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# In-Vitro Evaluation of the Hemolytic Effects of Augmented Venous Drainage

Randall K. Mathews BS, CCP; Joseph J. Sistino MPA, CCP

*Extracorporeal Circulation Technology Program, College of Health Professions, Medical University of South Carolina*

**Abstract:** Augmentation of venous drainage with either kinetic-assisted drainage (KAVD) or vacuum-assisted (VAVD) has been used clinically in order to overcome added venous resistance due to smaller venous cannulae or tubing. This in-vitro study evaluates the extent of hemolysis and sub-lethal red blood cell membrane damage than occurs with augmented (kinetic or vacuum) when compared to conventional gravity drainage. Four trials were conducted using each test circuit. The circuits were primed with 6 liters of fresh heparinized bovine blood, which was diluted to a hematocrit of 32% and was recirculated at 5 L/min for 8 hours. Hemolysis was determined by the change in plasma free-hemoglobin (Hb), hematocrit, and potassium at two hour intervals. The red cell osmotic fragility index was used to quantify the sub-lethal red blood cell membrane damage and was also measured every two hours. After 8 hours, the mean +/– SD of the plasma free-Hb were: 96.27 +/– 69.45 mg/dl for gravity, 83.87 +/– 48.14 mg/dl for vacuum-assist, and 134.45 +/–83.78 mg/dl for kinetic-assist. Two-hour increases in the plasma free-Hb revealed the following median values (mg/dL/2h): 16.90 for gravity, 13.75 for vacuum–assist, and 19.40 for kinetic-assist.

Analysis of the two-hour increases in plasma free-Hb with Kruskal-Wallis One-Way ANOVA did not reveal a significant difference among the groups. After 8 hours, the red cell osmotic fragility test results at the 0.55% sodium chloride concentration were compared. The medians of the percent hemolysis were 52.67% for gravity, 49.8% for vacuum-assist, and 57.2% for kinetic-assist. Analysis with the Kruskal-Wallis Wallis One-Way ANOVA did not reveal a significant difference among the groups. Therefore, there is no significant increase in hemolysis or sub-lethal red blood cell membrane damage associated with the use of augmented venous drainage. **Keywords:** vacuum-assisted venous drainage (VAVD), kinetic-assisted venous drainage (KVAD), centrifugal pump, gravity venous drainage. *JECT. 2001;33:15–18*

Perfusionists have been challenged to maintain adequate venous drainage from patients when smaller venous cannulas are used during minimally invasive and reoperative heart surgery. Both kinetic-assisted (KAVD) venous drainage, (2-6) and recently vacuum-assisted (VAVD) (1), have been incorporated into the cardiopulmonary bypass (CPB) circuits to overcome the added resistance of the smaller venous cannulae and tubing. Flows of up to 5.7 liters per min (LPM) have been achieved with augmented venous return (3-5).

When red blood cells are exposed to strong shear forces (7) such as negative pressure during blood salvaging (9-11) or when blood contacts CPB devices (8,10), damage to red blood cells produces an increase in red blood cell fragility and hemolysis. Hemolysis releases free hemoglobin into the plasma portion of the blood. Plasma free-hemoglobin levels increase when the haptoglobin, which binds free hemoglobin, becomes saturated.

Address correspondence to: Randall K. Mathews, BS, CCP, Memorial Hospital, 2525 DeSales Avenue, Chattanooga, TN 37411, respfusion@aol.com
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The free hemoglobin in the plasma is then filtered by the kidney, reabsorbed by the proximal renal tubular cells, and broken down into iron, globin, and porphyrin moieties.

Hemoglobinuria occurs when the capacity of the renal tubule is exceeded. The hemoglobin then combines with the Tamm-Horsfall protein, which precipitates out in the distal tubules forming casts (8,12). These hemoglobin-Tamm-Horsfall casts can cause blockage of the distal tubule, proximal tubular necrosis, and acute renal failure (8).

Hemolysis also causes a release of potassium into the plasma. A significant increase in serum potassium can induce electrocardiogram irregularities such as t-wave abnormalities and can lead to cardiac arrest. Therefore, hemolysis is an important consideration in the design of new CPB techniques and devices.

With the use of augmented venous drainage, additional negative pressure is applied to the venous blood, which may increase red cell damage. The rate of hemolysis was measured in order to determine if augmented venous drainage (kinetic or vacuum) causes more damage than standard gravity venous drainage.

