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Case Study

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Recovery of residual curarization after red blood cell transfusion

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Background: The muscle-relaxing effects of succinylcholine are terminated via hydrolysis by plasma cholinesterase. There are multiple genetic variants of this enzyme and clinical circumstances that might influence the activity of plasma cholinesterase and eventually lead to prolonged neuromuscular blockade following succinylcholine application.

Case Report: Here, we report a parturient woman with atonic bleeding who suffered significant blood loss (hemoglobin 6.0 $g \cdot dL^{-1}$). For surgical curettage, general anesthesia was performed by using short-acting succinylcholine. By the end of the 105-minute procedure, the patient's trachea was extubated. After extubation she showed signs of the prolonged neuromuscular blocking action of succinylcholine. At this time, the patient received an AB0-compatible red blood cell transfusion and recovered instantly from neuromuscular blockade. The plasma cholinesterase (3.200 $U \cdot L^{-1}$) was below the normal range (4.900–12.000 $U \cdot L^{-1}$). Patient's blood DNA analysis revealed heterozygously the genetic K variant of plasma cholinesterase. After red blood cell transfusion, serum potassium was elevated (5.7 $mmol \cdot L^{-1}$; 4.4 $mmol \cdot L^{-1}$ prior to transfusion).

Conclusions: Pregnancy, blood loss and genetic variation contributed to impairment of plasma cholinesterase. Due to high-speed red blood cell transfusion, hemolytic release of erythrocyte cholinesterase might have terminated the neuromuscular blocking succinylcholine effect.

key words: **succinylcholine • plasma cholinesterase • neuromuscular blockade • red blood cell transfusions**

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Background

The rapid action of succinylcholine makes this depolarizing muscle relaxant favorable for facilitating tracheal intubation in emergency patients and clinical situations with high aspiration risk [1]. The neuromuscular blocking effects of succinylcholine and mivacurium are terminated by rapid hydroxylation by the butyrylcholinesterase enzyme (BChE; plasma cholinesterase) [2,3]. Unfortunately, approximately 25% of individuals in a white population have a hereditary variation of the enzyme, extending the neuromuscular blocking effects of both muscle relaxants up to several hours [4,5]. Apart from genetic variability, acquired diseases such as hepatic failure or physiologic changes during pregnancy are known to reduce the amount of plasma cholinesterase or the efficiency of its enzymatic action [6]. Therapeutic alternatives are few; either the patients are ventilated for 4–8 hours until the end of prolonged neuromuscular block, or injection of cholinesterase may lead to a shorter duration of action of the neuromuscular blocking agent mivacurium [7]. Here, we report a parturient woman with severe atonic bleeding and prolonged succinylcholine block after uterine abrasion under general anesthesia, whose prolonged muscle relaxation was terminated by application of packed red cells.

Case Report

A 31-year-old parturient woman (70 kg body weight) without history of previous anesthesia was admitted to the hospital with atonic bleeding after 25-hour labor preceding successful delivery at home. In order to replace perinatal blood loss, 1 L colloid and 1 L crystalloid solution were given by the emergency team before the patient arrived at the hospital. At admission the patient appeared fully conscious, and heart rate [HR] and blood pressure [BP] were measured to be 90 beats·min^{-1} and 120/60 mmHg, respectively. Blood gas analysis revealed a hemoglobin level as low as 6.0 g·dL^{-1}. Prompt uterine curettage was required, as bleeding was sustained. After rapid sequence induction of general anesthesia with 200 mg propofol, 100 mg succinylcholine (1.25 mg·kg^{-1}), and 1 mg rapifen, the tubus was successfully placed into the trachea. During general anesthesia maintained with sevoflurane (1.5 Vol-%), blood pressure and heart rate remained stable, obviating the need for immediate blood transfusion with AB0-untested red packed cells. As blood coagulation appeared to be clinically impaired, 4 g fibrinogen and 2 g tranexamic acid were given intravenously. Removal of residual placenta was complicated by a retroflected uterus, prolonging the surgical procedure to 105 minutes. After extubation of the trachea at stable cardiovascular conditions, the HR increased to 140 bpm, the tongue was obstructing the airway, and tachydyspnoea could be observed. Oxygenation was maintained by applying jaw thrust and supply of 100% oxygen using a face mask. Neuromuscular monitoring, manually tested, showed no fading of the "train of four", thereby excluding dual block. The patient was awake but she could not open her eyes or give hand signs. Furthermore, uncoordinated muscle activity was visible. As at this time, automatic BP stopped measuring values in a detectable range, making blood loss the most likely cause. Consequently, AB0-compatible red blood cells (250 mL) were transfused at high flow by using a pressure bag and a warming system (Ranger®). While reinduction of general anesthesia was prepared, the patient immediately regained neuromuscular function, tachydyspnoea stopped, and she was able to open her eyes, give hand signs, and speak. Simultaneously, the HR decreased to 90 beats·min^{-1} and automatic BP displayed values in the normal range, enabling transfer to the intermediate care unit.

