The Role of Isotonic and Hypertonic Solutions in the Resuscitation of Shocked Patients

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SUMMARY: The role of intravenous salt solutions in resuscitation is reviewed historically. A brief account of the pathophysiology of shock is given. The particular use of hypertonic solutions in the resuscitation of severely shocked patients is reviewed and its mechanism of action discussed. It is considered that hypertonic solutions may find a role in any future major military conflict. Two hypertonic solutions that are suggested for consideration in this context are 12% sodium chloride (2mmol/ml) and 8.4% sodium bicarbonate (1 mmol/ml).

ISOTONIC SALT SOLUTIONS

I Introduction

The use of intravenous (IV) salt solutions to resuscitate patients was first carried out in a logical, competent manner during the 1831 cholera epidemic in the UK. In cholera massive amounts of alkaline fluid are lost in the watery stool, leading to depletion of the extracellular fluid and a profound metabolic acidosis. The biochemical changes in the blood were elegantly summarised by O'Shaughnessy.¹ Latta and his colleagues at the Cholera Hospital, Leith, successfully resuscitated several patients using a hypotonic salt solution given intravenously. The composition of this fluid was approximately:

NaCl 60 mmol/l
NaHCO₃ 10 mmol/l

and 9 l was infused over 12-h in one patient.² It was appreciated at the time that the solution needed to be warmed to body temperature prior to administration, and the importance of avoiding air embolism was also known.³ This fascinating early work is fully reproduced in photocopy form in Howorth.²

Unfortunately, when the cholera epidemic burnt itself out this knowledge and experience were completely forgotten, perhaps because in 1833 Latta died and O'Shaughnessy emigrated to India where he later became the first Director General of the Indian Telegraph Service. (His work in linking Calcutta by telegraph to Bombay and Madras proved to be of great value in suppressing the Indian Mutiny.⁴

The value of IV salt solutions was rediscovered some 50 to 60 years later by obstetricians who realised that women dying of acute haemorrhage in childbirth still had enough blood remaining within the cardiovascular system to sustain life if only the blood volume could be restored. The use of blood transfusion itself was known to be risky; at that time ABO blood groups had not been discovered and it was not known how to prevent blood from clotting *in vitro*.

Thus Coates⁵ described the resuscitation of a patient after a massive post-partum haemorrhage by the IV in-

fusion of 22 oz (660 ml) water warmed to 100°F. This was no wild adventure since Coates had previously tried a saline-alcohol infusion in another patient, and he explained that although in theory IV water might result in "the red globules to swell up and cause them to yield their pigment" this did not occur as checked by microscopy. Coates was later largely instrumental in forming the Volunteer Medical Staff Corps in Manchester which was taken over by the War Office in 1887 and is the direct ancestor of the present-day 207 (Manchester) General Hospital RAMC (TA). Elder⁶ has given a full account of Coates's remarkable career.

Later on the use of "normal saline" gradually became established in treating acute haemorrhage⁷. In 1891 the famous surgeon W Arbuthnot Lane concluded a paper on this subject with the aphorism "No person should die of haemorrhage"⁸. It took nearly fifty years for this precept to become normal medical practice.

World War One

In the handbook issued to RAMC medical officers in 1915 there is no mention of IV saline or of blood transfusion⁹. However by the end of the war it was accepted that IV saline was of value in treating shock¹⁰. Cannon also realised that shock is accompanied by metabolic acidosis (described as a low alkaline reserve) and recommended IV bicarbonate to correct this¹¹. Unfortunately the importance of this observation was overlooked when blood transfusion became more frequently used to supplement IV saline therapy.

World War Two

In the Western Desert in 1941 it was understood that shocked, dehydrated casualties needed resuscitation with IV fluids before surgery could be safely undertaken. With the setting up of the new Army Blood Transfusion Service (a brilliant achievement) the early use of IV saline was complemented by IV plasma and ABO-compatible whole blood. During the 1944 Normandy campaign each

100 casualties received on average 63 pints of whole blood, 63 pints of plasma, and a larger volume of IV saline⁹.

Post-World War Two

It was gradually learned from using IV salt solutions to treat burns shock that inadequate volumes of fluid had been given in the past, since only about 1/3 of infused saline is retained in the circulation^{12,13}.

More recently there has been a move away from infusing saline towards more "physiological" salt solutions such as compound Na lactate (Hartmann's solution). The K at 5.0 mmol/l is intended to correct any tendency towards hypokalaemia, although hyperkalaemia usually accompanies the metabolic acidosis of shock. The lactate is converted into bicarbonate (27 mmol/l) in the liver, unless hypoxia is present, so that conversion will be slow in shock until recovery begins.

