


The influence of reducing fever on blood oxygen saturation in children

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Abstract Laboratory-based studies on the oxyhemoglobin dissociation curve (ODC) suggest that high blood temperature decreases the affinity of hemoglobin for oxygen. The aim of the study was to evaluate the influence of pyrexia on oxygen saturation (SpO₂) in children presenting to the emergency department. Normoxemic children with body temperature at or above 38.5 °C were included. Patients with a dynamic respiratory disease were excluded. SpO₂ was measured before and after antipyretic treatment. The changes in body temperature and SpO₂ were assessed and compared to the changes predicted from the ODC. Thirty-four children completed the study.

Mean temperature at presentation was 39.17 ± 0.549 °C and mean SpO₂ was 96.15 ± 2.21%. The mean decrease in temperature after antipyretic treatment was 1.71 ± 0.67 °C and mean increase in SpO₂ was 0.95 ± 1.76%. Among children in whom pyrexia decreased by 1.5 °C or more, the mean increase in SpO₂ was 1.45 ± 1.57%. The measured increase in SpO₂ was close to the increase anticipated from the ODC.

Conclusion: Pyrexia was associated with decreased SpO₂ in normoxemic children. The influence of pyrexia in children with low-normal oxygen saturation is expected to be much higher because of the non-linear shape of the ODC. Physicians treating patients with fever should be aware of this effect, especially in patients with borderline hypoxia.

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What is Known:

- High blood temperature decreases the affinity of oxygen to hemoglobin.
- It is not known whether fever would decrease SpO₂.

What is New:

- Fever is associated with decreased SpO₂.

Keywords Fever · Oxygen saturation · Oxyhemoglobin dissociation curve

Abbreviations

ODC the oxyhemoglobin dissociation curve
SaO₂ hemoglobin oxygen saturation
SpO₂ oxygen saturation measured by pulse oximetry

Introduction

Non-invasive measurements of hemoglobin oxygen saturation (SaO₂) by pulse oximetry (SpO₂) have become routine in

emergency settings, and SpO₂ has been labeled the “fifth vital sign” [11]. Pulse oximetry is a measurement that reliably estimates SaO₂ in arterial blood [6, 7, 9]. Single or serial measurements of SpO₂ significantly influence decision-making in regard to workup, treatment, and hospitalization of patients. Many factors have been shown to influence SaO₂ including: partial pressure of O₂ and CO₂ in blood, 2,3 DPG level, blood pH, and temperature [2]. Increased blood temperature decreases the affinity of oxygen to hemoglobin, so that increasing blood temperature leads to a decrease in SaO₂.

To the best of our knowledge, the effect of pyrexia upon SpO₂ has not been quantified in children. Theoretically, pyrexia may affect the oxygen-hemoglobin dissociation curve directly, but it also may affect SpO₂ through indirect mechanisms. For instance, pyrexia is associated with tachypnea which decreases Pco₂ causing a shift of the oxygen-hemoglobin dissociation curve and increasing SpO₂. Additionally, pyrexia causes tachycardia and increased cardiac output which might shorten blood transit time in the lungs, leading to reduced oxygen uptake.

The aim of the current study was to evaluate the influence of pyrexia on SpO₂ in a “real world” setting. For this purpose we measured SpO₂ in febrile children presenting to the emergency room before and after antipyretic treatment. We compared our findings to those calculated from the oxygen dissociation curve.

Methods

Patients Children up to the age of 12 years old, who presented to the emergency department of our institution with pyrexia, were included in the study. Inclusion criteria were body temperature at or above 38.5 °C and intention to use an antipyretic. Exclusion criteria were SpO₂ below 90% and the presence of dynamic respiratory disease such as an asthma exacerbation, wheezing, bronchiolitis, or laryngitis. Patients with stable “respiratory disease” such as pneumonia without oxygen supplementation were included in the study.

Antipyretic treatment and vital signs measurements Oral acetaminophen 15 mg/kg or oral ibuprofen 10 mg/kg was given depending upon the preference of the ER physician. Before administration, we measured baseline vital signs including heart and respiratory rate, temperature, and oxygen saturation. Temperature was measured using a digital thermometer (Welch Allyn SureTemp® Plus 690 with a disposable tip) either orally or rectally, ensuring that the same method was used for all measurements for each child. Approximately 90 min after administration of antipyretics, vital signs including SpO₂ and temperature were again measured.

