In This Issue . . .

ARTICLES

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An Analysis of Osmolarity and Sodium Content

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Page 26
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INTRODUCTION

As the morbidity and mortality from the number one killer, namely disease of the blood vessels, continues to increase, many surgical and nonsurgical techniques offering a treatment of the affected individual have come and gone. The current surgical procedure in vogue is the multiple bypass surgery in the individuals with coronary artery disease while the medical therapy of choice involves nitrates, B-blockade and more recently slow channel physiological calcium blockers (Conn., 1981). There are, however, a number of doctors using an innovative medical treatment known as intravenous chelation therapy in which a number of infusions (approximately 30) of Disodium Ethylene Diamine Tetra-acetate (EDTA) are injected into the body. The patient is evaluated before and after for improvement in circulation to the heart and the affected limbs. Side effects are minimal in this therapy. It was felt by early researchers that use of EDTA could damage the renal tubules. However, a recently completed study (McDonagh, JHM, Fall, 1982) indicated that if used properly, it may actually improve renal function. Two transient side effects noted are some pain on injection (which can usually be corrected with additional magnesium chloride for injection) and mild peripheral edema. Most of the focus of attention on treatment protocol by individuals using this therapy is on what to add to the bottle. The purpose of this report is to examine the intravenous carrier solution along with the additives. Specifically, this report is designed to answer five basic questions:

1) What is the osmolarity of common intravenous infusions used in chelation therapy?

2) What is the sodium content of the intravenous infusions commonly used in chelation therapy?

3) What combination of additives plus intravenous solutions are best for patients in both 500 cc and 1,000 cc quantities?

4) What combinations of additives plus intravenous solutions are problems to critically ill patients especially those with coronary artery disease, tendencies to congestive heart failure and hypertension?

5) How can the physician compute easily, the approximate hypo- or hyper-tonicity to the fluids being used?

REVIEW OF THE LITERATURE

There is a myriad of papers in the literature that refer to chelation therapy but the main focus in these papers is the additives with only a few papers mentioning the carriers. The protocol for the chelation therapy published by the American Academy of Medical Preventives refers to "appropriate" carrier solutions being used.
including 0.5 Normal Saline, 5% Glucose, 10% Glucose, 10% Fructose and Lactated Ringers solution (AAMP, 1981). Perry and Schroeder in their investigation of cholesterol levels following EDTA used 5% Dextrose as carrier (Perry, 1955). Clarke in investigating occlusive vascular disease with EDTA used 5% Dextrose and Normal Saline as a carrier (Clarke, 1960). Kittrell in his study on the treatment of coronary artery disease with EDTA used Normal Saline and 5% Glucose as a carrier (Kittrell, 1963). Olwin in evaluation of plasma lipid levels in atherosclerotic patients following EDTA therapy used 5% Dextrose as a carrier solution (Olwin, 1968). In papers published by this author (McDonagh, 1981, 1982), the main carrier used in the earlier studies was 0.45% Sodium Chloride with Dextrose being used in patients with hypoglycemic tendencies. There are many other references to EDTA in the literature. The ones that report what carrier solution used (many do not) appear to use primarily 5% Glucose, and secondarily physiological Saline (0.9% Sodium Chloride).

### MATERIALS AND METHODS

As the subject of this paper is the computation and definition of a number of solution parameters as opposed to the collection of new data, it might be best for the reader to review and define terms as well as showing some of the basic calculations that were determined. Hence, the following are offered for the readers review:

**Osmolarity - \( O_s \)**

The amount of osmotic pressure exerted by 1 mole or gram formula weights (GFW) of ions is one liter of solution. If a mole of substance is composed on "N" ions, then the osmolarity of that solution is equal to N times the number of moles present.

\[
O_s = \frac{\text{Wt. of substance}}{\text{G.F.W.}} \times N
\]

The osmolarity of a solution calculated by the above equation is expressed in osmoles. Since most values are less than one, the more common unit is Milliosmoles in which

1 Osmole = 1,000 Milliosmoles.

**Osmolarity of Plasma**

For the purpose of this paper, all osmolarity calculations were based on the Physiological Saline (0.85% Sodium Chloride) which contains approximately 290 milliosmoles per liter. The osmolarity of the various carrier solutions used in this study are expressed in Table I.

