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EXTRACORPOREAL HEMOLYSIS OF BLOOD IN A MICROWAVE BLOOD WARMER

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Abstract Marked hemoglobinemia and hemoglobinuria developed in a 13-year-old girl during an operative repair for scoliosis. Residual blood from 1 of 5 U of whole blood, preheated in a microwave blood warmer and administered during the procedure, was found to be hemolyzed. The blood warmer was studied in an effort to reproduce extracorporeal hemolysis. Faulty placement of the blood container in the heating unit was found to produce improper heating through nonrotation of the container. No change in plasma hemoglobin or red-cell filterability was found when normally heated samples were compared with unheated control samples. Improperly heated blood revealed a marked increase in plasma hemoglobin (maximum, 949 mg per 100 ml) and a reduction in filterability of residual cells (maximum, 19 per cent). Morphologic changes (e.g., budding) were identified in improperly but not properly heated red cells. These studies indicate the production of extracorporeal hemolysis and reduced viability of a population of nonhemolyzed cells through improper heating of blood in a microwave blood warmer.

IN recent years, increasing attention has been paid to the problem of iatrogenic disease in hospitalized patients. Technologic advances have had a positive impact on modern medical practice, but the benefits of such technology have not been without risk.[1] A recent development in the field of anesthesia has been a microwave blood warmer designed to heat whole blood to a temperature of 32°C in something less than one minute.[2,3] In the case reported below, severe hemoglobinemia and hemoglobinuria followed the transfusion of blood improperly heated in a microwave warmer. In vitro studies of blood heated in the microwave unit confirmed the potential for extracorporeal hemolysis.

CASE REPORT

K.N., a 13-year-old girl, suffered cardiac arrest during surgical repair of congenital scoliosis at Strong Memorial Hospital on October 30, 1970. Successful closed-chest cardiac massage was followed by termination of surgery and transfer to the recovery room, where physical examination showed normal vital signs, decerebrate rigidity and no response to painful stimuli. The hematocrit was 32 per cent, the blood urea nitrogen 15 mg per 100 ml, and the serum potassium 3.1 mEq per liter. Urinalysis revealed clear pink urine, with a 2+ test for protein and a 3+ test for blood (Hematest), and no red blood cells were observed on examination of the sediment. The serum was pink, and the hemoglobin, determined on the following day, was 251 mg per 100 ml. Multiple blood cultures revealed no growth. The patient failed to regain consciousness and died on November 19.

During the operation the patient had received 5 U of whole blood heated in a microwave warmer. Retyping of all blood units received, together with direct and indirect Coombs testing of the patient's blood, gave no evidence of serologic incompatibility. Examination of residual blood from the 5 U administered disclosed gross hemolysis in 1 U with a plasma hemoglobin of 4878 mg per 100 ml. The pilot tube for this unit was not hemolyzed. The lack of evidence for serologically mediated intravascular hemolysis coupled with the finding of large amounts of free hemoglobin in one of the preheated units of blood administered during surgery suggested the possibility of extracorporeal hemolysis through improper heating in the microwave warmer. The studies described below were undertaken to confirm this hypothesis.

MATERIALS AND METHODS

The Ohio Model 987 microwave blood warmer (Ohio Medical Products, 1400 East Washington Avenue, Madison, Wisconsin) used on the day of surgery was employed throughout. This unit utilizes microwave radiation to heat whole blood to 32°C in a little less than one minute. Proper heating is effected by 1 U of blood contained in a standard 500-ml plastic bag placed into a plastic cylinder, which in turn is placed inside the blood warmer. A bag temperature of less than 25°C, sensed by means of a thermal probe, activates a light signal, which in turn activates a magnetron microwave generator and a cylinder rotator motor. Rotation and heating occur simultaneously. The light signal is extinguished when the bag temperature reaches a preset level of 32±2°C, and at that point heating and rotation stop. A timing circuit automatically overrides the magnetron generator if the heating cycle length exceeds a period of 80 seconds.

Attempts were made to hemolyze blood through improper heating. The only way in which improper

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heating could be induced was when the plastic container and blood unit were placed into the microwave unit in such a fashion that the magnetron generator was activated but rotation did not occur owing to incomplete engagement of the cylinder head with a rotating-gear assembly.

The following observations were made on six-day-old, two-week-old and outdated samples of whole blood before and after both proper and improper microwave heating: plasma hemoglobin[4]; per cent hemolysis[5]; red-cell filterability[6]; osmotic fragility[7]; and examination of Wright-stained blood smears. Calculations of per cent hemolysis were based on an assumed packed cell volume of 40 per cent and hemoglobin of 13 g per 100 ml. Filterability values are reported as the percentage of red cells filtered in relation to normal, fresh control erythrocytes.

