ORIGINAL ARTICLE

FFP:RBC Resuscitation Ratio and Post-Shock Fluid Uptake

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Objective: To assess the effects of the fresh frozen plasma (FFP) to red blood cell (RBC) ratio and balanced electrolyte solution (BES) to RBC ratio during resuscitation of severely injured patients on the duration of the postoperative fluid uptake period (phase 2) as well as the fluid (BES) needs, weight gain, and hypoproteinemia in phase 2.

Design, Setting, and Patients: The 316 patients were hypotensive (systolic blood pressure = 81 mm Hg) and tachycardic (117/min), with an average shock time (systolic blood pressure < 80 mm Hg) of 31 minutes in the operating room (OR); they received 14.2 RBC units, 854 mL of FFP, and 11.5 L of BES while in the OR. Phase 2 averaged 29.2 hours, where the patients gained 8.4 kg, had a serum albumin level of 2.6 g per day, and received 8.6 L of BES. The phase 2 time, BES needs, weight gain, and hypoproteinemia were correlated with systolic blood pressure, admission pulse rate, arterial pH, shock time, RBC, FFP, and BES; the FFP:RBC, BES:RBC, and BES:FFP ratios were given in the OR.

Results: Shock time had the best correlation with RBC, FFP, and BES administration in the OR as well as with phase 2 duration, BES needs, weight gain, and hypoproteinemia. There was no significant correlation with OR FFP:RBC, BES:RBC, or BES:FFP ratios and phase 2 hypoproteinemia or weight gain. The FFP:RBC ratio in the OR correlated directly with phase 2 duration and BES needs ($P = .001$); in contrast, the BES:RBC ratio in the OR correlated ($P < .001$) inversely with phase 2 duration and BES needs.

Conclusions: The severity of shock is best predicted by shock time and the RBC, FFP, and BES infusions in the OR. Contrary to recent reports, the FFP:RBC ratio in the OR correlates directly with duration and BES needs of phase 2, whereas the BES:RBC ratio correlates inversely with phase 2 duration and BES needs.

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THE HEMORRHAGIC SHOCK INsult (HSI) is uniformly associated with postresuscitation extravascular fluid sequestration.[1,2] The extent of extravascular fluid sequestration, in turn, reflects the shock insult and the volume requirements during emergency department and operating room resuscitation (phase 1). This sequestration occurs within both the intracellular fluid (ICF) space and the interstitial fluid space (IFS).[1,3] The ICF expansion is associated with altered cell membrane potential, which, in animal models, decreases from a normal of −90 mv to −60 mv during severe hemorrhagic shock; a HSI causing the cell membrane potential to fall below −60 mv is usually lethal.[1,4] This severity of lethal insult is associated with an increase in the ICF sodium concentration from a normal of 9 mEq/L to 15 mEq/L.[1] Consequently, the maximum amount of ICF sodium sequestration after a HSI in the 70-kg patient with 28 L of ICF would approximate 230 mEq, or less than 2 L, of normal saline.[4] Thus, most extravascular fluid sequestration following resuscitation from the HSI is within the expanded IFS.[5]

The severity of the HSI correlates with the duration of the fluid sequestration period (phase 2), the volume of balanced electrolyte solution (BES) needed in phase 2, and the extent of consequent phase 2 weight gain and hypoalbuminemia.[1,3] These phase 2 indices of the severity of hemorrhagic shock have been equated to the degree of organ dysfunction affecting morbidity, hospital length of stay, and mortality.[5] Recent studies, especially from the military sector, have suggested that increasing the fresh frozen plasma (FFP) to packed red blood cell (RBC) ratio would reduce the extent of

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Table 1. Phase 1 Emergency Department and Operating Room Condescriptives of 316 Patients

Parameter	Mean (SE)
Admission SBP	81.40 (1.80)
Admission pulse rate	117.20 (2.30)
Shock time, min[a]	30.73 (1.89)
Phase 1	
Time, h	8.69 (0.33)
RBC	14.22 (0.50)
FFP, mL	853.80 (36.77)
BES, L	1153.67 (270.70)
UO, mL	2061.78 (63.37)

Abbreviations: BES, balanced electrolyte solution; FFP, fresh frozen plasma; RBC, red blood cell; SBP, systolic blood pressure; UO, urine output.
[a] Shock time = SBP < 80 mm Hg.

