
Reduction of Mechanical Hemolysis by Urea and Potassium Cyanate

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Abstract

Urea and potassium cyanate were tested to find out if they could reduce mechanical hemolysis of normal human red blood cells. Blood treated by urea and cyanate was circulated for four hours in an extracorporeal system. The results were compared to matched controls. Urea and potassium cyanate reduce mechanical hemolysis in vitro.

Introduction

Mechanical hemolysis of a moderate degree is seen in extracorporeal circulation and sometimes after insertion of a valve and/or prosthesis. Occasionally the hemolysis becomes severe and in rare cases necessitates, for example, exchange of the valvular prosthesis.^{1,2}

Urea and cyanate reduce hemolysis in hemolytic disease where the mechanism is a lessening of the resistance of red blood cells to mechanical trauma (sickle cell anemia).^{3,4,5}

In this study the ability of urea and cyanate to reduce hemolysis caused by mechanical trauma to normal human red blood cells was tested by circulating blood in an in vitro model.

Material and Methods

Eighteen experiments were performed. For each experiment one unit of human blood not

more than two days old was used. It was heparinized with 2500 IU of heparin. Each unit was then divided into three parts. The first was mixed with a solution giving a concentration of 300 mg urea/100 ml blood. The second part was mixed with a solution giving a concentration of 4 mg cyanate/100 ml blood. A five percent invertose solution was added to obtain equal volumes for the three parts of blood.

The blood was circulated in three identical sterile perfusion systems consisting of a glass bottle, a PVC tube 120 cm long and 3/8" in inner diameter^a, a blood transfusion filter^b, and a three-way stop cock. Circulation was accomplished by a roller pump^c giving a flow of 500 ml/min (Figure 1).

Circulation was maintained for four hours and samples were taken before the pump was started and at hourly intervals to measure total plasma hemoglobin (P-HB)⁶ and hematocrit.⁷

The paired T-test comparing the differences of the mean plasma hemoglobin produced in the three parts of blood was used for statistical analysis.⁸

Results

Less hemolysis was seen in the systems treated with urea or cyanate (Figure 2). The accumulated P-HB at the end of the perfusion was significantly reduced (Figure 2). Expressed as a percentage of the mean P-HB in the untreated system, the

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^b Triplus, Kungsbacka, Sweden.

^c Sarns, Inc., Ann Arbor, MI 48103.

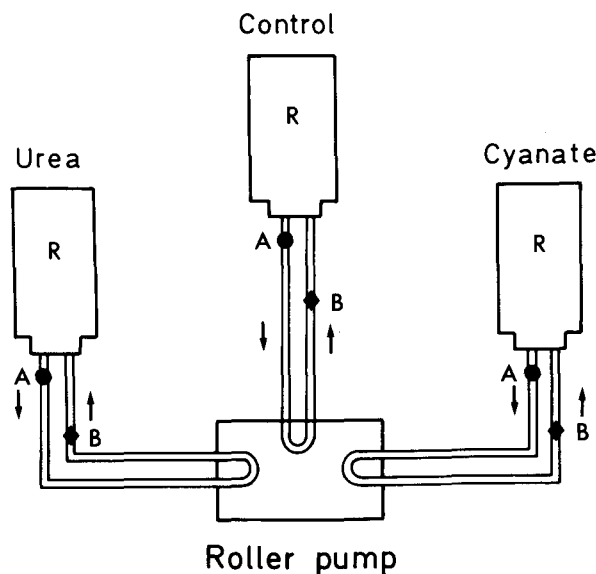


FIGURE 1. Schematic representation of the blood traumatizing model showing the roller pump pumping blood in the direction of the arrow through a three-way stop-cock (B) into the reservoir bottle (R) containing blood, down through a blood filter (A) and then back towards the pump. Blood samples for estimating plasma hemoglobin were drawn through the three-way stop-cock (B).

hourly reductions in the urea treated blood were 62, 46, 44 and 32 and in the cyanate treated blood were 58, 49, 43 and 31 at 1 to 4 hours respectively.

The hematocrit did not show any significant changes.

Discussion

Mechanical hemolysis, seen in extracorporeal circulation and other situations where prosthetic materials are in contact with blood, is usually of moderate degree but can in rare cases become a severe problem. It is, however, desirable to minimize hemolysis whenever it occurs. The perfusion system used in this study produced hemolysis (P-Hb levels) that are often seen during the use of the extracorporeal system in open heart surgery. Thus the measurable traumatic effect seen as an increase in plasma hemoglobin is comparable in these two situations.

Urea and cyanate have been used for treating patients with hemolytic anemia and the dosage of urea used in this study is comparable with that noted in clinical experience.^{9,10} The mechanism by which these drugs reduce hemolysis is not fully

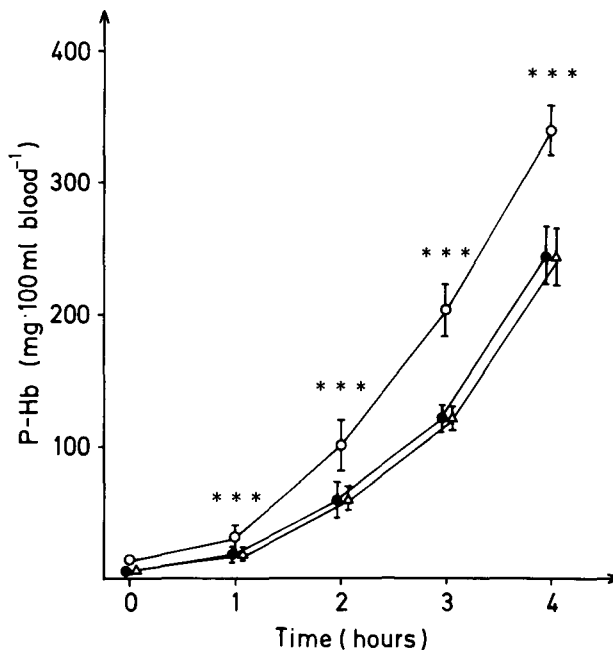


FIGURE 2. Mean plasma hemoglobin (\pm SD⁻¹) produced during four hours perfusion. \circ = untreated blood, \bullet = urea treated blood, Δ = cyanate treated blood, * = $P \leq 0.001$.

understood, but it has been suggested that cell membrane proteins are affected, thereby improving membrane deformability.^{3,4,5}

The cumulative effects of the trauma and lack of nutrition that is normally available could contribute to the increased hemolysis in the fourth hour in both treated and untreated blood.¹¹ This situation is also reflected in the reduced protection that is seen in the treated blood as perfusion time increases.

Urea or potassium cyanate treated blood resists in vitro mechanical stress significantly better than untreated blood. This might be of clinical significance but must first be further investigated experimentally.

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