The following morning, plasma cholinesterase level was 3.200 U·L^{-1}, which is below the normal range (4.900–12.000 U·L^{-1}), and the patient's blood DNA testing revealed that she was a heterozygous carrier of the K variant of plasma cholinesterase.

Discussion

In our patient, signs of physical stress and the inability of automatic blood pressure measurement (probably due to shivering) were misinterpreted to be caused by intravascular volume deficiency, in particular as a hemoglobin level as low as 6.0 g·dL^{-1}. Retrospectively, it became clear that she had a prolonged action of succinylcholine due to a genetic variation, namely, the K variant of the butyrylcholinesterase enzyme. The frequency of the K variant of plasma cholinesterase is described to be at 13%, and the enzyme activity is typically decreased by 30% [8]. Even in patients carrying the heterozygous K variant, effects of mivacurium or succinylcholine might be prolonged [9,10]. Pregnancy and hemodilution as a result of volume therapy might have further contributed to decreased plasma cholinesterase activity. Furthermore, significantly lower levels of plasma cholinesterase are described to occur in up to 10% of parturients [11].

It can be assumed that the immediate improvement of neuromuscular distress was either caused by plasma cholinesterase in the residual serum of packed red cells, or by release from hemolyzed erythrocytes. Epstein et al have shown that the activity of serum cholinesterase in stored whole blood was around 87% of initial values after 21 days [12]. It has been demonstrated in patients with K variant that administration of plasma cholinesterase reverses the effect of mivacurium [7]. Further, Lainé-Cessac et al. measured cholinesterase activity in erythrocytes and plasma by hydrolysis of acetyl-, butyryl-, and succinylcholine [13]. Erythrocyte acetylcholinesterase was tested after red cells were hemolyzed. Determination of activity correlated well among the 3 substrates ($r>0.94$), with erythrocyte acetylcholinesterase being 3.7-fold more effective compared to plasma cholinesterase [13]. Our patient recovered, most probably due to transfusion of red blood cells, which were hemolyzed in part by high speed transfusion, leading to an increase in serum potassium from 4.4 mmol·L^{-1} to 5.7 mmol·L^{-1} after transfusion. Lovely et al reported a patient with compromised plasma cholinesterase activity undergoing first surgery without prolonged succinylcholine blockade, but experiencing it after a second intervention [14]. The authors assumed that packed red blood cells given perioperatively masked atypical plasma cholinesterase the first time succinylcholine was administered. In another study, concentrations of the short-acting opioid remifentanil were lower when incubated with red blood cells compared to plasma incubation, suggesting a role of erythrocyte cholinesterase in remifentanil esterase-dependent metabolism [15]. Moreover, in organophosphorus poisoning, erythrocyte cholinesterase might be a bioscavenger when given as whole blood transfusion, as reported by Ryniak et al. [16].

In addition to the K variant of plasma cholinesterase, there are other genetic mutations, like the atypical (A) and silent (S) variant, with different impact on enzyme activity [17,18]. Although the modest reduction of plasma cholinesterase due to the K variant (67% of normal enzyme activity) usually does not cause significant prolongation of succinylcholine effect, the combination with another variant, chronic illness, organophosphorus poisoning, or, as in our case, pregnancy and major blood loss, might lead to clinical appearance [4,8,19]. This is in line with the study of Levano et al, who genotyped 9 patients with prolonged neuromuscular block after succinylcholine, but 2 of them displayed normal molecular genetic results [4].

Conclusions

Anesthesiologists should be aware of lower levels of plasma cholinesterase occurring in parturient women [6]. Application of succinylcholine or mivacurium in these patients must be carefully considered, since rapid-sequence induction can be performed alternatively with rocuronium [20–22]. The routine use of red blood cells to determine prolonged muscle dysfunction is certainly not recommended, but it helped in the case reported.

Disclosure

All authors have no conflict of interest to declare. Written consent of the patient for publication of this case report was obtained.

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