IFS sequestration and thereby ameliorate multiple organ dysfunction.[6-8] This potential benefit is thought, in part, to be related to a reduction in the BES:RBC ratio needs in phase 1 because the expansion of plasma volume by the FFP would theoretically restore perfusion pressures more efficiently with less BES.[7,8]

This premise was evaluated in a large group of severely injured patients who had prospective monitoring of the FFP:RBC and BES:RBC ratios not only during emergency department and operating room resuscitation (phase 1) but also in the subsequent fluid uptake period (phase 2) and the later fluid mobilization period (phase 3). The severity of the HSI was judged by the fluid and blood product needs during operation, the shock time during which the systolic blood pressure (SBP) was less than 80 mm Hg, the intraoperative arterial pH (ApH), the duration and BES needs during phase 2, and the extent of weight gain and hypoproteinemia during phase 2.

METHODS

This study included 316 patients who were severely injured and required massive transfusions prior to the end of an operation for control of bleeding. Inclusion criteria for the study included the need to transfuse 8 or more RBC units if the injured patient never had a SBP of less than 80 mm Hg or the need to infuse 6 or more RBC units if the patient was documented to have a SBP of less than 80 mm Hg; these transfusion requirements had to be met during operation for control of bleeding. Patients not meeting these criteria were not considered to have had a severe enough physiologic insult to warrant the time expenditure and expense of multidisciplinary monitoring and long-term data storage. Consequently, the patients reported herein represent a small percentage of those patients treated by the authors during the study years. All data were collected and stored prospectively for later retrospective analysis; all patients were de-identified, meeting institutional review board guidelines. There were 281 patients who had sustained penetrating wounds, primarily gunshot wounds, and 35 patients who had sustained blunt injury. All patients arrived from the inner eastern quadrant of the Detroit Trauma System with an average transit time of less than 5 minutes. Because of the rapid transit time, many patients received no prehospital infusions and none are known to have received more than 500 mL of BES; prehospital infusion volumes were not collected. Most patients were rapidly resuscitated in the process of going to the operating room for control of bleeding and treatment of injuries. Phase 1 was defined as the time from arrival to the hospital until the end of the operation for control of bleeding and repair of organ injuries. Parameters measured during phase 1 included admission SBP; admission pulse rate (PR); ApH; resuscitation needs of RBC, BES, and FFP; and urine output (UO). During Phase 1, the shock time was determined by noting, in 5 minute segments, the number of minutes that the SBP was less than 80 mm Hg.

Following operation, the patients were treated in a surgical intensive care unit and had ongoing measurements of the previously noted vital signs, with additional monitoring of central pressures in most patients. Total inputs were monitored hourly in terms of BES, RBC, and FFP infusion; total outputs were monitored hourly in terms of UO, nasogastric tube output, and other output (drains and ostomies). Serial measurements were made of serum protein dynamics including total serum protein and serum albumin (SA). Each morning, a balanced scale was used to monitor daily patient weight; patients whose fractures had been splinted or casted with plaster or who had fractures that were treated with external fixators were excluded. Transferring the patient to the bedside scale during weighing precluded error induced by wet sheets and bed clothing. Based on the sequential changes in vital signs—namely, an increase in pulse pressure, an increase in UO, the need to reduce the infusion rate to maintain desired vital signs, and the intake and output records—a judgment was made as to when the fluid uptake period (phase 2) ended and the subsequent mobilization period (phase 3) began. Using the previously mentioned parameters, the distinction between phase 2 and phase 3 could be easily identified within a 2-hour interval in all patients. The fluid uptake period (phase 2) averaged 29.2 hours. The patients then entered into a fluid mobilization phase during which continued intake and output records were monitored on an hourly basis and continued daily weightings were made to judge when the fluid mobilization ended and the patient went back into a positive fluid balance. The fluid mobilization (phase 3) averaged 5.3 days.