**Absolute Osmotic Pressure**

The absolute osmotic pressure is the total pressure exerted by the ions in solution and it is this pressure that affects the red blood cells. The red blood cells will either swell and can burst (if solution is hypo-osmolar) or they may crenate (if solution is hyper-osmolar). The total or absolute osmotic pressure is due to both metabolizable and non-metabolizable substances in the infusion solution (Table II). In figures 1 through 5, the metabolizable osmolarity is depicted as stippled (dotted), whereas the non-metabolizable osmolarity is shown as non-stippled.

### TABLE 1

**Composition of Carrier Solutions**

<table>
<thead>
<tr>
<th>Volume</th>
<th>Sodium (Mg)</th>
<th>Sodium (MEQ)</th>
<th>Milliosmoles (Per liter)</th>
<th>Osmotic Yield (Absolute)</th>
<th>Osmotic Yield (Non-Metabolizable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextrose</td>
<td>500 cc</td>
<td>0</td>
<td>0</td>
<td>277</td>
<td>0.95</td>
</tr>
<tr>
<td>(5%)</td>
<td>1,000 cc</td>
<td>0</td>
<td>0</td>
<td>277</td>
<td>0.95</td>
</tr>
<tr>
<td>Dextrose</td>
<td>500 cc</td>
<td>0</td>
<td>0</td>
<td>555</td>
<td>1.91</td>
</tr>
<tr>
<td>(10%)</td>
<td>1,000 cc</td>
<td>0</td>
<td>0</td>
<td>555</td>
<td>1.91</td>
</tr>
<tr>
<td>Fructose</td>
<td>500 cc</td>
<td>0</td>
<td>0</td>
<td>555</td>
<td>1.91</td>
</tr>
<tr>
<td>(10%)</td>
<td>1,000 cc</td>
<td>0</td>
<td>0</td>
<td>555</td>
<td>1.91</td>
</tr>
<tr>
<td>Saline</td>
<td>500 cc</td>
<td>880</td>
<td>38</td>
<td>155</td>
<td>0.54</td>
</tr>
<tr>
<td>(45%)</td>
<td>1,000 cc</td>
<td>1,760</td>
<td>76</td>
<td>155</td>
<td>0.54</td>
</tr>
<tr>
<td>Saline</td>
<td>500 cc</td>
<td>1,760</td>
<td>76</td>
<td>310</td>
<td>1.08</td>
</tr>
<tr>
<td>(9%)</td>
<td>1,000 cc</td>
<td>3,520</td>
<td>152</td>
<td>310</td>
<td>1.08</td>
</tr>
<tr>
<td>Lactated</td>
<td>500 cc</td>
<td>1,500</td>
<td>65</td>
<td>290</td>
<td>1.00</td>
</tr>
<tr>
<td>Ringers</td>
<td>1,000 cc</td>
<td>3,000</td>
<td>130</td>
<td>290</td>
<td>1.00</td>
</tr>
<tr>
<td>Water</td>
<td>500 cc</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>Sterile</td>
<td>1,000 cc</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.00</td>
</tr>
</tbody>
</table>
The physician should closely read the Vitamin C (Ascorbic Acid) bottle as the fine print says pH adjusted with Sodium Bicarbonate or Sodium Hydroxide and at pH of 7.4 the Ascorbic Acid is in the form of Sodium Ascorbate to the extent of 95+%. In the graphs in Figs. 1-7, the following abbreviations are used: (1) KCl = 40 Meq. of Potassium Chloride; (2) MgCl₂ = Magnesium Chloride, 1 gram, equivalent to 5 cc of 20% Magnesium Chloride; (3) Vit. C = Sodium Ascorbate, 10 grams; (4) EDTA = 3 grams of Disodium Ethylenediamine tetra-acetate or 20 cc of a concentration of 150 mg/cc.

