Nuitiv™ Clear Needlefree Connector Hemocompatibility Study

Report of a study commissioned by ICU Medical, Inc. and conducted by WuXi AppTec

Background

Hemolysis is the breakdown of red blood cells with the subsequent release of their intracellular contents. In the context of blood administration, hemolysis can be classified as either immune hemolysis or nonimmune hemolysis. Nonimmune hemolysis can be due to thermal, osmotic, and/or mechanical injury to red blood cells or other blood products.[1]

Coagulation is one complication that can come from hemolysis[2–3], where it can introduce a thrombus in the catheter line or the patient. Using Nuitiv Clear needlefree connectors may help reduce the risk of hemolysis and coagulation.

Introduction

The purpose of the study was to assess the potential of the Nuitiv Clear connector to cause hemolysis or coagulation during the administration of blood. This evaluation was performed by measuring the hemolytic index and partial thromboplastin time (PTT) of blood samples infused through 5 Nuitiv Clear connectors in comparison to a blood sample infused through an open male luer.

Methods

Whole human blood was infused by gravity flow through the Nuitiv Clear connector attached to the male luer of a gravity infusion set. The same gravity infusion set with an open male luer was used as a control article. Blood samples were taken after approximately 100 mL, 300 mL, and 500 mL of blood had flowed through the Nuitiv Clear connector and were assayed for hemolysis per ASTM F756-13 and ISO 10993-4. After 500 mL of blood had flowed through the set, samples of blood were assayed for PTT. The testing was performed using 5 test article replicates.

Test Procedure

A 500 mL unit of freshly drawn, whole human blood was connected to each test or control article. A 15 mL sample of each of these units of blood was taken directly from the bag prior to infusion through the set in order to establish a pre-exposure baseline. The entire unit of blood was allowed to flow through each Nuitiv Clear test article by gravity. After approximately 100 mL and 300 mL of blood had flowed through the Nuitiv Clear test article, 5–10 mL samples of blood were collected. A final blood sample of 15 mL was collected once the entire 500 mL unit of blood had flowed through the Nuitiv Clear test article. This procedure was repeated for a total of 5 Nuitiv Clear test articles and 1 open male luer control article.

The samples of blood collected after 100 mL, 300 mL, and 500 mL of infusion for hemolysis evaluation were centrifuged for 15 minutes at 800 x g. The hemolytic index for each test and control sample was calculated based on the absorbance results and compared to the pre-exposure hemolytic index value for each bag of blood.

The additional blood samples were collected after 500 mL of infusion. After sample preparation, the length of time required for the formation of a clot was determined by photo-optic detection. If a sample did not clot within 300 seconds, the maximum value of 300 seconds was applied. The clotting time values were compared to the pre-exposure values in order to assess the activation of the intrinsic coagulation pathway.

Evaluation Criteria

The evaluation criteria for the hemolysis and PTT assays are listed in Tables 1 and 2 below, respectively.

Table 1. Hemolysis

% Hemolytic Index Corrected for Pre-exposure Value	Hemolytic Classification
0.0–2.0	Nonhemolytic
2.1–5.0	Slightly hemolytic
Greater than or equal to 5.1	Hemolytic

Table 2. PTT

% Clotting Time of Pre-exposure Sample	Thrombogenicity
Greater than or equal to 100	Nonactivator of intrinsic coagulation pathway
75–99	Minimal activator
50–74	Mild activator
25–49	Moderate activator
Less than 25	Activator

Results

The hemolysis percentag for each Nuitiv Clear test article at each volume point, corrected for pre-exposure hemolytic index, was 0.0%. The hemolysis percentage for the control article at each volume point, corrected for pre-exposure hemolytic index, was also 0.0%. Negative results were reported as 0.0. The hemolysis results are listed in Table 3 below. A clotting time of 300 seconds was applied for each Nuitiv Clear test article and the control article since no clots were detected. This represents 100% of the pre-exposure clotting time. The PTT results are listed in Table 4 below.

Table 3. Hemolysis Results

Test/Control Article	% Hemolysis at 100 mL		% Hemolysis at 300 mL		% Hemolysis at 500 mL	
	Average % Hemolytic Index	Average Pre-exposure Corrected % Hemolytic Index	Average % Hemolytic Index	Average Pre-exposure Corrected % Hemolytic Index	Average % Hemolytic Index	Average Pre-exposure Corrected % Hemolytic Index
Test Article 1	0.3	0.0	0.4	0.0	0.4	0.0
Test Article 2	0.6	0.0	0.6	0.0	0.7	0.0
Test Article 3	0.2	0.0	0.2	0.0	0.2	0.0
Test Article 4	0.6	0.0	0.6	0.0	0.7	0.0
Test Article 5	0.4	0.0	0.5	0.0	0.5	0.0

Table 4. PTT Results

Test/Control Article	PTT (seconds)		
	Pre-exposure Assay Time	Post-exposure Assay Time	Percentage of Pre-exposure
Control Article	300.0	300.0	100
Test Article 1	300.0	300.0	100
Test Article 2	300.0	300.0	100
Test Article 3	300.0	300.0	100
Test Article 4	300.0	300.0	100
Test Article 5	300.0	300.0	100

Conclusion

The Nuitiv Clear connector is considered nonhemolytic and a nonactivator of the coagulation pathway. No differences were observed between the blood samples that had flowed through the Nuitiv Clear connectors and the open male luer control article. Therefore, the Nuitiv Clear needlefree connector can be used for the transfusion of blood and blood products.

References

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