

R. Ubbink¹, P.A.W. te Boekhorst², E.G. Mik¹

1. Department of Anesthesiology, Erasmus MC – University Medical Center Rotterdam, Rotterdam, The Netherlands
2. Department of Hematology, Erasmus MC – University Medical Center Rotterdam, Rotterdam, The Netherlands

Introduction:

Red blood cell (RBC) transfusion is aimed at restoring adequate oxygen delivery in case of too low hemoglobin (Hb) level. Unfortunately, blood transfusion is not without risks [1]. What is low, however, differs widely between individuals. Therefore, positive effects of blood transfusion should certainly outweigh the risks in selected patients, and unnecessary (over) transfusions should be avoided [2]. Transfusion guidelines use Hb-level to indicate blood transfusion. Since they are based on mean data they incorporate a safety margin and might lead to unnecessary transfusion in individual cases.

To date no objective, clinically useful methods are available to determine an individual need for RBC transfusion [3, 4]. Since ultimately the mitochondria are the target for oxygen delivery, it seems reasonable to use mitochondrial oxygen tension (mitoPO₂) as a measure for the transfusion need. In animal experiments a correlation between a sudden drop in cutaneous mitoPO₂ and the critical hematocrit has been found [5]. The recent development of the COMET monitor allows cutaneous mitoPO₂ measurements in humans [6].

Methods:

Two cases are selected from a single-center randomized study in Erasmus Medical Center Rotterdam, in patients with chronic anemia, who receive a RBC transfusion on a regular basis. Subjects were asked informed consent if they would receive a transfusion coming weeks. Mitochondrial oxygen tension was measured during the transfusion with COMET.

The COMET (Photonics Healthcare BV, Utrecht, The Netherlands) seen in Figure 1a uses the protoporphyrin IX-Triplet State Lifetime Technique (PpIX-TSLT) to measure the mitoPO₂ [7]. Protoporphyrin IX (PpIX) is the final precursor of heme in the heme biosynthetic pathway and is synthesized inside the mitochondria [8]. The conversion of PpIX to heme in the mitochondria is a rate-limiting step. Therefore, administration of the porphyrin precursor 5-aminolevulinic acid (ALA) enhances the mitochondrial PpIX concentration.



Figure 1: a) COMET monitor with skin sensor, b) Skin Sensor position on the chest

Delayed fluorescence can be observed after pulsed excitation of PpIX as delayed luminescence has the same spectrum as prompt fluorescence (red light). In contrast to prompt fluorescence delayed fluorescence has a lifetime of tens to hundreds of microseconds [7]. Delayed fluorescence is the result of photon emission due to spontaneous relaxation of the excited triplet state via bi-directional intersystem crossing. Oxygen is a very effective quencher of the excited triplet state PpIX.

In the process of quenching, energy is transferred to oxygen and PpIX relaxes to the ground state without emission of a photon. This causes the lifetime of the triplet state, and thus the lifetime of the emitted delayed fluorescence, to be oxygen-dependent.

For the study the 5-aminolevulinic acid (ALA) patch is applied the evening before the RBC transfusion. The Skin sensor was fixated on the chest position is seen in Figure 1b. COMET measurement time interval was 1 min. The transfusion protocol 10 min slow 60ml/h and than infusion of 300ml/h.

Results

Two RBC transfusion cases are presented. First case is a man with myelodysplastic syndrome Hb 4.8 mmol/L, mitoPO₂ decreased during RBC transfusion.

Second case is a man with X-linked sideroblastic anemia Hb 3.8 mmol/L, mitoPO₂ increased during transfusion, seen in Figure 2.

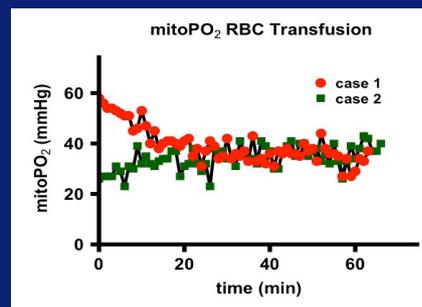


Figure 2 : Two red blood cell transfusion cases measured with COMET, case 1 (red) mitoPO₂ decreases and case 2 (green) mitoPO₂ increases upon red blood transfusion

Discussion

The two presented cases are preliminary data from a study recently finished enrolment. It shows that COMET is able to detect changes in humans during a RBC transfusion. The decrease seen in the first case could be the result of free hemoglobin. Free hemoglobin after a certain storage period can lead to vasoconstriction and results in a decrease the mitoPO₂ [8]. On the contrary in case two the hemoglobin level was 3.8mmol/L resulting in a direct increase of oxygen delivery in the skin. This beneficial delivery outweighs the vasoconstriction of the free hemoglobin. The measured mitoPO₂ is the balance between the delivered and consumed oxygen inside the cells.

Conclusion

Our preliminary data show that COMET is able to detect opposing responses of mitoPO₂ during red blood cell transfusion. A novel clinical tool for research in transfusion medicine.

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