Pulse oximetry measurements Pulse oximetry was measured using a Masimo Radical-7 motion resistant pulse oximeter (Masimo, Irvine, California, USA) incorporating Masimo SET v7.6.2.1 software. All measurements were conducted by the same investigator (S.H.). Measurements were conducted while the children were sleeping or awake and quiet (not feeding, fussy, or crying) before and after antipyretic therapy. Measurements were performed either on the palm of the hand or the foot (infants), or on a digit in older children. Both measurements for each child were performed at the same site. Using an averaging mode of 12 s, the measurements were conducted for a period of at least 90 s after a stable and sharp pulsatile pulse waveform appeared and the perfusion index (PI) was steadily > 1, all in accordance with the manufacturer’s recommendations. We used trend data for analysis collected with Masimo Trendcom software provided by the manufacturer. SpO₂, pulse rate, and perfusion index values (including alerts of low SpO₂ signal quality) were recorded at 2-s intervals. Trend data were omitted from analysis at least for the first 12 s of each recording and until 6 s of steady SpO₂ recording was obtained. Any recordings that were missing a value or had a low SpO₂ signal quality alert were also omitted from analysis. The average of all reliable SpO₂ measurements was used.

Predicting the expected influence of blood temperature on SpO₂ In order to calculate the expected influence of pyrexia on SpO₂, we first calculated the expected alveolar Po₂ (PAO₂). For this purpose we used the alveolar gas equation: $PAO_2 = FiO_2 (PB - P_{H_2O}) - PACO_2 [FiO_2 + (1 - FiO_2) / R]$ (where FiO₂ is the fractional inspired oxygen concentration in air, PB is the atmospheric (barometric) pressure, P_{H₂O} is the partial pressure of water, and PACo₂ is the partial CO₂ alveolar pressure, while R is the respiratory quotient [1]). Assuming P_{H₂O} = 47 mmHg, PACo₂ = 40 mmHg, and R = 0.8, the PAO₂ in a healthy examinee breathing room air at sea level (760 mmHg) is expected to be 101.7 mmHg. The current study was done in Jerusalem, which is located at 800 m above sea level, where the barometric pressure is 697 mmHg giving an anticipated PAO₂ of 88.5 mmHg. Assuming that the alveolar-arterial gradient is 10 mmHg, the anticipated arterial Po₂ (PaO₂) is 91.7 mmHg at sea level and 78.5 mmHg in Jerusalem. In order to calculate the SpO₂ from PaO₂, we used an Internet-based calculator called “The Interactive Oxyhemoglobin Dissociation Curve” [8]. The software requires PaO₂, Pco₂, pH, and temperature of the patient to calculate SpO₂ and is based on the classic oxyhemoglobin dissociation curve equation developed by Kelman [3] and from data obtained by Severinghaus [10]. The calculations were all performed based upon the assumptions that Pco₂ is 40 mmHg and pH is at 7.38. The expected changes in SpO₂ were calculated separately for each patient according to the temperature measured before and after antipyretic treatment.

Table 1 Vital signs and oxygen saturation (mean \pm SD) before and after administration of antipyretic medication

	Baseline	After antipyretics	Difference (before–after antipyretics)	<i>p</i> value
Temperature ($^{\circ}$ C)	39.17 \pm 0.54	37.46 \pm 0.59	1.71 \pm 0.67	<i>p</i> < 0.0001
Respiratory rate (breaths per minute)	35.65 \pm 15.87	28.97 \pm 12.54	11.65 \pm 6.68	<i>p</i> = 0.002
Heart rate (beats per minute)	156.33 \pm 21.8	136.44 \pm 22.41	19.9 \pm 14.5	<i>p</i> = 0.001
SpO ₂	96.15 \pm 2.13	97.1 \pm 2.13	- 0.95 \pm 1.76	<i>p</i> = 0.0034

Statistical analysis

We used the Minitab 15 statistical software (Minitab, State College, Pennsylvania) for statistical analyses. We assessed the effect of fever reduction on SpO₂ and other vital signs using paired *t* tests. A *p* value of < 0.05 was considered significant.

