
Is Commercially Prepared Albumin Excreted Through the Kidneys?

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Introduction

Unexplained volume loss during cardiopulmonary bypass is a commonly observed phenomenon. A common belief is that the volume loss may be attributed to a reduction in plasma albumin levels thus causing a fluid shift from the vascular to the extra vascular compartments.

The hypothesis is that commercially prepared albumin is denatured or otherwise altered during preparation such that it is rapidly excreted through the kidneys creating a reduction in plasma osmotic pressure and resultant "third spacing."

This study was undertaken in an attempt to determine if significant quantities of albumin did exist in the urine and, if so, at what rate the albumin depletion did occur.

History

Methods of purifying and crystallizing albumins in concentrated salt solutions were introduced during the last century by Hoppe - Seylor and Hofmeister and were later perfected by Hopkins and Sorensen. Through the work of Hopkins and Sorensen, it was noted that proteins may be precipitated-out not only by "salting-out"; but also by the addition of alcohols, acetone or other water-miscible organic solvents to their solutions. However, it was noted such additions at ordinary temperatures generally lead to protein denaturation⁽²⁾.

In 1947, new conditions for protein fractionation in alcohol-water mixtures at low temperatures were introduced by Edwin J. Cohn⁽³⁾⁽⁴⁾⁽⁵⁾. Under these conditions protein denaturation was minimized. It is this

method that has gained wide acceptance and is used by many manufacturers today.

Under normal conditions as much as 30 grams of protein filter into the glomerulus of the kidney each day. This would be a great metabolic drain on the body if the protein were not returned to the body fluids. The protein molecule is reabsorbed in the proximal tubule of the kidney, by a process known as pinocytosis. Consequently, the appearance of a protein such as albumin in the urine would indicate signs of renal disease and/or a systemic disorder⁽⁶⁾⁽⁷⁾.

