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Transfusion-Associated Hyperkalemia: Implications for Pediatric Cardiac Health

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INTRODUCTION

Transfusion-associated hyperkalemic cardiac arrest (TAHCA) is an adverse event that can occur after the transfusion of red blood cells (RBCs). During refrigerated storage, RBCs undergo a series of morphological, functional, and metabolic changes that are collectively termed 'the red blood cell storage lesion'. Specifically, refrigeration impairs cation transporters, including Na+/K+ ATPase, which leads to a progressive increase in extracellular potassium within the RBC unit. Rapid or large volume transfusions of RBC units with elevated potassium can predispose patients to hyperkalemia, electrical instabilities, and cardiac arrest.

Expert panels recognize that pediatric patients are a sensitive population that are at an increased risk of developing a transfusion reaction compared to their adult counterparts. Despite this, many studies have focused on the adult population. Human-induced pluripotent stem cell derived cardiomyocytes (hiPSC-CM), mimic immature heart tissue and allows for the characterization of cardiac responses to a variety of treatments and exposures.

Studying the electrophysiological differences that are provoked by aged RBCs as well as the irradiation status of the blood unit has typically been done on animal models; but in-vitro examination of human stem cell derived cardiomyocytes, on a microelectrode array allows for high throughput, rapid analysis of many clinically relevant cardiac endpoints.

Objective

We aimed to review the literature on the incidence of transfusion-associated hyperkalemia, highlight the association with cardiac electrical instabilities, and identify potential mitigation strategies to reduce the risk of hyperkalemia in pediatric patient populations.

Experimentally, we examined the direct electrophysiological effects of RBC storage age on hiPSC-CM, using a microelectrode array system.

RESULTS

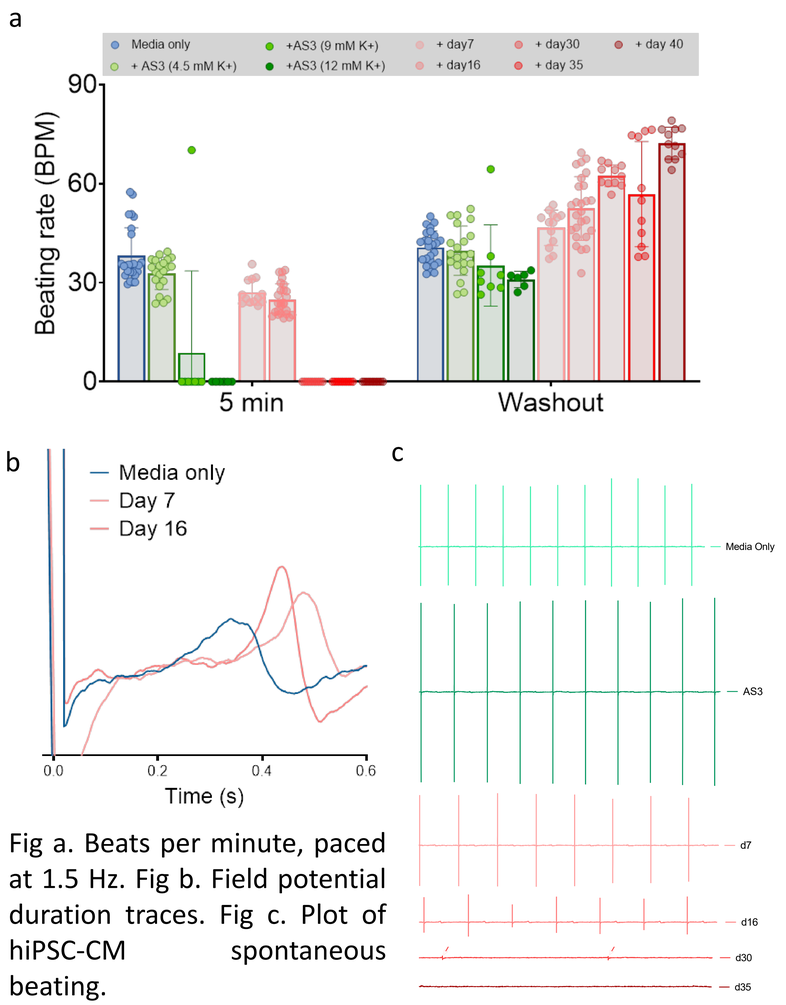

Fig a. Beats per minute, paced at 1.5 Hz. Fig b. Field potential duration traces. Fig c. Plot of hiPSC-CM spontaneous beating.

Fresh (< 7 days) and standard issue (1-2 week old) blood products increased the field potential duration time, a psuedo-QT interval, in hiPSC-CM MEA experiments. Older blood products nearing expiration arrested the cells and a FPD measurement could not be measured. Immediately post removal of the blood product, all hiPSC-CM field potential duration measurements returned to baseline levels. Cardiac electrical disturbances were worse with chronological aging leading to increasing numbers of hiPSC-CM wells capturing at half the pacing frequency or having a complete loss of capture, suggesting increased refractoriness.

RESULTS

We identified 21 case reports and case series documenting TAHCA in pediatric patients. Hyperkalemia and cardiac arrhythmias were reported in pediatric patients when blood products were transfused quickly, were delivered directly to the heart without time for electrolyte equilibration, or when blood products accumulated extracellular K+ due to storage time or irradiation. We note that hyperkalemia and/or TACHCA may be underreported due to incomplete hemovigilance reporting. Collectively, these reports suggest that the risk of hyperkalemia may be mitigated by using fresh blood products, reducing storage time after blood product irradiation, and implementing manipulations that wash or remove excess extracellular K+.

	Days of Storage			
Parameter (mmol/L)	KH media	7	30-35	40
pH	7.38 ± 0.01	7.40 ± 0.01	7.41 ± 0.01	7.40 ± 0.003
K^+	4.48 ± 0.04	5.82 ± 0.16*	***9.28 ± 0.41****	***9.28 ± 0.33****

Table 1. Biochemical analyses of sRBC diluted to 10% volume in KH-buffered media. Storage age was associated with deviations in the electrolyte composition of sRBC samples. Mean ± SEM,
*value differs significantly from control KH buffer, or **value differs from day 7 sample ($p<0.05$). n=3-10 per group

	Central line	Peripheral line	Age range	Surgical	Medical	Small volume	Large volume
# of cases	13	13	1 hour – 17 years	63%	36%	15	15

Table 2. Review article stats.
Total of 36 cases reported in 21 publications.

CONCLUSION

Advances in transfusion medicine have improved the health of RBCs during storage, yet vulnerable patient populations experience transfusion-associated hyperkalemia. Additional mitigation strategies are warranted to reduce the risk of TAHCA, which has a low rate of survival in pediatric patients.

ACKNOWLEDGMENTS

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