Results

Forty-five patients were recruited for the study, and 34 (64.7% males) completed the study protocol. The other 11 children did not complete the study protocol mostly because they were either crying or because they were not in the same state of arousal at the time of the second measurement. One patient was asleep during both measurements and all the others were awake at both measurements.

Twelve patients (35%) were diagnosed with suspected viral infection, nine (26%) with pneumonia, three (9%) with acute gastroenteritis, three (9%) with febrile seizures, and seven (21%) with other diagnoses including tonsillitis, acute otitis media, familial Mediterranean fever, and lymphadenitis.

Mean patients' age was 37.5 \pm 14.8 months, ranging 0.45–192 months, and mean weight was 14.2 \pm 10.5 kg. Nineteen of the patients (55.9%) were treated with acetaminophen and the rest (44.1%) with ibuprofen.

Vital signs and oxygen saturation before and after administration of antipyretic agent are depicted in Table 1. In all participants, body temperature decreased, with a mean decrease of 1.71 \pm 0.67 $^{\circ}$ C (*p* < 0.001). Both respiratory and heart rates decreased significantly. SpO₂ increased significantly by 0.95 \pm 1.76% (*p* = 0.0034). SpO₂ increased in 73.5% (25/34) of the whole cohort and in 90% (18/20) of children in whom body temperature decreased by 1.5 $^{\circ}$ C or more. There was a significant correlation between the decrease in temperature and the increase in SpO₂ (*p* = 0.031, *R* = 0.34, Fig. 1). The mean measured increase in SpO₂ was only 56 \pm 114% of that expected when using Kelman's equation. Taking only patients (*n* = 20) in whom the temperature decreased by \geq 1.5 $^{\circ}$ C, the measured increase in SpO₂ was much closer to the anticipated increase (90 \pm 105%, Table 2).

Discussion

In this study, we measured the SpO₂ in febrile children in the emergency room and the influence of defervescence upon SpO₂. We also compared our findings to expected changes based upon theoretical calculations using Kelman's equation. We found that most, but not all patients, had an increase in SpO₂ concomitant with the decrease in body temperature. Moreover, a larger increase in SpO₂ after defervescence correlated with a greater reduction in temperature. Finally, in patients in whom the decrease in temperature was greater (1.5 degrees and above), the mean increase in SpO₂ was very close to the calculated theoretical increase.

To the best of our knowledge, there is only one study in the English written literature quantifying the influence of temperature upon SpO₂ in patients with fever [4]. This study involved adults hospitalized in an intensive care unit and included patients receiving ventilator support and supplemental oxygen. An increased median temperature from 38.1 to 39.0 $^{\circ}$ C was accompanied by a decrease in SpO₂ from 98.0 to 97.6%. Since the change in temperature was small and some (numbers are not given) of their patients were on ventilatory support, their findings might not be applicable to children breathing room air and with higher temperature changes. A previous study quantifying the influence of temperature upon SpO₂ on 22 children was published by our group in Hebrew [5]. We determined the level of SpO₂ by documenting the values as appeared on the pulse oximeter screen and not by averaging recorded values as was done in the current study. The results were similar to the current study. The mean decrease in

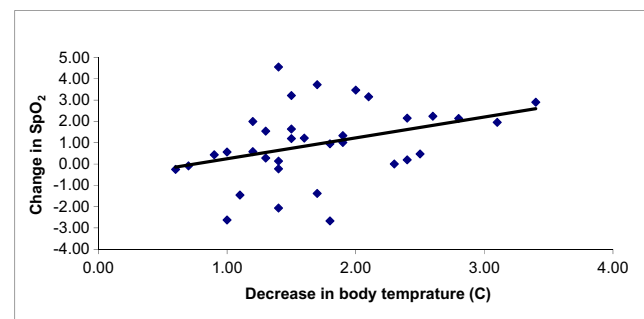


Fig. 1 The association between the change in body temperature and the change in SpO₂ (*p* = 0.031, *R* = 0.34)