To examine the possibility that the hemolyzed donor red cells in this case were intrinsically abnormal, blood was obtained from the donor and the following studies were performed: examination of Wright-stained blood smears; hemoglobin electrophoresis; glucose-6-phosphate dehydrogenase assay; and plasma hemoglobin and red-cell filterability before and after proper heating of 1 U of the donor blood in the microwave oven.

Results

Normal Heating

Proper use of the microwave blood warmer attained an average unit temperature of 30.7°C in an average of 35.5 seconds. No appreciable change in plasma hemoglobin, red-cell filterability, osmotic fragility or red-cell morphology over control values was observed after proper heating (Table 1).

Improper Heating

Improper heating through nonrotation of the cylinder often resulted in the rupture of the plastic blood-containing bag. If the bag did not rupture, the blood usually heated for well over 50 seconds. Examination of the nonruptured but overheated bags always revealed a brown area of coagulated blood the size of a nickle at the point of maximum heating. The congealed blood at this spot could be dispersed by gentle massage. The average temperature reached by the overheated blood never exceeded 39°C, and the term "overheated blood" thus refers only to blood focally overheated through nonrotation of the cylinder.

Improper heating with or without rupture resulted in marked increases in plasma hemoglobin and a reduction in red-cell filterability (Table 1). The magnitude of these changes was directly proportional to the duration of improper heating and not to the age of the blood. The fourfold difference between per cent hemolysis and per cent decrease in red-cell filterability indicates critical damage to approximately three times as many red cells as were hemolyzed.

Wright-stained smears of blood from overheated units revealed morphologic changes of membrane budding and early fragmentation consistent with heat-induced erythrocyte injury.[8] The osmotic fragility of overheated red cells was not uniformly affected although a small population of fragile cells was identified in several units. The morphologic and osmotic changes noted also correlated only with increased heating time.

Donor Blood

RBC morphology and hemoglobin electrophoresis

Table 1. Effects of Proper and Improper Heating of Stored Whole Blood in Microwave Blood Warmer.

Heating	Storage Age (Days)	Heating Time (Sec)	Hemoglobin/100 Ml		Filterability (% Normal)	
			Before Heating	After Heating	Before Heating	After Heating
Proper	6	31.0	16*	22*	78*	80*
	6	35.0				
	14	38.0				
	15	38.0	22*	22*	73*	74*
	23	36.0				
	25	35.0	62*	63*	62*	64*
Mean	15	35.5	33	36	71	73
Improper (Bag rupture)	15	32.0	7	115	90	82
	25	34.0	35	233	83	79
	16	47.0	8	252	87	80
Mean	19	37.7	17	200	87	80
Improper (Bag intact)	6	31.0	23	296	87	80
	23	59.0	38	424	71	54
	6	63.0	17	949	77	58
Mean	12	51.0	26	556	78	64

*Average value, 2 U.

of the donor blood was normal. Unexpectedly, glucose-6-phosphate dehydrogenase deficiency was identified. Proper heating in the microwave oven resulted in no hemolysis of this blood, however (plasma hemoglobin 5.4 mg before and 7.6 mg per 100 ml after heating).

Discussion

The data support the hypothesis that extracorporeal hemolysis due to improper heating of blood was responsible for the hemoglobinemia and hemoglobinuria observed in the subject of the case report. Marked increases in plasma hemoglobin were observed in samples of blood heated after faulty placement of the blood container in the microwave unit. A review of the events that took place during the morning of surgery disclosed that the unit in question required a particularly long time to heat and that, after heating, it had "a brown film on the inside of a small area of the bag" similar to the experimental observations noted.

The potential hazards of infusion of hemolyzed blood or damaged cells by the means described are clear. It is difficult, however, to attribute the cardiovascular collapse in the case reported to the infusion of damaged blood.

Microwave warming of blood for use during surgical procedures is a comparatively recent development predicated on the known benefits of warmed blood given to patients requiring multiple transfusions.[9] Few studies of the effects of microwave heating upon blood have been reported. The in vivo survival of canine red cells tagged with radioactive chromium (^{51}Cr) after whole-body microwave radiation is shortened.[10] In vitro studies of blood heated in microwave warmers indicate no increase in plasma hemoglobin.[2] Preliminary reports by the manufacturer of the unit in question also suggest no important decrease in the ^{51}Cr survival of human cells heated in this fashion.[3] The ability of red cells to deform or to pass through microscopic filter pores has been found to correlate well with in vivo survival.[6] The demonstration in the current report of normal filterability and absence of gross hemolysis of cells heated properly by microwaves is consistent with the manufacturer's report. On the other hand, the data indicate that improperly heated blood not only results in overt hemolysis of red cells but also produces a population of damaged but intact erythrocytes whose in vivo survival can be expected to be shortened.

The ease with which improper heating could be induced by the microwave warmer in question requires that this and similar machines, if they are to be employed in clinical medicine, be equipped with safety devices sufficient to preclude the possibility of overheating blood. The manufacturer of the unit involved has been apprised of our findings and has arranged to recall and equip all units with appropriate safety features.

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