The severity of the HSI was quantified in the postoperative period by the duration and volume needs of phase 2, the estimated weight gain, and the reduction in serum protein levels, primarily SA. These gauges of the severity of the HSI were correlated with several factors of resuscitation including the admission SBP and PR; the amount of RBC, BES, and FFP given during phase 1; the ApH; the FFP:RBC, BES:RBC, and BES:FFP ratios given during phase 1; and the phase 1 shock time. Finally, the patients who received an FFP:RBC ratio of less than 0.3 during phase 1 were compared with patients who received an FFP:RBC ratio of greater than 0.45 during phase 1 for severity of insult, parameters of phase 2 HSI, postoperative respiratory function as judged by the arterial oxygen tension to fraction of inspired oxygen ratios, and outcome.

RESULTS

The admission SBP and PR in the 316 patients averaged 81 mm Hg and 117, respectively; the average shock time during phase 1 was 31 minutes (**Table 1**). During the 8.6 hours of phase 1 (emergency department and operating room resuscitation), they received an average of 14.2 RBC units, 11.5 L of BES, and 853 mL of FFP (Table 1). Following operation, the patients entered into an average (SE) of 29.2 (1.1) hours of fluid sequestration (phase 2) during which time they received 2.4 (0.1) RBC units, 235 (23) mL of FFP, and 8.6 (0.5) L of BES, while having 2.6 (0.1) L of UO, 803 (65) mL of nasogastric tube output, and other out-

Table 2. Correlations Between Severity of HSI and Resuscitation[a]

	P Value			
HSI Parameter	Serum Albumin	Phase 2 Weight Gain	Phase 2 Time	Phase 2 BES
Admission SBP	.43	.21	.03	.16
Admission PR	.43	.66	<.001	<.001
Shock time	<−.001	<.001	.001	.006
Phase 1				
RBC	.002	<.001	.01	.002
FFP	.01	<.001	<.001	<.001
BES	<.001	<.001	.58	.09
Ratio				
FFP:RBC	−.30	.40	.001	.01
BES:RBC	.87	−.24	−.001	−.02
BES:FFP	−.87	.53	<−.001	−.07

Abbreviations: BES, balanced electrolyte solution; FFP, fresh frozen plasma; HSI, hemorrhagic shock insult; PR, pulse rate; RBC, red blood cell; SBP, systolic blood pressure.

[a]With postoperative albumin, weight gain, shock time, and BES infusion.

put (526 [78] mL). A significant portion of the phase 2 UO occurred within the first 2 hours of operation when the kidneys, subjected to a HSI, have impaired concentrating ability probably related to an innermedullary washout due to a reduction in renal component 1 perfusion associated with severe hemorrhagic shock; the breakdown between this early phase 2 UO and later phase 2 UO was not stored in the database.[9,10] The average (SE) weight gain was 8.4 (0.4) kg. During phase 2, there was a uniform reduction in all serum proteins with the SA level falling to 2.6 (0.8) g/dL (to convert to grams per liter, multiply by 10) and the total serum protein level decreasing to 4.6 (0.9) g/dL (to convert to grams per liter, multiply by 10.0).

The admission SBP correlated significantly with the duration of phase 2 but did not correlate with the phase 2 hypoalbuminemia, weight gain, or the required volume of BES (**Table 2**). Likewise, the admission PR did not correlate with the phase 2 hypoalbuminemia or subsequent weight gain but did correlate significantly ($P < .001$) with the duration of phase 2 and the volume of BES required during phase 2 (Table 2). The severity of acidosis as determined by the ApH did not correlate with the phase 2 weight gain or the phase 2 duration but did correlate significantly with the SA level and the volume of BES required during phase 2 (Table 2). There was a highly significant correlation between the shock time and the subsequent duration and fluid needs during phase 2 and with the phase 2 hypoalbuminemia and weight gain (Table 2). The volume of RBC and FFP given during phase 1 had a highly significant correlation with all 4 of these phase 2 monitors of the HSI (Table 2). The volume of BES given during phase 1 correlated with the subsequent degree of hypoalbuminemia and weight gain but did not correlate with the duration of phase 2 or the volume of BES required during phase 2 (Table 2).

