Original Article

An Evaluation of Three Methods for Determining Colloid Osmotic Pressure

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ABSTRACT

Plasma colloid osmotic pressure (COP) is an important determinant in edema formation. Three methods for assessing the COP were evaluated. Direct measurement of COP using the 4420 Wescor Colloid Osmometer was compared to the estimation of COP from both serum total protein and total serum solids (TSS) determinations. Blood samples from twenty adult patients (mean age = 64 years) undergoing cardiopulmonary bypass surgery were collected for COP assessment. Sample collection was performed prior to heparinization/hemodilution, during hypothermic bypass and at the conclusion of bypass following protamine administration. The results obtained from each method were analyzed by a two-way analysis of variance. The Bonferroni technique was used for comparison of sample means when the difference was significant ($p<0.05$). Correlations were reported by linear regression analysis. A statistically significant difference ($p<0.01$) was found between the three methods. A regression equation for the estimation of COP from total serum solids is offered:

$$COP = (3.02 * TSS) + 0.65.$$

Prospective clinical testing between the direct COP measurement and the estimation of COP from TSS using the equation (n=38) revealed a significant correlation ($R2 = .932$) and no significant difference between the two ($p > 0.05$).

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INTRODUCTION

Many patients undergoing cardiopulmonary bypass surgery experience a decrease in circulating blood volume and an increase in extracellular fluid volume during the early postoperative period (1). Rapid shifts of fluids between body compartments can lead to the development of edema, particularly pulmonary edema. (2).

In 1896, Starling identified colloid osmotic pressure (COP) as the primary force opposing capillary hydrostatic pressure for maintaining normal fluid distribution between the intravascular and extravascular compartments (3). The Starling equation states:

$$\text{Fluid Movement} = K\,(P_c + \pi_{if} - P_{if} - \pi_{pl})$$

where:

K= is the filtration coefficient in ml/sec/cm^2/mmHg

P_c=is the capillary hydrostatic pressure in mmHg

π_{if}=is the interstitial fluid COP in mmHg

P_{if}=is the interstitial hydrostatic pressure in mmHg

π_{pl}=is the osmotic pressure of plasma proteins (COP) in mmHg

The effect of plasma COP in edema formation and absorption was studied in 1937 by Kerkoff (4). The purpose of his study was twofold: to determine normal plasma COP levels in the adult population and to identify the critical COP level at which edema was present. Kerkoff determined the normal colloid osmotic pressure to be 21.4 ± 2.5 mmHg and found whenever edema was present the COP was always lower than 15 mmHg and when the COP = 16 mmHg or greater , edema was absent.

Direct measurements of colloid osmotic pressure, in the past have proven to be cumbersome and unreliable (5). Regression equations have been derived to estimate the plasma COP from total protein concentrations. The COP is determined by the concentration of plasma proteins. In a steady state at physiologic pH, one gram of protein retains approximately 15 ml of fluid in the intravascular space and the COP can be derived from the van't Hoff's theory and the Donnan effect (6). Marty, Prather and Matloff studied the oncotic effect of albumin , dilutional cardiopulmonary bypass and diuretics and derived an equation using the total protein to estimate COP (7).

$$\text{COP} = 4.57 \bullet \text{total protein} + 0.19$$

Total serum solids (TSS) measurements by the refractometer method are a direct reflection of serum proteins. The ease and availability of this methodology has prompted other investigators to determine the correlation between TSS values and COP (8). Wu and associates found good correlation when predicting COP from TSS levels. They reported the reference range for infant plasma COP to be 17.4 ± 0.4 mmHg. Whole blood colloid osmotic pressure reference ranges for infants have been reported as 16.1 ± 3.1 mmHg (9). Beshere, Camerlengo and Dearing reported a regression equation when describing the relationship between COP and TSS (10).

$$\text{COP} = (3.32 \bullet \text{TSS}) - 2.0$$

Morissette and associates used a modification of the osmometer described by Prather, et al, (11) to re-evaluate the expected values of COP in adults. This study took such variables as age, sex, temperature, pH and the patient's health status into consideration when evaluating the correlation of the calculated COP versus directly measured values. Their study showed poor correlation between the two. The authors attributed the poor correlation to the lack of proportional changes in protein and salts, as well as the interaction between proteins. In agreement with other investigators, this group regarded the direct measurement of COP as the only option in instances where quantitative measurement of COP is considered to be important (12).

Perfusion protocols for the management of patients during cardiopulmonary bypass at the Medical University of South Carolina include the estimation of colloid osmotic pressure using the American Optical Refractometer[a] for TSS determinations. The estimated post-dilutional COP derived from the "Beshere" formula should be 15 mmHg for pediatric patients. For adults, the COP value is subject to faculty intervention and albumin is often added to the prime if the value is estimated to fall below 12 mmHg (Riley JB, Bishop DB, et al. MUSC/Extracorporeal Technology Dept. Perfusion Protocols).