Virgilio et al¹⁴ showed that the circulation could be satisfactorily maintained after heavy blood loss due to major surgery (aortic reconstruction) by packed red cells and simple balanced electrolyte solutions, since in this situation the patient is not allowed to develop shock.

Operation Corporate

A simple and straightforward policy was adopted for resuscitation of casualties during the Falklands Islands campaign of 1982. IV fluids were given by large bore cannula into the forearm vein. All patients who required circulatory resuscitation received 1 l compound Na lactate, followed by 0.5 L polygeline (Haemaccel). If further fluid was required this sequence was repeated or ABO-group compatible blood was given¹⁵.

Conclusion

We can summarise the above work by saying that resuscitation with isotonic electrolyte solutions is quite feasible provided that:

- (1) there are sufficient red cells in the circulation to transport adequate amounts of oxygen to the tissues.
- (2) the patient is not badly shocked, which depends not so much on the amount of fluid lost as on the time interval between trauma and resuscitation.

II Patho-physiology of shock

Before discussing the role of hypertonic solutions in resuscitation, it would be helpful to outline the sequence of changes which may follow trauma and result in progressive cardiovascular collapse, or shock. Although shock can result from sepsis and cardiac causes, we are mainly concerned here with hypovolaemic shock due to trauma and haemorrhage. Shock is usually described in four stages:

Stage 1: Vasoconstriction

Trauma or haemorrhage result in the sudden secretion

of catecholamines and other vasoactive substances which cause intense arteriolar vasoconstriction. However blood flow is maintained in vital organs, particularly the heart and brain. Sympathetic stimulation results in the well-known features of early shock such as the pale, sweating skin and rapid thready pulse.

Stage 2: Expansion of the vascular space

The generalised vasoconstriction causes the cells to become hypoxic and a metabolic acidosis ensues. As a result of oxygen demand from the tissues all capillaries open up resulting in a slowing of capillary perfusion which further aggravates the acidosis. The blood becomes hypercoagulable, and the viscera (lungs, liver, kidneys) are congested.

Stage 3: Disseminated intravascular coagulation

In late shock capillaries become blocked by clots and the blood may then become incoagulable resulting in oozing of blood from wounds even if sutured. Cells formerly nourished from the blocked capillaries start to die. Shock at this stage is resistant to treatment but is still reversible.

Stage 4: Irreversible haemorrhagic shock

It is never clinically certain when tissue death and necrosis have reached the point of no return, since death of cells begins as a local event and becomes progressive. Given that attempts at resuscitation are made, the capillary circulation may be restored since clots will be lysed by endogenous fibrinolysin. Depending upon the extent of necrosis "multiple organ failure" may result in death¹⁶.

Shock affects the major organs in different ways:

Heart

Myocardial depression is the main feature and is thought to follow myocardial ischaemia or the release of myocardial depressant factor from hypoxic pancreatic acinar cells.

Lungs

Shock respiratory distress syndrome results from pulmonary oedema and alveolar collapse. Although in early shock there is often a low PCO₂ and normal PO₂ due to hyperventilation, in severe cases the PO₂ may be low from the outset.

Kidneys

The kidney is very vulnerable to ischaemia since the renal blood flow is normally 25% of the cardiac output and during shock the renal blood flow and oxygen consumption fall markedly, particularly in the cortex. Urine output ceases when the arterial BP drops to 50 mm Hg. As renal perfusion falls so Na reabsorption is reduced in the tubules allowing Na loss into the urine. In severe shock acute renal failure may develop.

Liver

Liver damage is an early, common finding in shock and follows reduction in hepatic blood flow and oxygen consumption. Centrilobular necrosis is seen histologically.

With adequate resuscitation recovery of liver function is usual and persistent jaundice is a bad prognostic sign¹⁷.

III Resuscitation using hypertonic solutions

We have seen that significant advances in resuscitation techniques were made in both World Wars. It is easy to anticipate that in the event of a major conflict in the future there may be resupply problems with both colloids and whole blood. It is of interest therefore to review the small but valuable literature on the use of hypertonic solutions to resuscitate dogs and humans in severe shock (Stages 2-4). Three types of hypertonic solution have been used:

- (1) neutral saline (NaCl)
- (2) alkaline (NaHCO₃)
- (3) non-electrolyte (glucose or mannitol).

Mixtures have also been used.

(1) Brooks *et al*¹⁸

Brooks *et al*¹⁸ experimented on 39 dogs bled to a mean arterial BP 40 mm Hg giving acute haemorrhagic shock of 90 min duration. Dogs did not survive resuscitation with isotonic fluids, but survival was excellent after resuscitation with either 2.74% NaHCO₃ (325 mmol/l) or 1.8% NaCl (300 mmol/l). There was a small suggestion that NaCO₃ was better than NaCl; it has the theoretical advantage of correcting the metabolic acidosis of shock. 10% glucose (555 mmol/l) was found to be ineffective in dogs.