The ratio of FFP:RBC given during phase 1 did not correlate with the subsequent hypoalbuminemia or weight gain; however, the FFP:RBC ratio did correlate significantly with an increase in phase 2 time and the volume of BES required during phase 2 to maintain appropriate or desired vital signs (Table 2). The BES:RBC ratio given during phase 1 did not correlate with the subsequent phase 2 weight gain or hypoalbuminemia. In contrast to the FFP:RBC ratio, the BES:RBC ratio correlated inversely in a highly significant manner, with a reduction in phase 2 duration and the volume of BES required during phase 2 (Table 2). The BES:FFP ratio during phase 1 showed no significant correlation with the degree of phase 2 weight gain or hypoalbuminemia; however, there was a significant inverse relationship to the duration of phase 2 and an insignificant ($P = .07$) reduction in the volume of the BES required during phase 2 (Table 2).

The initial vital signs, shock time, and resuscitation needs were similar for the 117 patients who had an FFP:RBC ratio of less than 0.3 compared with the 100 patients who had an FFP:RBC ratio of more than 0.45; however, the admission SBP was significantly lower in the patients with the FFP:RBC ratio of less than 0.3 (**Table 3**). By definition, the volume of FFP administered during operation was decreased in those patients with a FFP:RBC ratio of less than 0.3. The SBP, diastolic BP, PR, and SA during phase 2 were similar for those patients with the FFP:RBC ratio of less than 0.3 compared with those with the FFP:RBC ratio of greater than 0.45 (Table 3). The phase 2 duration, phase 2 BES needs, and phase 2 weight gain were significantly less in those patients receiving a FFP:RBC ratio of less than 0.3 during phase 1 compared with those patients who received a FFP:RBC ratio of more than 0.45 (Table 3). There was no difference in the arterial oxygen tension to fraction of inspired oxygen ratio during either the first half or the second half of the fluid uptake phase (Phase 2) but there was a significant increase in the arterial oxygen tension to fraction of inspired oxygen ratio during the first 48 hours of the later fluid mobilization period (phase 3) in those patients receiving the FFP:RBC ratio of less than 0.3 compared with those who received the FFP:RBC ratio of greater than 0.45 (Table 3). Likewise, the hospital length of stay was decreased in those patients receiving the lower FFP:RBC ratio (20.5 [1.5] days) compared with those receiving the higher FFP:RBC ratio (26.1 [2.1] days) (Table 3).

There were no significant differences in the mortality rate between the 2 groups. Seven of the 117 patients who received the lower FFP:RBC ratio died; 5 of the 7 deaths were judged to be directly related to the HSI,

Table 3. Resuscitation FFP:RBC Ratios and Outcomes

Parameter	FFP:RBC Ratio, Mean (SE)		
	<0.30 (n = 117)	0.30-0.45 (n = 99)	>0.45 (n = 100)
Admission SBP	7.5 (2.6)[a]	74.0 (2.3)	79.0 (3.1)
Admission PR	132 (3.7)	116 (3.9)	114 (4.7)
Phase 1			
Shock time, min	32 (3)	30 (3.6)	30 (2.8)
RBC	13.6 (0.9)	12.9 (2.1)	14.3 (0.8)
FFP	406 (41)[b]	931 (53)	1315 (66)
BES	10.3 (0.4)	9.3 (0.4)	12.1 (0.4)
ApH	7.43 (0.6)	7.40 (0.3)	7.42 (0.6)
Phase 2			
A PaO_2:FIO_2[c]	312 (14)	300 (11)	320 (14)
B PaO_2:FIO_2[d]	290 (15)	300 (13)	320 (14)
Phase 3			
A PaO_2:FIO_2[e]	322 (11)[b]	299 (15)	274 (12)
B PaO_2:FIO_2[f]	297 (11)	309 (13)	306 (14)
Length of stay, d	20.0 (1.5)[a]	26.5 (1.9)	27.5 (3.2)
Phase 2			
SBP	140 (2)	133 (1.9)	145 (2.5)
DBP	87 (1.4)	81 (1.9)	85 (2.1)
PR	101 (1.4)	100 (1.2)	100 (1.6)
SA	2.6 (0.7)	2.5 (0.7)	2.6 (0.9)
BES	7.7 (0.6)[b]	8.1 (0.8)	9.7 (0.9)
UO	3.2 (0.6)	2.9 (0.7)	2.3 (0.2)
Weight gain	8 (0.5)	8.7 (0.6)	9.1 (0.5)
Time	25 (1.2)[b]	31 (2.1)	36 (2.6)