The two columns on the left in each figure represent osmotic yield or relative osmotic pressure on both 500 cc and 1,000 cc of solution respectively. The two columns on the right represent the sodium content in both 500 cc and 1,000 cc of solution. The dotted lines on the bar graph show the contribution of metabolizable substances to the osmolarity. The remainder of the ingredients are non-metabolizable. That portion of the bar graph containing multiple dots represents the influences of the carrier solution to both osmolarity and sodium content.

**DISCUSSION**

The data presented in Figs. 1-7 shows the problems and advantages of each carrier. We will consider the pros and cons of each fluid and the physician may decide the best solution suited for his patient.

**0.9% Sodium Chloride**

This solution is, basically historical (i.e. it was commonly available) and its use today should be the same (i.e. historical). One can see from Figure 1 that the sodium content is extremely high, especially when 1,000 cc is used (i.e. over 5 grams) and the osmolarity is over 1.6 even if 1,000 cc is used without Potassium Chloride. Hence, 1,000 cc is undesirable based on sodium content and the 500 cc is undesirable based on osmolarity. The use of this solution, especially in the hypertensive individual and in those individuals with congestive heart failure is not recommended.

**Ringers Lactate**

This solution starts out at the osmolarity and sodium content of plasma and any additives do precisely that - add to the sodium content and osmolarity as seen in Figure 2. These bottles contain anywhere from 3.0 to 4.6 grams of sodium slightly less than 0.9% Sodium Chloride, but slightly more than helpful. The osmotic yield is also 1.5 or greater depending on size so the same factors that make 0.9% Chloride undesirable also...
Figure 3.

Figure 4.

Figure 5.

Figure 6.
make the use of Ringers Lactate somewhat limited. There are pros and cons to Ringers Lactate that should be analyzed. On the positive side is the fact that some people feel Lactate also acts as a chelator in synergism with the EDTA - a contribution which is at the most, minimal. The major "con" to Ringers Lactate is illustrated in Table V, namely that Ringers Lactate contains 3 millimoles of calcium per liter and this effectively consumes a portion of the EDTA rendering it inactive even before infusion.

### TABLE V
**EDTA and Ringers Lactate**

<table>
<thead>
<tr>
<th>R.L. Contains 3.0 Millimoles Calcium</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 GM. EDTA Contains 8.9 Millimoles EDTA</td>
</tr>
<tr>
<td>34% Neutralization</td>
</tr>
</tbody>
</table>

30 Grams of Vitamin C in Ringers Lactate

This bottle became popular because many physicians, through a fear of potential nephrotoxicity which has been subsequently disproven (McDonagh, JHM, August, 1982), would give a bottle every 2nd, 3rd, or 4th treatment containing high doses of Vitamin C (also supposed to be a calcium chelator) and lactate, the two together thought to have chelating abilities of 10 to 50% of an EDTA infusion. The merits of this are not being decided but rather the sodium content and osmolality, which as noted in Figure 3, are the highest of any of the combinations. It is suggested that extreme caution be used with this particular combination, especially in the cardiac decompensated patient.

**0.45 Sodium Chloride**

Figure 4 illustrates one of the better sodium containing intravenous fluids available for chelation physicians. The 1 liter size is slightly high in sodium (about 3.3 grams) but the osmolality is almost perfect and by slightly reducing the Vitamin C to 7.5 grams (that currently used in the McDonagh protocol) one brings the sodium to under 3 grams and osmolality to 1.0 in the 1,000 cc size. The 500 cc size is, without Potassium Chloride, relatively low in sodium (less than 2.5 grams) and has an osmotic yield of about 1.7. This solution can be used safely in chelation therapy, however, precautions in the severely hypertensive and/or cardiac decompensated patient must still be considered.