The development of the Wescor Colloid Osmometer[b] allows for rapid determination of either plasma or whole blood colloid osmotic pressure. The instrument directly measures the COP of solutions using a flow-through membrane system which is selectively impermeable to protein molecules. The membrane separates the specimen solution (in the sample chamber) from the reference solution (0.9% NaCl) located in the reference chamber. When the protein containing solution is placed in the sample chamber there is a net migration of water molecules and diffusable solute ions from the reference chamber into the sample chamber. The resultant negative pressure in the reference chamber is sensed by the pressure transducer. The signal from the pressure transducer is converted directly to millimeters of mercury (mmHg), centimeters of water (cmH_2O) or kiloPascals (kPa) (Wescor 4420 Colloid Osmometer Instructions for Use: Wescor Inc., Logan, Utah).

This study was undertaken to compare the whole blood colloid osmotic pressure measurements of the Wescor Osmometer to the calculated COP from the total protein and total serum solids measurements. The null hypothesis states: there is no difference between the TSS estimated COP, total protein estimated COP and directly measured whole blood colloid osmotic pressure in patients undergoing cardiopulmonary bypass procedures.

a American Optical Company, Buffalo, NY 14240

b Wescor Inc., Logan, Utah 84321

Figure 1
Direct COP vs. Event
Cold CPB = hypothermic cardiopulmonary bypass; COP = colloid osmotic pressure; POST-CPB = after termination of cardiopulmonary bypass; PRE-CPB = prior to CPB

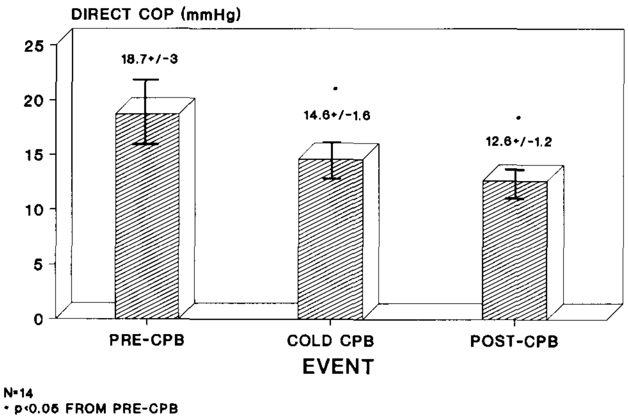
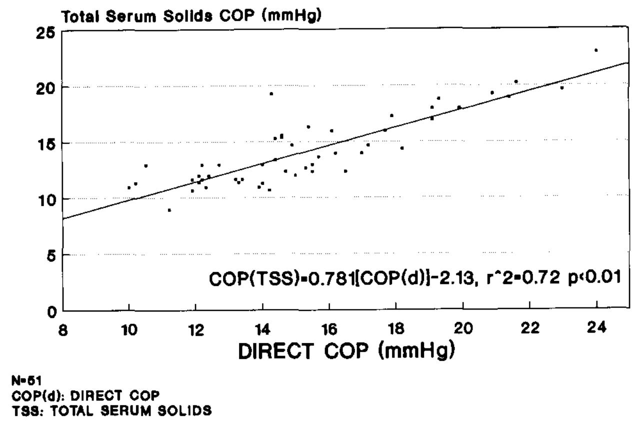


Figure 2
COP (TSS) vs. Direct COP
COP = colloid osmotic pressure; COP(d) is the directly measured colloid osmotic pressure; COP(TSS) = the colloid osmotic pressure estimated from total serum solids; TSS = total serum solids



MATERIALS AND METHODS

Two ml of non-heparinized blood were collected from patients undergoing cardiopulmonary bypass surgery prior to hemodilution or heparinization, five minutes after the initiation of bypass, and following protamine administration. Six hundred microliters of whole blood were transferred to a heparinized (green) microcontainer bullet[c] and sent to the Chemistry Laboratory for total Protein analysis on the Beckman Chemistry Analyzer[d].

One hundred-fifty microliters of whole blood were placed in two heparinized capillary tubes and sealed with clay. The tubes were centrifuged for 3 minutes and the plasma collected for TSS measurements using the AO Refractometer[a]. Each TSS measurement was performed in duplicate. The refractometer was calibrated daily using distilled water and 0.9% NaCl.

Three hundred-fifty microliters of whole blood were placed into the 4420 Colloid Osmometer for direct measurement of the colloid osmotic pressure. The instrument was calibrated according to manufacturer's recommendations.

Values obtained from each determination were recorded on the data collection sheet. The regression equation used by Marty, et al, was employed to estimate the COP from total protein measurements (7). The equation for determining the COP from TSS measurements was the one reported by Beshere and associates (10).

Differences between the groups were determined using two-way analysis of variance. Differences in sample means were determined using the Bonferroni Method ($p<0.05$). A total of 51 determinations were made based on a=0.05, b=0.20 and a power of 80%.

Correlations between the three methods were calculated and a new regression equation for the estimation of COP from total serum solids is offered.