Abbreviations: ApH, arterial pH; BES, balanced electrolyte infusion; DBP, diastolic blood pressure; FFP, fresh frozen plasma; FIO_2, fraction of inspired oxygen; PaO_2, partial pressure of oxygen (arterial); PR, pulse rate; RBC, red blood cell; SA, serum albumin; SBP, systolic blood pressure; UO, urine output.

[a] $P = .05$ for patients with FFP:RBC ratio of 0.03 compared with patients with FFP:RBC ratio of greater than 0.45.

[b] $P = .005$ for patients with FFP:RBC ratio of 0.03 compared with patients with FFP:RBC ratio of greater than 0.45.

[c] During the first half of phase 2.

[d] During the second half of phase 2.

[e] During the first 48 hours of phase 3.

[f] During the second 48 hours of phase 3.

whereas 2 of the deaths from head injury were considered to be unrelated to the severity of the hemorrhagic shock. Of the 100 patients, there were also 7 who died who had received the FFP:RBC ratio of more than 0.45; all 7 of these deaths were thought to be directly related to the pathophysiologic effects of the HSI.

COMMENT

The lack of a significant correlation between the admission SBP and the phase 2 weight gain, hypoalbuminemia, and BES needs is not surprising because many factors, such as alcohol and drugs, may affect the admission SBP in the severely injured but still conscious patient. The systemic release of catecholamines accompanying the arrival into an emergency department where a team of resuscitation personnel take control of one's body is very understandable. Furthermore, there often is an inappropriately low admission SBP when a patient with moderate injury is under the influence of alcohol.

The better correlation between the admission PR and the duration and BES needs in phase 2 is expected; however, bradycardia in severely injured patients may occur.[11,12] More recently, several authors have noted an altered heart-rate variability that alters the expected pulse response to a severe HSI.[13,14] However, most of the patients herein responded with the typical tachycardia expected with a severe HSI. The positive correlation between the ApH and the degree of hypoalbuminemia as well as the BES needs for maintaining postoperative vital signs and perfusion reflects the cellular insult of the severity of the HSI independent of the effects of associated alcohol or street drugs.

The best correlation was seen between the shock time and the indices for severity of the HSI. This reflects the accumulative total body hypoperfusion when the catecholamine response has been blunted by general anesthesia. The level of 80 mm Hg was chosen herein on the basis of prior studies showing that the duration of hypotension below 80 mm Hg was the best reflection of the HSI.[2,3] The very high correlation between shock time and the phase 2 duration and BES needs along with the hypoalbuminemia and weight gain reinforces the decision to use 80 mm Hg as the best indicator of the total body HSI.

The strong correlations between the amount of RBC, FFP, and BES given during phase 1 resuscitation and the subsequent gauges of severity of the HSI reflect this total body insult as the RBC units and BES are needed to correct acute anemia and hypoperfusion supplemented by the FFP used to correct coagulation needs seen during acute hemorrhage. These factors, in turn, would predict the extent of total body insult. The large volume of phase 1 BES infusion reflects this insult, which is associated with both ICF and IFS expansion during phase 2.