**5% Dextrose**

This solution, as can be seen in Figure 5, has many merits. The sodium content is in the range of 1.5 grams, independent of bottle size, making it a highly desirable fluid. If the 500 cc size is used with Potassium Chloride, the osmotic yield is over 2.5 of which 1.2 to 1.6 units are due to non-metabolizable constituents. Hence, one should not have a problem with this solution unless it is infused too fast. It is recommended that this bottle be infused in no less than the 3 hour time period due to its high osmolality. The Dextrose solution, as did Ringers Lactate, has other pros and cons. First, it is a sugar and one infuses 25 gm. or 50 gm. I.V. in 500 cc and 1,000 cc size respectively. Diabetics, especially juvenile onset ketogenic types, may not handle this sugar well. Adult type diabetics may get a hyperglycemic response, but it is probably not acutely detrimental. Some physicians feel Dextrose is contra-indicated in hypoglycemics but the infusion of 10-15 grams of Glucose per hour is probably not enough to develop more than a marginal insulin response and this may be the bottle of choice in the hypoglycemic individual. This bottle can be used safely in both sizes.

**10% Fructose**

This solution was popular 3-5 years ago because many physicians felt that since fructose did not elicit a major insulin response and made simple carbohydrate available to the brain, that this had the potential of being the fluid of choice in chelation therapy. A metabolic problem
encountered in the use of Fructose is that it is rapidly metabolized and when such a large quantity is introduced (1 liter contains 100 grams of Fructose) there is rapid conversion to triglycerides which can cause rolesque formation in the red blood cells making it difficult for them to penetrate small arterioles resulting in angina in the patient with coronary artery disease. The Frederickson Type IV individual should probably not receive Fructose, especially if severe coronary artery disease is present. Additionally, as seen from Figure 6, Fructose has merit in the fact that it is very low in sodium. In the 500 cc size, however, it is the most hyperosmolar solution used and should be infused very slowly.

10% Dextrose has the same osmotic properties as 10% Fructose but differing metabolically in that it is less of a tendency to elevate plasma triglycerides. It has more tendency to give problems to juvenile diabetics and possibly hypoglycemic patients since the glucose infusion rate for a 3 hour bottle would be 30-35 grams/Hr.

Sterile Water

In the past, sterile water has been used on a limited basis as the carrier solution when chelating patients, but there are several qualities which, as seen in Figure 7, truly make it the bottle of choice, especially in the 500 cc size. Both bottle sizes have less than 2 grams of sodium. The 500 cc size without Potassium Chloride is almost isotonic with plasma. The 1,000 cc size tends to be somewhat hypotonic and if the patient is hyponatremic due to diuretics or for other reasons the 1,000 cc size is not advisable. The 1,000 cc size may, by adding either 20 or 40 meq of Potassium Chloride, an additional 2 to 5 grams of Vitamin C, and/or 10 grams of Glucose, be the best liter sized bottle available.

SUMMARY

From the data presented in Figures 1 through 7, the following conclusions can be reached:
1. Use of Normal Saline should be avoided.
2. Use of Ringer's Lactate should be avoided.
3. Sugar solutions should be infused slowly due to their high osmolarity.
4. When using sugar solutions, metabolic aberrations of carbohydrate and fat metabolism should be evaluated.
5. 0.45% saline can be used effectively but should be used cautiously in hypertensive or cardiac decompensated patients.
6. Sterile water is the best vehicle in the 500 cc size with regular additives.
7. Sterile water should be used with caution in the 1,000 cc size as it is hypo-osmolar, a phenomena corrected by adding Glucose, Potassium Chloride or additional Vitamin C.

The author would like to thank the editors of IAPM for considering this because, although it is not original research, it is information vital to the care of patients undergoing this mode of cardiovascular therapy.

REFERENCES