Values obtained using the new regression equation for the estimation of COP from TSS determinations were compared with the directly measured COP (n=38). Sample means were compared using the paired t-test.

c Becton-Dickinson, Rutherford, New Jersey 07070
d Beckman Instruments Inc. Healthcare Products, Brea, CA 92621

RESULTS

The direct colloid osmotic pressure measurements read 1.2 mmHg higher ($p<0.05$) than the estimation of COP based on total serum solid measurements during all phases of bypass. The COP estimation from the laboratory total protein values was 4 mmHg higher than the direct measurement during all phases of CPB ($p<0.01$). The COP estimation from the total protein results averaged 5.2 mmHg higher ($p<0.01$) than the calculated COP from total serum solids.

Figure 1 represents the direct measurement of colloid osmotic pressure during the three phases of cardiopulmonary bypass. A significant decrease in COP exists between each phase ($p<0.01$). The colloid osmotic pressure varied from a baseline mean of 18.7 ± 3.0 mmHg to a mean of 14.6 ± 1.6 mmHg during hypothermic bypass. The post-protamine measurements decreased to a mean of 12.6 ± 1.24 mmHg.

Figure 2 illustrates the comparison of the current clinical practice of estimation of COP from total serum solids using the "Beshere" method and the actual measured colloid osmotic pressure. A significant difference between the two methodolo-

Figure 3
Direct COP vs. TSS
COP = colloid osmotic pressure; TSS = total serum solids; COP(d) = direct measurement of colloid osmotic pressure

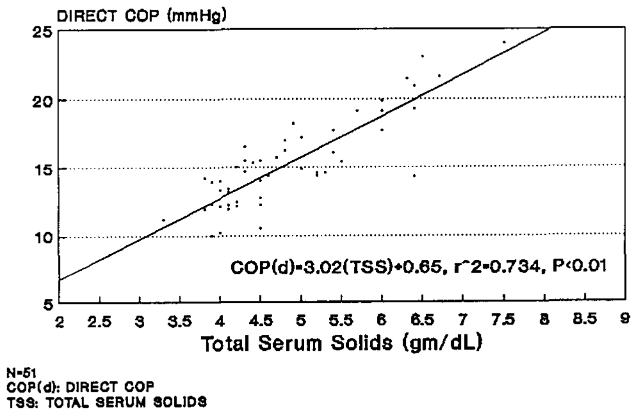
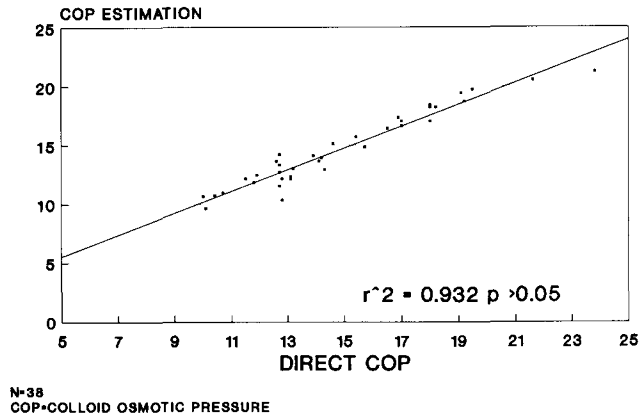


Figure 4
Direct COP vs. COP Estimation
COP = colloid osmotic pressure



gies was discovered ($p<0.01$).

Figure 3 demonstrates the relationship between total serum solids and the values obtained by direct measurement of COP. A new regression equation for the estimation of the colloid osmotic pressure from serum solids is reported.

$$COP = (3.02 * TSS) + 0.65$$
$$R^2 = 0.734 \quad p<0.01 \quad N = 51$$

Figure 4 confirms the relationship between the directly measured COP and the values obtained from TSS estimation using the new regression equation.

$R^2 = 0.932$
$p < 0.01$
$N = 38$

Patient Demographics

Age	64 ± 11.6 yr
Weight	80 ± 14 kg
Arterial pH	7.433 ± 0.054
Hematocrit	32.95 ± 5.7
% Male	75%

DISCUSSION

Many investigators regard the direct measurement of colloid osmotic pressure superior to estimation in instances where quantitative measurement of COP is considered to be important. In this study, we found the use of the osmometer to be time consuming and often labor intensive. The instrument did not perform consistently and often required additional sample to reach plateau. This is a major disadvantage where infant and pediatric patients are concerned. Twenty microliters of serum was sufficient for TSS determinations used in the calculation of COP. This method is inexpensive and requires little equipment maintenance.

Currently, we clinically use COP estimation based on TSS determinations as our standard of care. Based on these results our clinical practice underestimates the colloid osmotic pressure in adults before, during and after cardiopulmonary bypass. The established protocol of the addition of 25% albumin to the bypass circuit when the COP falls below 12 mmHg in adult patients and 16 mmHg in pediatric patients results in an additional $135.00 charge to the patient. The use of the Beshere method of COP estimation may add unjustified charges to patient.

We recommend the use of the new regression equation for COP estimation based on total serum solids. The new regression equation more accurately represents the actual colloid osmotic pressure. The estimation of COP provides the perfusionist with a rapid and true depiction of the oncotic pressure.

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