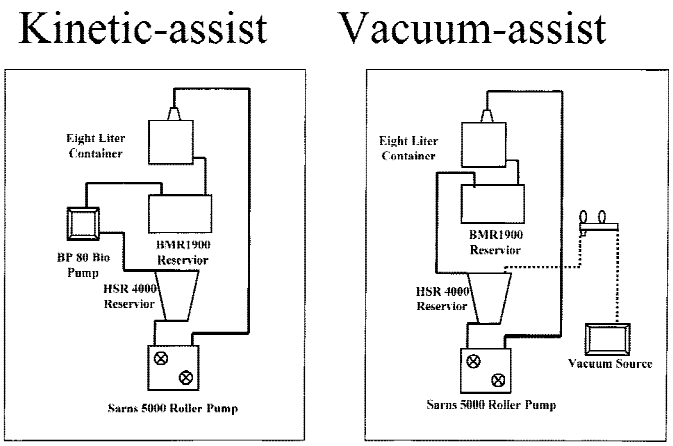


**Figure 1.** Kinetic assist and Vacuum assist diagram.

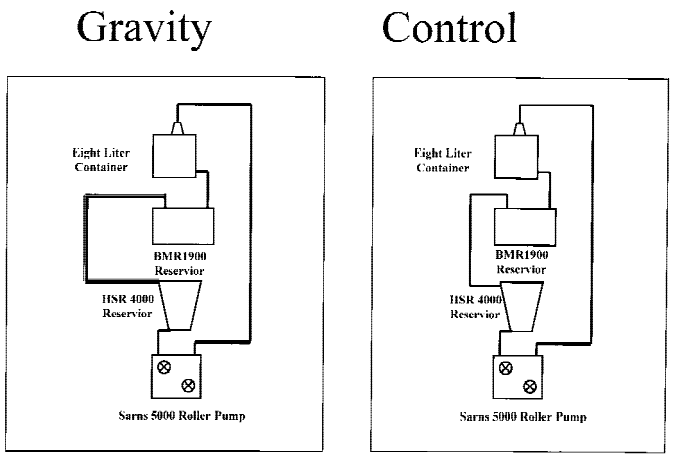


**Figure 2.** Gravity and control diagram.

## MATERIALS AND METHODS

Four in-vitro CPB circuits were designed to test plasma free-Hb levels, potassium levels, hematocrit, and osmotic fragility during recirulation. Four trials were run using each of the following in-vitro circuits. Each of the four CPB circuits was set up using a roller pump console (Sarns 5000, Terumo-Sarns Healthcare Corp., Ann Arbor, MI), a 1/2″ arterial pump head, a venous reservoir (HRS 4000 and BMR 1900, Jostra-Bentley Division, Irvine, CA), a 3/8″ arterial line, and an 8-liter plastic container. The venous reservoir bag was used to simulate the right atrium of the heart, while an 8-liter plastic container with a 1/2″ outlet was used as the primary volume reservoir. The venous reservoir bag was placed 24 inches above the inlet to the lower venous reservoir. The 1/2 inch venous line of the control circuit was connected directly to the venous reservoir without a venous cannula for venous drainage.

The first test circuit, which was used for gravity drainage, incorporated a 6 foot long 1/2″ diameter polyvinyl chloride tubing connected to a TAC2 Model # 92348 two-stage 34/48 Fr venous cannula (Medtronic-DLP Inc., Grand Rapids, MI). The second circuit incorporated the vacuum-assisted venous drainage system with 6 feet of 3/8-inch diameter polyvinyl chloride tubing connected to a FLEX11022 22Fr venous cannula designed specifically for vacuum-assist (Jostra-Bentley Division, Irvine, CA). The third circuit using kinetic-assist, incorporated a 6 foot long 3/8 inch diameter polyvinyl chloride tubing venous line with a BP-80 centrifugal pump (Medtronic-Biomedicus, Eden Prairie, MN) inline connected to another FLEX11022 22 Fr venous cannula (Baxter Research Medical, Inc., Midvale, UT) (Figs. 1 and 2). The fourth circuit was used to determine the amount of hemolysis produced by the roller pump returning blood to the upper reservoir. A pressure monitor (Medtronic-DLP Inc., Grand Rapids, MI) was placed in the venous line to measure negative pressure.