Brooks also gave a case-report on the use of a hypertonic IV fluid on a 72-year-old man with acute renal failure.

The composition of the fluid was:

NaHCO ₃	166 mmol/l
NaCl	75 mmol/l
Glucose	119 mmol/l
Total	360 mmol/l

(2) McNamara *et al*¹⁹

McNamara and his colleagues¹⁹ studied 31 Vietnam War combat casualties admitted to the US 24th Evacuation Hospital in hypovolaemic shock (arterial BP <90 mm Hg; pulse rate > 120/min). Their patients had already received conventional resuscitation en route including IV electrolytes and blood transfusion. They reported that 50% glucose, 1 ml/kg, injected IV over 45 sec gave the best results, with significantly sustained elevation in BP and pulse pressure. Blood lactate fell but blood pH altered little. Saline given as 3% NaCl (510 mmol/l), 2.7 ml/kg, or mannitol, 25% solution, 2 ml/kg, given as an equivalent osmotic load were both less effective than IV glucose; elevations in BP and pulse pressure occurred but were lower and of shorter duration.

(3) Jelenko *et al*²⁰

Jelenko and colleagues²⁰ resuscitated 12 civilian burns

casualties using two hypertonic solutions:

(1) NaCl	120 mmol/l
Na lactate	120 mmol/l
Total	240 mmol/l

- (2) As above, plus added albumin, 12.5 g/l.

Resuscitation was found to be more rapid and required lower volumes using solution (2), but the hypertonic electrolyte solution (1) was still superior to ordinary IV Ringer-lactate solution (130 mmol/l).

(4) de Felipe *et al*²¹

de Felipe and colleagues²¹ attempted to resuscitate 12 patients admitted to their intensive care unit at Sao Paulo in refractory shock (Stage 3-4). Patients had been in shock 5-22 h, had arterial hypotension (BP < 70 mm Hg) and had low or absent urine flow. Shock was reversed in 11/12 patients by giving 7.5% NaCl (1280 mmol/l), 100-400 ml IV, although three patients subsequently died. The immediate effects seen were a moderate rise in arterial BP, the resumption of urine flow, and recovery of consciousness. These effects lasted for several hours.

Discussion

It has been standard medical practice for the last 50 years to resuscitate shocked patients with IV isotonic electrolyte and colloid solutions, adding packed red cells or whole blood if the haematocrit falls to 30%. Trends in recent years have been to use compound Na lactate as electrolyte and polygeline as colloid in place of simple saline and Dextran. Polygeline is not mentioned in the 1981 Field Surgery Pocket Book²², although it was the colloid of first choice in the 1982 Falklands campaign¹⁵.

The wisdom of replacing IV saline (150 mmol/l) by compound Na lactate (140 mmol/l) can be questioned. Although intended to correct the metabolic acidosis of shock it will be least effective in the worst injured patients, since it requires an active liver to convert lactate to bicarbonate. It is now obsolete to give IV Na lactate in diabetic ketoacidosis; when correction of serious metabolic acidosis is necessary (arterial H⁺ greater than 100 mmol/l: pH less than 7.0) 50-100 mmol IV NaHCO₃ are given, with measurement of arterial blood pH to monitor the procedure³.

This paper was written primarily to suggest the use of hypertonic solutions to resuscitate severely shocked patients in any future major military conflict. There is insufficient evidence in the papers cited above to decide which of the various solutions used is the best. Saline alone is simplest and cheapest, and meets military requirements about availability under arduous field conditions, but the work of McNamara *et al*¹⁹ using 50% glucose (2.8 mmol/ml) would merit investigation if the opportunity arose. Brooks²³ commented that the strength of hypertonic solutions used by different workers is arbitrary, but that since isotonic electrolytes will have already been infused it would be logical to use stronger

solutions such as 10% sodium chloride. The best clinical results in the work reviewed above were obtained by McNamara et al¹⁹ and de Felipe et al²¹ using 50% glucose (2.8 mmol/ml) and 7.5% NaCl (1.3 mmol/ml) respectively.

The mechanism whereby hypertonic solutions produce a dramatic response in shock is presumably that they correct the almost isotonic shift of sodium and water from the extra-cellular fluid into the cells which is known to occur in haemorrhagic shock²⁴. Using ¹³¹I-albumin to measure plasma volume and ³⁵S-sulphate to measure extra-cellular fluid water Shires²⁴ was able to demonstrate quite clearly that in haemorrhagic shock the loss of extra-cellular fluid volume was much greater than the actual blood volume lost from the circulation. By measuring resting transmembrane potential (P.D.) in skeletal muscle cells Carrico et al²⁴ showed a fall in membrane P.D. accompanied by a fall in blood pressure and rise in extra-cellular fluid potassium concentration in haemorrhagic shock. The hypoxia of shock leads to impaired functioning of the Na/K-activated AT-Phase which controls Na transport; raising the plasma osmolality may help to correct the ionic shifts in "sick cells" and their surroundings.