Table 2 Comparison of the measured increase in SpO₂ after antipyretic treatment to the predicted increase in SpO₂. The comparison was performed on the whole cohort and then only on patients with a decrease in body temperature of 1.5 °C or above

		Temperature (°C)	Measured SpO ₂ (%)	Calculated SpO ₂ (%)
All participants (<i>n</i> = 34)	At baseline	39.17 ± 0.54	96.15 ± 2.21	93.70 ± 0.53
	After antipyretic administration	37.46 ± 0.59	97.10 ± 2.13	95.08 ± 0.4
	Difference	− 1.71 ± 0.67	0.95 ± 1.76	1.38 ± 0.55
Only participants with temperature decrease of 1.5 °C or more (<i>n</i> = 20)	At baseline	39.34 ± 0.58	96.1 ± 1.8	93.53 ± 0.57
	After antipyretic administration	37.24 ± 0.55	97.6 ± 1.6	95.21 ± 0.42
	Difference	− 2.125 ± 0.55	1.45 ± 1.57	1.68 ± 0.47

temperature was 2.03 °C and the average rise in SpO₂ was 1.55 ± 1.79% (*p* = 0.001).

In the current study, by definition, baseline SpO₂ was above 90% in all patients. We speculate that the influence of an increase in body temperature on SpO₂ in patients with low baseline SpO₂ may be greater than that found in our study. This is because the oxyhemoglobin dissociation curve is much steeper when Po₂ is lower than 60 mmHg. Indeed, according to Kelman's equation, when the Po₂ is 60 mmHg with a blood temperature of 37 °C, the anticipated SpO₂ is 91%. When the blood temperature is increased to 40 °C, the anticipated SpO₂ decreases to 85.8%.

It is important to note that the calculation presented above is based upon the assumption that the values of PACo₂, *R* value, *P*_{H2O}, barometric pressure, and the alveolar-arterial oxygen gradient are constant and equal to the values presented in the methods section. In practice, these values differ between patients and days. Moreover, the influence of compensatory mechanisms such as an increase in the respiratory rate is not known. Hence, the influence of an increased body temperature upon oxygen saturation will vary between patients and should be measured individually. We suggest that in a febrile patient, with borderline oxygen saturation, the decision to give supplemental O₂, or to hospitalize, should be postponed until after the administration of antipyretics.

Study limitation The main limitation of the study is the absence of hypoxemic patients. It is anticipated that in those patients the influence of temperature upon SpO₂ would be greater. We did not include them in the current study because those patients usually receive supplemental oxygen. Another study incorporating hypoxemic patient is required.

Conclusion Increased body temperature is associated with decreased SpO₂ as suggested by the oxyhemoglobin dissociation curve. The relationship is not completely predictable. Physicians treating patients with fever should be aware of the potential significant influence of temperature on SpO₂, especially in patients with borderline saturation. An increase in SpO₂ in a patient after fever reduction should not be automatically interpreted as an improvement in the patients'

respiratory condition. Similarly, a low SpO₂ in a patient with high fever does not always imply significant respiratory compromise.

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Authors' contributions Shmuel Goldberg: Dr. Goldberg conceptualized and design of the study, interpreted the results, reviewed and revised the manuscript, and wrote the final manuscript as submitted.

Shmuel Heitner: Dr. Heitner enrolled all participants, recorded the clinical and demographic data, performed all measurements, summarized the results, and approved the final manuscript as submitted.

Francis B. Mimouni: Prof. Mimouni helped conceptualizing and designing of the study, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Leon Joseph: Dr. Joseph helped conceptualizing and designing of the study, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Reuben Bromiker: Dr. Bromiker obtained the equipment support, critically reviewed the manuscript, and approved the final manuscript as submitted.

Elie Picard: Prof. Picard aided in the design of the study, initial analysis and interpretation of the results, critically reviewed the manuscript, and approved the final manuscript as submitted.

Compliance with ethical standard

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Shaare Zedek Medical Center Ethic Committee, study number 43/12.

Informed consent Written informed consent was obtained from all individual participants included in the study.

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