A most important finding herein is the lack of correlation between the ratios of FFP:RBC, BES:RBC, and BES:FFP administered during phase 1 on the subsequent phase 2 hypoalbuminemia and weight gain. These findings suggest that, within limits, the body will relocate BES and proteins according to the geometric alterations in the interstitial space matrix that, in turn, reflect the severity of the HSI rather than the specific infusion ratios given during phase 1.[3] The phenomenon of rapid BES relocation into the extravascular space has been clinically apparent in patients who gain significant weight.[1-3] Prior studies have demonstrated that this weight gain is a reflection of the expansion of the IFS as measured by acute expansions in the inulin space.[3] Likewise, rapid relocation of proteins out of the vascular system has been demonstrated by increases in prenodal and postnodal lymphatic concentration of albumin and globulin following the administration of human SA in severely hypoalbuminemic conditions.[5,15,16] Similar changes have been identified following BES resuscitation with and without colloid supplement in canine hemorrhagic shock models.[17,18] This rapid relocation of colloids out of the plasma into the interstitial space in canine models of hemorrhagic shock has been shown to markedly increase following the administration of different colloid solutions.[17-19]

A most interesting and unique finding herein was the completely divergent effects that the phase 1 FFP:RBC ratio had on phase 2 duration and BES needs in contrast to the BES:RBC and BES:FFP ratios of phase 1 resuscitation. These findings are contrary to recently pub-

lished reports suggesting that a higher FFP:RBC ratio will decrease the BES needs during and following operation.[20-22] However, these reports have not correlated the FFP:RBC ratio with the duration of the postoperative fluid uptake period, the extent of postoperative hypoalbuminemia, and the volume of BES needed to maintain perfusion and vital signs. Possibly, these divergent findings reflect the bias of individual patient selection. Many of the civilian reports recommending or showing the advantage of a 1:1 FFP:RBC resuscitation ratio had been multiinstitutional retrospective studies of patients who sustained blunt trauma in contrast to the overwhelming majority of patients herein who had been victims of penetrating wounds.[20-22] Moreover, the patients reported to have a better outcome with the 1:1 FFP:RBC ratio following military injury may have experienced more concussive and tissue-destructive forces not typically seen in civilian trauma centers.[8] Likewise, the military casualties would not be under the influence of alcohol and street drugs, which are common comorbid conditions following inner-city penetrating trauma.[23,24] Regardless of these differences, the proponents of the higher FFP:RBC phase 1 resuscitation ratio of 1:1 have suggested that the so-called survival benefits of the higher FFP:RBC ratio are due to a reduction in extravascular BES relocation, thereby preserving organ function. The significant prolongation in phase 2 duration ($P = .001$) and BES needs ($P = .01$) associated with the higher FFP:RBC phase 1 resuscitation ratio suggests protein relocation from the infused FFP into the IFS is delaying fluid mobilization from the interstices.[25,26] This phenomenon has been observed in a prospectively randomized supplemental albumin resuscitation regimen in humans.[25-27] Likewise, supplementation of hemorrhagic shock resuscitation with albumin and other artificial colloids in a controlled canine shock model has shown an increased colloid-induced relocation of protein into the IFS.[15-17] However, when this same canine hemorrhagic shock model was used to study the effects of fresh (nonfrozen) plasma–supplemented resuscitation, no abnormal protein relocation was seen with supplemental fresh plasma compared with control animals without supplemental plasma.[26] The only apparent differences between the FFP administered in the patients reported herein and the previous studies in which 1 group of animals received fresh plasma and the control group received no plasma was the process of freezing.[26,27] The plasma used in the controlled canine model was obtained from separate canine donors 1 day prior to the experimental studies and was appropriately stored within a refrigerator without being frozen. The marked differences in the physiologic handling of protein and the consequent effects on IFS dynamics suggest that the freezing process itself conveys alterations in some of the protein fractions that, in turn, initiate changes in the IFS matrix; these changes, in turn, may cause a delay in fluid and protein mobilization from the IFS following a specific HSI. Such a delay would explain the prolongation of phase 2 and the increased BES needs during phase 2 in patients receiving higher FFP:RBC ratios. This suspicion needs to be tested in a controlled model.