It is likely that administration of hypertonic fluids will be most effective when first used and that repetition will bring a diminishing response. There is only a relatively small amount of water in the cells which can be "pulled out" over and above the entry in shock referred to above. In severe dehydration death occurs when about 12.5% body weight has been lost, equivalent to about 9 l water or 1/5th total body water in a 70 kg adult, but in this situation water is usually lost over several days. In acute haemorrhage death usually occurs if more than 3-4 l blood is lost without fluid replacement.

Since under field conditions a simple IV resuscitation regime is required it is suggested the two hypertonic solutions might be used in severe (Stage 2-3) shock. As a simple saline solution 12% NaCl containing 2.0 mmol/ml and given in 100 ml quantities would make for simplicity in recording therapy. A second solution to be considered is 8.4% NaHCO₃ which is generally available and contains 1 mmol/ml. Up to 50 ml could be safely given in severe shock without measurement of blood gases, but if these measurements were available more could be given if required. de Felipe et al²¹ gave up to 500 mmol NaCl as a 7.5% solution; 200 ml 12% NaCl and 50 cl 8.4% NaHCO₃ contain 450 mmol and would therefore be comparable therapy with the added advantage of helping to correct the acidosis of shock which has been recognised as necessary for over 150 years^{1,3}.

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THE ROLE OF ISOTONIC AND HYPERTONIC SOLUTIONS IN THE RESUSCITATION OF SHOCKED PATIENTS

From Col R Scott, L/RAMC, Professor of Military Surgery

The interesting paper by Colonel P J N Howorth brings to mind the discussions concerning the role of hypertonic solutions in the treatment of cholera victims.

This treatment was gradually given up in favour of isotonic saline and in a recent authoritative review Flear et al recommend isotonic rather than hypertonic solutions for the correction of salt depletion.²

Although the wounded soldier may be dehydrated, and in some areas may also be salt depleted, blood loss is the principal reason for the need to restore the circulatory volume. The biochemical changes following blood loss are so complex that it takes a chemical pathologist to

understand them; nevertheless military surgeons have been impressed by the value of replacement of lost blood by Ringer lactate solution, providing that it is not used in amounts in excess of 2 litres.

There may be logistic advantages in the stock-pile and use of hypertonic solutions and this is currently being investigated in the United States. We await the outcome of these investigations with interest but, in the meantime, we do not think that there should be any change in the resuscitation policy or in the holding policy for resuscitation fluids.

R SCOTT

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A Light Yellow Look at Purple Matters (Or a Weak Reply)

I find it surprising that you found the time
To sit at your desk and write verses in rhyme,
Instead of improving your plan so sublime
Yes you Sir, Sir Henry and Martyn!

In defining your plan, did you use tricks
To conjure the appropriate brown and blue mix,
Or did you resort to Jim Saville to fix?
Did you Sir, Sir Henry and Martyn?

But you can depend on us loyal men and true,
Whatever our Service or uniform's hue
To make Yellowlees work is what we will do
For you Sir, Sir Henry and Martyn.

To be in bright and early we will rise with the larks,
We'll rip into paperwork, like blood-frenzied sharks,
But why, why oh why didn't you leave us some clerks?
Yes you Sir, Sir Henry and Martyn.

We'll work out the answers to the tasks you foresaw
And to the ones that you didn't which comprise many
more,
Our letters will fly to Command, Fleet and Corps,
For you Sir, Sir Henry and Martyn.

To manage all three by one is a game,
So you say in your words, which tend to inflame,
But the languages used just are not the same,
Oh no Sir, Sir Henry and Martyn.

Appointers and posters, packs and files,
Heads and cabins, it goes on for miles,
To good humoured officers it causes large smiles!
Not you Sir, Sir Henry and Martyn.

The enjoyable part comes from the pleasures
Of finding staff matters that are absolute treasures
So that Pongos can tell Admirals and Air Marshals the
measures,
Ho ho Sir, Sir Henry and Martyn.

The commitment and toil of the tri-Service staff
Will ensure that it works, with perhaps the odd laugh!
(But don't turn your backs chaps, they'll cut us in half)
I mean you Sir, Sir Henry and Martyn.

Enough nonsense, there's plenty of work so infernal,
Though you found the time to write for the Journal,
Is this the way to Brigadier for a Colonel?
Much obliged for the lead sir, Sir Henry and Martyn.