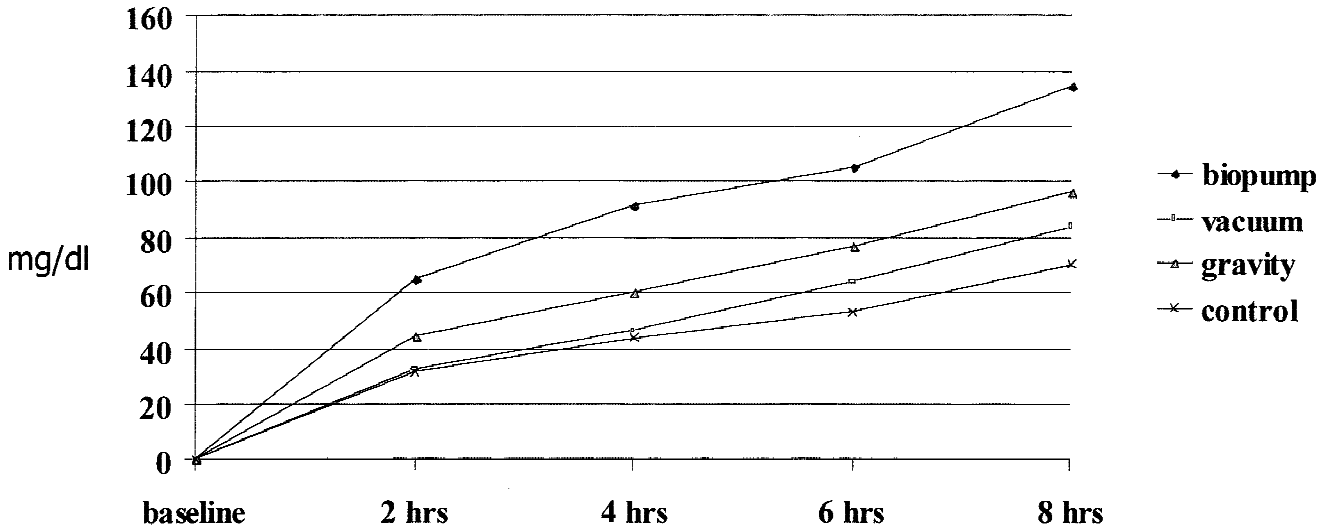


**Figure 3.** Plasma-free hemoglobin (n = 4).

**Table 1.** Mean plasma-free hemoglobin after 8 hours.

| | Mean | SD |
|---|---|---|
| Gravity | 96.27 | 69.45 |
| Vacuum-assist | 83.87 | 48.14 |
| Kinetic-assist | 134.45 | 83.78 |
| Control | 70.15 | 19.86 |

Corrected for baseline plasma free hemoglobin level (n = 4).

**Table 2.** Median two-hour increases in plasma-free hemoglobin

| | Median |
|---|---|
| Gravity | 16.90 |
| Vacuum-assist | 13.75 |
| Kinetic-assist | 19.40 |

**NS**
One-way ANOVA

(n = 4)

Each circuit was primed with 6 liters of fresh (<3 hours), heparinized (8,000 units/liter) bovine blood which was filtered through a 40 micron cardiotomy reservoir, then diluted to a hematocrit of 32% with normal saline. The blood was circulated at 5.0 ± 0.2 L/min for 8 hours. Blood samples were taken at two-hour intervals for plasma-free hemoglobin, hematocrit, potassium, and determination of the red cell osmotic fragility index (Becton Dickinson Inc., Franklin Lakes, NJ).

The median values for the each two-hour increase in plasma-free hemoglobin levels were calculated after correcting for the initial plasma-free hemoglobin level and the hemolysis generated by the control roller pump circuit. These were compared using Kruskal-Wallis one–way analysis of variance (ANOVA).

The red cell osmotic fragility test results using 0.55% sodium chloride concentration were compared for the three groups. These median values of the percent hemolysis at the 0.55% sodium chloride concentration were also compared using Kruskal-Wallis ANOVA.

## RESULTS

Pressure in the vacuum-assisted venous drainage system ranged from –75 to –78 mm Hg and in the kinetic assist drainage system, the pressure measured –88 to –97 mm Hg at 5 L/min of blood flow.

The hematocrit during the 8 hours ranged from 30% to 32%, while the serum potassium levels remained within the normal range throughout each of the four trial runs (3.8mEq/L, 2.7 mEq/L, 3.0 mEq/L, 4.6 mEq/L).

The results for 8 hour plasma-free Hb are shown in Figure 3 and Table 1. There was no statistically significant difference among plasma hemoglobin levels.

Two-hour analyses of the plasma free hemoglobin are shown in Table 2. This includes the hemolysis generated by the control pump. Analysis after correction for initial plasma free-hemoglobin levels did not reveal a significant difference among the three groups.

After correcting for the initial plasma-free hemoglobin level and the hemolysis generated by the control roller pump circuit, the mean values for the 2 h plasma-free hemoglobin levels were: kinetic-assist 16.07 ± 26.65 mg/dL, vacuum-assist 3.43 ± 13.95 mg/dL, gravity 6.53 ± 18.16 mg/dL. There was no significant difference found among the three groups. Correction for baseline was done due to the wide range in baseline plasma free-hemoglobin levels (30.8 mg/dL, 20.7 mg/dL, 39.7 mg/dL, and 75.5 mg/dL for the 4 trials).