Based on these findings, we recommend that ongoing treatment of hemorrhagic shock during phase 1 should include sufficient RBC to correct ongoing anemia recognizing that the RBC has both oncotic and oxygen-carrying capabilities. The supplementation of FFP should be designed to correct coagulopathy, which is readily achieved by a FFP:RBC ratio of 0.3:1.[28] This supports the observation by Teixeira and colleagues,[29] who showed that a FFP:RBC ratio of more than 0.5:1 is not beneficial. Defining a specific optimal FFP:RBC ratio for all patients is an unreasonable objective because of the variability in shock time, severity of tissue injury, mechanism of injury, transport time, and promptness of operative intervention. Despite these limitations, we recommend that the immediate response to a level I trauma activation or to some other type of hemorrhagic insult include 4 units of sex-specific type O blood. Any patient receiving fewer than 5 RBC units will have ample replenishment of procoagulants from the IFS without FFP supplementation. However, additional bleeding will deplete the IFS stores so that the subsequent deliveries of 4 RBC units from the blood bank should include 2 units of FFP, insuring a minimal 0.3:1 FFP:RBC ratio by the time 10 units are infused. Additional transfusion should follow the 2:4 FFP:RBC ratio until hemostasis is obtained. The additional infusion of FFP to increase oncotic pressure and reduce BES infusion is not indicated because the infused protein particles likely enter into the IFS and, like other colloids, prolong phase 2. In this setting, the use of prethawed FFP likely would not alter these findings.[20] Consequently, the administration of BES during phase 1 should be guided by the ongoing vital signs and UO, recognizing that most of the BES will enter into the IFS in proportion to the severity of the HSI and organ ischemia. This subsequent relocation into the plasma should not be aborted by colloid or excess FFP supplementation. These basic physiologic responses to a severe HSI cannot be altered by the administration of fixed BES:RBC, FFP:RBC, or BES:FFP ratios.

This prospective study has a number of limitations. First, the extent of weight gain in phase 2 was calculated from pre-injury estimates, which may not be a perfect reflection of the patients' true weight. However, recent studies suggest that this technique using pre-injury weight is reasonably accurate.[30] The duration of phase 2 is judged by the changing hemodynamics and fluid balance, representing a best guess. However, that there are highly significant correlations between estimated weight gain and the shock time suggests this is a satisfactory method. Second, another limitation reflects the fact that the FFP:RBC ratios given during operation ranged from 0.2:1 to 0.75:1; thus, none of the patients received the 1:1 FFP:RBC ratio that is currently recommended by many authors.[6-8] However, previous studies from this unit have demonstrated that patients receiving a 0.3:1 FFP:RBC ratio have appropriate restoration of procoagulants.[28,29]

Third, another limitation of this study reflects the range of the BES:RBC ratio. This ratio ranged from 1.7:1 to 2.9:1, with none of the patients having the extraordinarily high ratios of greater than 3.5:1, which, in theory, could be associated with pulmonary dysfunction. The classic canine studies by Shires and colleagues[1] identified a 3.0:1 ratio as being ideal for restoring perfusion pressure and

UO. Prior clinical studies from our unit demonstrated that the ideal BES:RBC ratio is 2.5:1 when administering packed cells as opposed to 2.0:1 when resuscitating with whole blood.[2,3]

In conclusion, the severity of the HSI will best correlate with shock time and the phase 1 volumes of BES, FFP, and RBC. There will be no such correlation between the phase I FFP:RBC, BES:RBC, and BES:FFP resuscitation ratios and the phase 2 weight gain or degree of hypoalbuminemia. A higher FFP:RBC ratio during phase 1 was associated with a prolonged phase 2 duration and BES needs. In contrast, a higher BES:RBC phase 1 resuscitation ratio was associated with a reduced phase 2 duration and fluid needs.

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