Original Article

Effects of Hyperosmotic Solutlon on Platelet Aggregation and ATP Secretion

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Summary

This study has investigated effect of two hypertonic solution, a 50% dextrose solution and a 10% saline solutilon, on platelet function after incorporation into blood samples drawn from healthy volunteers, these two group of mixtures then referred to as the D group and the S group, respectively. Four strengths of each hyperosmotic solution were tested in the mixtures: 0.25, 0.50, 0.75 and 1.00 ml, which were then labeled as samples S1 to S4, respectively. Next, 1 ml of a 3.2 % solution of trisodium citrate was added to each sample, so that the total volume of each sample amounted to 10 ml. For control purposes, blood samples with no additives were used, these samples assigned the designation S0. After adding either adenosine diphosphate(ADP)or collagen to each mixture, the platelet aggregation and the adenosine triphosphate(ATP) platelet secretion were measured by a Lumi-Aggregometer. These measurements revealed that both the platelet aggregation and platelet ATP secretion decreased in both groups. Further, when the volume of the hyperosmotic solution was increased in the mixture, an even more remarkable reduction in platelet function occurred. The collagen S3 and the ADP and collagen S4 platelet aggregations significantly differed between the two groups but the ATP platelet secretion did not.

These findings are consistent with a tendency towards hemorrhagic shock patients undergoing a hyperosmotic infusion.

For trauma victims in severe hemorrhagic shock, a rapid infusion of a crystalloid or colloid solutions in the cornerstone of early therapy. However, while the infusion of a large volume of an isotonic solution has proven highly successful and internationally used for the initial treatment of hemorrhagic shock, it may be that a smaller volume of a hyperosmotic solution is also equally effective as a resuscitating fluid for victims of hemorrhagic shock.

To investigate this possibility, using blood samples drawn from healthy volunteers, this study has compared platelet function after an infusion of a hyperosmotic solution has been incorporated.

Materlals and methods

To determine the effect of a hyperosmotic solution on platelet function, blood samples were drawn from l7 healthy volunteers, after which a hyperosmotic solution was added to these blood samples. The blood samples were divided into two groups based on the hyperosmotic solution that was added; one set of 8 samples received a 50 % dextrose solution(2,800 mOsm/liter)and was labeled group D and the other set of 9 samples received a 10 % saline solution(3,333 mOsm/ liter) and was labeled group S. Further, each hyperosmotic solution was added to blood samples in 4 ml different doses of 0.25, 0.50, 0.75 and 1.00 ml, which were respectively labeled S1 to S4 in that same order, so as to make the volume of each blood-solution mixture amount to 9 ml. Additionally, 1 ml of a 3.2% solution of trisodium citrate, an anticoagula-

nt, was added to each of the mixtures. Finally, for purposes of comparison, 9 ml blood samples that received no additive were used as controls and given the designation of S0.

The citrate blood samples were immediately centrifuged at 800 rpm for 10 min. at room temperature to obtain a platelet rich plasma (PRP). Then, on adding either adenosine diphosphate(ADP) or collaqen, the maximal platelet aggregation and maximal adenosine triphosphate(ATP) serection were measured with a Lumi-Aggregometer. The final concentration of the aggregating agents used were as follows: ADP, 1.82X10-5 mol and collagen, 4.55 μ g/ml.

All resulting values have been expressed as mean± standard deviation(SD). Differences within a group were analyzed by using the Student's paired t-test anddifferences between the groups were compared by using the unpaired t-test, with $p<0.05$ considered as statistically significant.

Results

The S0 platelet function values for both groups, including aggregation and ATP secretion, are shown in Table. As can be noted, platelet function did not significantly differ between the two groups.

Platelet aggregation on adding ADP significantly decreased in the S1 to S4 blood-solution mixture of both groups.

Similarly, on adding collagen, the platelet aggregation significantly decreased in the blood-solution mixtures of both groups, with the exception of the group D S1 blood-solution mixture. With an increase in the volume of the hyperosmotic solution mixed with the blood, a more remarkable reduction in platelet aggregation was observed. Further, the collagen S3 measurement and the ADP and collagen S4 measurements statistically differed between the two groups.

Maximal platelet ATP secretion significantly decreased in both the ADP and collagen groups. Further, with regard to platelet aggregation, with an increase in the volume of the hyperosmotic solution that had been mixed in with the blood, the greater was the tendency towards a reduction in the platelet ATP secretion. However, the amount of the platelet ATP secretion did not statistically differ between both groups despite any difference in the platelet aggregation.

Discussion

We have compared the effect on platelet function after an infusion of a hyperosmotic solution of either 50% dextrose or 10% saline had been incorporatedin to blood samples taken from healthy volunteers. Many reports have indicated that for cases of hemorrhagic shock, the infusion of a small volume of a hypertonic saline solution is a useful initial therapy to bring about resuscitation[1-5].

In this regard, Bitterman et al. have reported that for cases manifesting severe hemorrhagicshock, an intravenous infusion of highly concentration NaCl solution rapidly returns the blood pressure and acid-based equilibrium to normal parameters [3]. Further, many believe that a small volume of a hypertonic saline solution infused through a small-caliber needle over a few minutes into severe hemorrhaqic shock victims is a life-prolonging or, glven the overall status of the victim, a life-saving therapy.