At 8 hours, the red cell osmotic fragility test results using 0.55% sodium chloride concentration were compared (Fig 4). The median values of the percent hemolysis at the 0.55% sodium chloride concentration were 52.66% for gravity, 49.8% for vacuum-assist, and 57.23% for kinetic-assist. Analysis of the red cell fragility data did not reveal a significant difference among the three groups.

## DISCUSSION

This in-vitro comparison of augmented (kinetic or vacuum) against gravity drainage reveals there is no significant additional hemolysis or sublethal red cell injury using either of these techniques. This experiment was conducted in a controlled environment with no changes in flow rates or pressures. Negative pressure was controlled when using VAVD due the negative pressure regulator, which limits the maximum negative pressure to -80 mm Hg in the venous system. In a clinical setting using KAVD, the walls of the right atrium or vein may collapse around the cannula inlet during periods of hypovolemia. The kinetic-pump could generate higher negative pressures if the revolutions per minute of the centrifugal pump are increased to compensate for reduced venous return.

Even though this experiment was performed in a controlled laboratory setting, there are certain limitations to this study. There were differences in the initial plasma free-hemoglobin levels due to variations in the blood collection techniques (20.7 - 75.5 mg/dL). This source of error was corrected by subtracting the baseline plasma free-hemogobin concentrations from the measured values.

A roller pump was used in each the circuit to return blood to the upper reservoir in all of the systems tested. The four pumps on the Sarns 5000 console were alternated

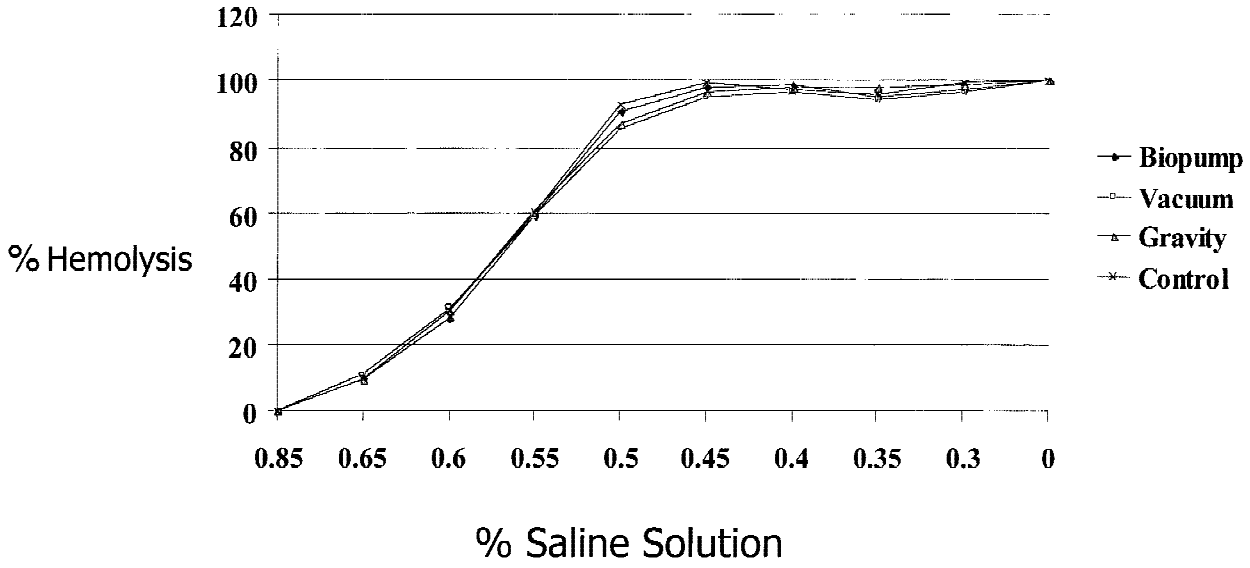


**Figure 4.** Red cell osmotic fragility after 8 hours (n = 4).

in each of the four trials to minimize experimental error. A comparison of the circuits included hemolysis contributed by the roller pump in all of the circuits tested. This was done to simulate the levels of hemolysis generated during a routine CPB with a roller pump in the arterial position. Additional hemolysis due to venous assist, when added to the hemolysis generated by the arterial roller pump, was not significantly different among the three groups. Therefore, we would not expect to see a clinically significant difference in hemolysis among any of the three methods of venous drainage when used in the context of a total CPB circuit.

Our findings show that either the kinetic-assisted or vacuum-assisted venous drainage system can be used to augment venous return through smaller venous cannulas without causing a significant increase in hemolysis, plasma-free hemoglobin, or red cell membrane damage. The vacuum-assist method for augmenting venous return can be of benefit in the clinical setting due to its reduced cost, and the added safety of limited negative pressure generation.

## ACKNOWLEDGMENT

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