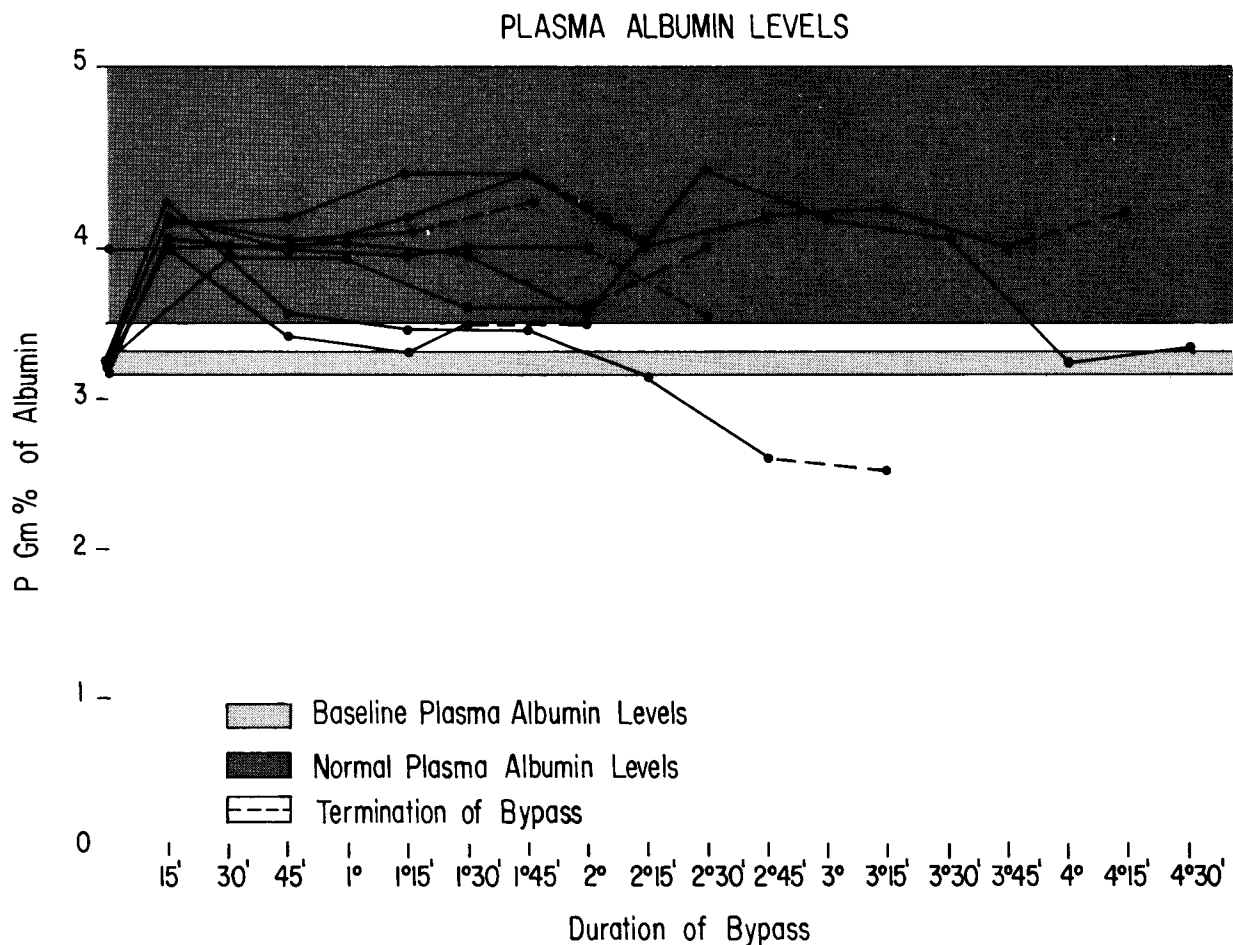
Methodology

Ten male patients, between the ages of 45 and 68 years were subjected to cardiopulmonary bypass. This was accomplished with the aid of the Travenol* TMO Oxygenator on eight of the patients, and the Shiley** Bubble Oxygenator on the remaining two patients. The pump priming solution was rendered iso-oncotic by the addition of salt-poor albumin to a concentration of 5 gm%. The duration of bypass varied from the shortest time of one hour and thirty minutes to the longest time of four hours and thirty minutes. Baseline blood and urine samples were drawn to determine plasma and urine albumin levels. Bypass blood and urine samples were drawn fifteen minutes after the initiation of bypass, every half hour thereafter, and thirty minutes after termination of bypass.

Whole blood additions were dependent upon the patient's hematocrit and fluid volume in the extracorporeal circuit. The minimum amount of whole blood

*Travenol Laboratories, Artificial Organs Division, Deerfield, Ill.

**Shiley Laboratories, Santa Ana, CA 92711



given to the patient during bypass was two units, the maximum being nine units.

Additional crystalloid volume during bypass varied from 750 ml to 2 liters. All of which was rendered iso-oncotic by the addition of salt-poor albumin to a concentration of 5 gm%.

A quantitative assay using Bromocresol Green Reagent and a Beckman BC-G Spectrophotometer was used to determine plasma and urine albumin levels. Each sample was measured three times, yielding a coefficient variation of .003%⁽¹⁰⁾.

Results

Studies to date revealed 90% of the patients studied had baseline plasma albumin levels ranging from 3.18 gm% to 3.38 gm%. The normal range of plasma albumin levels being 3.5 gm% to 5 gm%⁽⁶⁾.

The majority of the patients' plasma albumin levels were maintained above baseline and/or within normal ranges for the duration of bypass. However, one patient

did show a drop in his plasma albumin level to 2.6 gm% after two hours and forty-five minutes into bypass. The patient maintained this level through the termination of bypass.

Findings thus far indicate that patients receiving commercially prepared albumin show no significant amount of albumin in the urine during cardiopulmonary bypass. Of the aforementioned patients 50% received diuretic therapy consisting of mannitol and/or furosemide. This appeared to have no effect on the urine albumin levels which were virtually nonexistent.

Discussion

Results of the data to date may indicate that the loss in oncotic pressure caused by hemodilution during cardiopulmonary bypass is regained by the addition of salt-poor albumin to the priming solution at a concentration of 5 gm%⁽⁶⁾.

It would appear that by using commercially prepared albumin in the aforementioned concentrations, the

priming solutions sustain the osmotic integrity of the blood.

Other preliminary findings demonstrate that following the administration of commercially prepared albumin, there were no significant levels of albumin present in the urine.

Of substantial interest is the one patient whose plasma albumin level revealed a marked decrease, but whose urine albumin level remained unchanged. By itself this finding is significant enough to warrant further investigation. The albumin was not excreted through the kidneys, but what caused the reduction in the plasma albumin levels? Is commercially prepared albumin denatured or altered such that it is rapidly broken down into its amino acids and readily metabolized, or could commercially prepared albumin be altered such that it freely crosses the capillary membrane and is eventually consumed by the lymphatic system, thus causing a reduction in plasma albumin levels? At this point in time, it is difficult to substantiate what caused the reduction in the plasma albumin levels, we can only speculate.

Commercially prepared albumin has been shown to be an effective protein compound for the reduction of platelet adhesion and protein denaturation and has been used clinically in the priming solutions of extracorporeal circuits⁽⁸⁾⁽⁹⁾⁽¹¹⁾.

Summary and Preliminary Conclusions_____

Due to the limited number of patients studied thus far, we have not been able to totally disprove the orig-

inal hypothesis. In analyzing the data to date it does not appear premature to state that commercially prepared albumin is not excreted through the kidneys. Due to the many variables affecting plasma albumin levels and our lack of clinical data, we can only state that commercially prepared albumin appears to remain in the vascular compartments. We are hoping that future studies will provide more data to disprove the hypothesis as has been indicated by studies done thus far.

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