However, although a small volume of a hyperosmotic solution is known to effectively restore the hemodynamics in victims of severe hemorrhagic shock, the mechanisms through which these hyperosmotic solutions activate a restorative response have yet to be fully elucidated. Velasco et al. maintain that in response to an intravenous infusion of highly concentrated NaCl, myocardial contractility was restored and, as a consequence, cardiac efficiency increased, the precapillary vessels dilated, and capacitance in the vessels became constrlcted [1]. However, Ogata et al. have reported that after administering a hypertonic sallne solution in hemorrhagic shock victlms, the hematocrit did not markedly decrease and the combination of the preload elevation and the afterload reduction, brought about by the hypertonic saline solutlon, may have affected

improvement in the cardiac output. And the results of their study have indicated that a hypertonic saline solution administered after hemorrhagic shock may bring improvement and resuscitation not because of a plasma-expander effect but to blood redistribution[6]. In this regard, Welte et al. maintain that the instantaneous restoration of the central hemodynamics on resuscitation brought about by a small volume of hypertonic saline or dextran largely depends on the rapid augmentation of the ventricular preload due to plasma volume expansion and that resuscitation cannot be attributed to inotropic stimulation [7]. On the other hand, Bitterman et al., who investigated resuscitation from hemorrhagic shock that was brough on by a small volume of a 7.5% NaCl solution, have reported that the resuscitation was due to an attenuated accumulation of the myocardial depressant factor(MDF) in the plasma [3].

In another study, Gross et al. have reported that the hypertonic saline treatment of uncontrolled hemorrhagic shock victims increases the risk of blood loss, since the hypertonic saline can cause a rise in the blood pressure, the cardiac output, and peripheral vasodilation [8]. Our results also suggest that an infusion of hyperosmotic saline decreases platelet function, and in hemorrhagic shock patients this could lead to an increased blood loss. Therefore, such a risk should be given due consideration when treating victims of hemorrhagic shock.

In a study that investigated the hemodynamic effects of a hypertonic sallne infusion for treating severe endotoxic shock, Luypaert et al. have found that a saline solution rapidly restores the oxygen transport and tissue oxygen consumption in septic shock patients [9]. Based on this finding, we intend to investigate the efficacy of hypertonic saline as a treatment method not only for hemorrhagic shock victims but also for other kinds of shock.

In investigating the survival rates, the hemodynamic and metabolic effects of a hypertonic NaCl administration, and the non-electrolytes in victims of severe hemorrhagic shock, Roche-E-Silva et al. have found that infusions that provide a high plasma sodium content appear to be essential for survival, based on their finding that a higher survival rate was seen in hemorrhagic shock victims given a sodium solution rather than another type of solution [10].

In another study,Frey et al. have compared the respective effect of an equi-osmolar solutions(2,400 mOsm/liter) of sodium chloride (7.2%) and of sodium acetate(10.4%), the latter contained in dextran 60, on the central hemodynamics and metabolic variables in hemorrhagic shock victims and concluded that the sodium acetate solution offers no advantage over the sodium choride solution with regard to resuscitation from hemorrhagic shock [11]. Further, almost all fundamental studies of hyperosmotic solutions as a therapy for hemorrhagic shock favor a hypertonic saline solution. Additionally, hypertonic saline solutions are simple and inexpensive to make in comparison to other hyperosmotic solutions.

In treating hemorrhagic shock victims, a crucial consideration is the amount of the solution to be infused. With regard to hypertonic saline, some authors have infused 4 ml/kg of a saline solution(2,400 mOsm/liter) [1,3,4], whereas Ogata et al. have infused a 20% saline solution(6,666 mOsm/kg) at 1.5 ml/kg6). To cite an example of an infused volume, the infused amount of a hypertonic saline solution(2,400 mOsm/liter) for a man in hemorrhagic shock with a body weight of 70kg has been calculated to be 280ml. As for saline solution amounts to be infused based on the results of this blood sampling study, assuming that the hemorrhagic shock has caused a 4-liter reduction in the blood volume,the calculated amount of the S1 to S4 hyperosmotic solution strengths is as follows: 114, 235, 364 and 500 ml, respectively. Here it should be noted that the strengths of our blood-saline solution mixtures were clinically found to be of value, particularly the S1 and S2 strengths. When treating cases of hemorrhagic shock, care should be taken if the amount of the hyperosmotic solution

Table Changes in maximal platelet aggregation and maximal platelet ATP secretion in group D and group S

		S_0	S_1	S_2	S_3	S_4
Aggregation (%)						
ADP	D	65.4±6.5	60.3±5.8*	57.0±9.6*	51.8±8.9*	38.8±12.2** +
	S	68.7±9.8	57.3±10.3**	50.6±8.6**	42.3±10.7**	27.0±6.6**
Collagen	D	72.3±9.3	69.3±12.8	64.5±10.0**	58.8±12.8** +	47.3±11.7** +
	S	69.3±11.5	62.8±7.1*	55.0±9.2**	43.3±14.7**	26.0±18.7**
ATP secretion (μg)						
ADP	D	5.90±1.58	5.94±1.99	5.35±1.52*	4.91±1.74**	5.01±1.60*
	S	7.12±1.43	6.52±1.72*	5.40±1.86*	5.73±0.80**	5.21±0.39**
Collagen	D	2.88±1.17	2.48±1.14	1.74±0.79**	1.80±0.80**	1.04±0.64**
	S	2.27±0.78	2.19±0.68	1.49±0.67*	1.10±0.64**	0.79±0.48**

Values are the mean ± SD
**:P<0.01, *:P<0.05 versus control values (S0)
+:P<0.05 between group D and group S

to be infused is in excess of 4ml/kg.

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