse oximetry is evaluated in the same study in which the reflectance sensor is calibrated, the bias will be zero and will give no additional information.

The accuracy of various reflectance pulse oximetry systems has been reported in animal models. In two studies, a prototype sensor supplied by Nellcor was calibrated with either 660 and 925 nm LEDs [45], or 660 and 890 nm LEDs [46], and with a single photodetector placed 10 mm from both LEDs. The sensor was placed on the scalp of three [45], and two fetal lambs [46], respectively. Harris et al. found a precision of 5.5% over an oxyhemoglobin range of 6–81% [45] and Jongsma et al. found a precision of 3.5% above 30% SaO_2 and 6.6% below 30% SaO_2 [46]. Using the Nellcor 660/890 nm sensor Nijland et al. [36] found a

bias \pm precision of $4.7 \pm 7.3\%$ by placing the Nellcor 660/890 nm sensor on the neck of six fetal lambs over an SaO_2 range of 16–81%. In six piglets the precision was even less, using the same Nellcor 660/890 nm sensor, with a reported value of 12.9% over an SaO_2 range of 18–100% [47]. Mendelson et al. [48] developed a sensor with two pairs of 660/930 nm LEDs and a concentric row of six photodetectors and found a precision of 3.5, 4.1 and 4.8% for piglet scalp, neck and thigh measurements, respectively. The SaO_2 range was 30–100% [48]. Unfortunately, the number of animals is not stated [48]. Dassel et al. [49] also used a sensor of their own design with two LEDs for 660 and 940 nm and one photodetector at a distance of 7.5 mm from both LEDs on the fetal lamb scalp. They found a precision of 4.7% over an SaO_2 range of 17–82% in four fetal lambs [49]. Takatani et al. used a sensor with eight LEDs (four at 665 nm and four at 820 nm) placed in a circle around a single photodetector. Tissue was simultaneously warmed by additional 940 nm LEDs. The standard deviation of residuals was 2.5% for an SaO_2 range of 40–100% in five dogs [50].

4. New developments

From the reviewed studies it is clear that reflectance pulse oximetry is much more susceptible for all kind of physiological variables in the fetal SaO_2 range of 10–80% than transmission pulse oximetry in an SaO_2 range of 70–100%. Alternative approaches in sensor design must therefore be considered for intrapartum use. One theoretical suggestion is using three photodetectors at different distances of the LEDs [30].

Changing the red wavelength from 660 nm to 735 nm (Fig. 1) leads to less attenuation of the red light at low SaO_2 levels. In a theoretical Monte-Carlo model based on both absorption and scattering of light, Mannheimer [see Mannheimer P in this volume] predicted a significantly better similarity of light propagation for a 735/890 nm combination of LEDs than for a 660/890 nm combination of LEDs. A prototype reflectance sensor with a combination of 735 and 890 nm LEDs, and with a photodetector at a distance of 10 mm from both LEDs, developed by Nellcor, yielded much better results in six piglets compared with the 660/890 nm sensor [47], with a precision of 5.4%. A new version of this prototype sensor developed for intrapartum use, in which the LED-photodetector distance was changed from 10 to 14 mm was evaluated in two independent laboratories [36]. In seven piglets the sensor was calibrated. The precision was 4.7%. In a second series of four piglets this calibration was evaluated. The bias was -1.6% and the precision 5.4%. Measurements were made over an

SaO₂ range of 17–100%, with various sensors at several positions on each animal [36].

5. Conclusion

The aim of fetal surveillance during labour is straightforward: to identify fetal distress which may, if uncorrected, cause short-term morbidity, death, or possibly long-term morbidity. Undeniably, improved obstetrical care, together with cardiotocography, has led to a decrease in perinatal mortality in Western countries since 1940. The expected decrease in perinatal morbidity and long-term morbidity however was not observed, and due to a poor predictive value of cardiotocography, operative interventions during labour increased dramatically. In an effort to improve this unfortunate clinical situation it is tempting to rush for a new technique, like reflectance pulse oximetry.

Before reflectance pulse oximetry is used in obstetrical practice, it should be evaluated properly. First it should be evaluated in animal models, supported by quantitative support of in vitro models and theoretical models, and double sensor studies during labour. Several animal studies are needed in which the experimental set-up is varied. Second, if the accuracy has proven to be acceptable, clinical studies are needed to study the SaO₂ as a parameter for the fetal condition. Finally, if a clear understanding of the fetal SaO₂ monitoring together with cardiotocography has been established, a prospective randomized clinical trial can be performed.

From this review it is clear that reflectance pulse oximetry for fetal monitoring is susceptible for all kinds of physiological variables. Differences in blood volume, haematocrit and blood flow are major sources for inaccurate pulse oximetry readings with 660 nm sensors and cannot be overcome yet. Factors in the groups sensor-to-skin contact and technical problems can cause erroneous pulse oximeter values but may or have been solved. A new 735/890 nm Nellcor sensor demonstrated a promising accuracy but studies are limited.

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