The Turkish Journal of Pediatrics
Volume 20 / Nos. 1-2 / Jan.-April 1978 / pp. 17 – 23

Plasma Volume Determination with Two Different Methods in Children with Nephrotic Syndrome*

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Previous studies in patients with nephrotic syndrome have implied that plasma volume was reduced in the edematous state.[1-3] However, there are some reports about normal or even increased plasma and blood volumes in these patients.[4] This controversy is caused by the differences in the clinical status of the patients, the differences in the methods used for determination of plasma volume, and technical errors. Other factors that influence the results are the ways of expressing plasma volume according to body weight or body surface area and the use of venous hematocrit (Hct) instead of total body hematocrit for calculations.[5-7] In present study, we have compared two different methods of plasma volume determination.

Material and Methods

Seventeen patients with idiopathic nephrotic syndrome in the edematous state were studied. The diagnosis of nephrotic syndrome was made by massive proteinuria (>50 mg/kg/24 hrs), hypoalbuminemia (<3 g/dl), and edema.

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The study was performed before corticosteroids and diuretics were given and when the patient was on a sodium diet of 50 mEq per day and was allowed free activity. The control group included twelve patients who were hospitalized for different causes with no effect on plasma and blood volumes.

Plasma volume determinations were performed using two different radioisotopic methods:

1. ^{125}I Radioiodinated human serum albumin (RIHSA) method

Stock solutions containing 1.0 g protein per 100 ml were diluted with acid citrate dextrose (ACD) (Abbott) solution to a concentration of 10 uC per ml. One ml of the final solution with a dose of 0.5 uC/kg body weight, maximum 10 uC ^{125}I RIHSA was given intravenously The same amount of radioactive susbstance was diluted in 1000 ml distilled water and used as a standard (STD) solution. Heparinized blood samples were obtained at 5 and 15 minutes from the antecubital vein of the opposite arm with free flow, when the patients were in the supine position. The specific activity of radioiodine was counted from 2 ml of the patient's plasma and 2 ml of STD solution using 40-110 keV window in Gamma counter (Nuclear Chigago). Distribution of radioactivity of the 5 and 15 minute samples were corrected to zero time on semilogarithmic graph paper. Plasma volumes were calculated as follows:

$$\text{Plasma volume (total ml)} = \frac{\text{Std activity CPM/ml}}{\text{(0) time activity of plasma CPM/ml}} \times 1000$$

In order to reduce thyroidal uptake of radioiodine, Lugol's solution was administered one hour before and 48 hours after the test.

2. ^{51}Cr-labeled Erythrocyte Method

8-10 ml of the patient's blood or blood from an 0Rh (–) donor was drawn into 2 ml of ACD solution using aseptic technique. The blood sample was mixed with 1.5-2 uC $Na^{51}CrO_4$ per ml of blood and incubated at room temperature for 30 minutes. 250 mg of vitamin C was added to the bottle to prevent the binding reaction of ^{51}Cr.

After 3 Minutes

a) 2 ml of blood from the above mixture was taken to measure the radioactivity and Hct.

b) 2 ml of blood was diluted in 100 ml of distilled water and then 2ml of this solution was used as a standard; radioactivity and Hct were measured.

c) Some of the blood was centrifuged and radioactivity was counted from 2ml of plasma.

d) 2 ml of blood was administered to the patient intravenously. A 5ml heparinized blood sample was obtained from the antecubital vein of the opposite arm after 30 minutes using free flow when the patient was in the supine position. Hct. and specific acitivity of ^{51}Cr were determined.

e) Radioactivity was counted from 2 ml of the patient's plasma by a Gamma counter on 280-360 keV windov. Plasma volumes werecalculated from blood volumes:

$$\text{Blood volume (total ml)} = \frac{\text{(axb) (dilution factor)-C(1,00-STD Hct)}}{\text{d-e(1.00-patient's Hct)}}$$

Erythrocyte volume = Total blood volume x Hct.

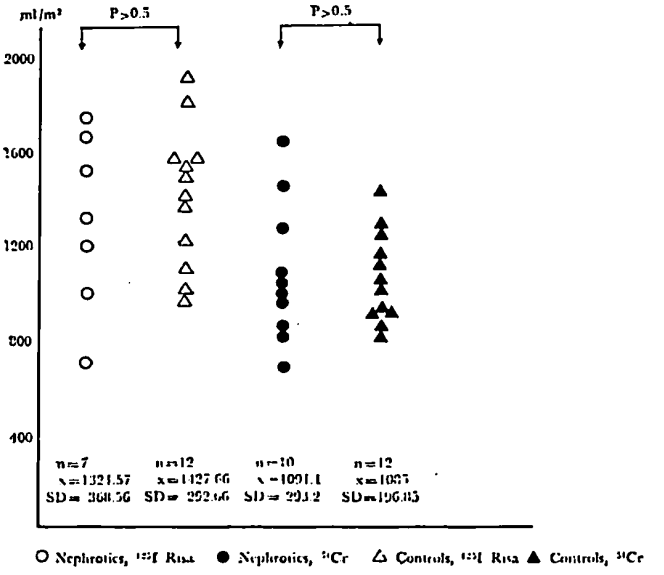
Plasma volume (total ml) = Total blood volume – Erythrocyte volume

In each case plasma volume was presented as total ml, ml/kg (body weight), and ml/m^2 body surface area. The X^2 test was used for statistical analysis and values are given as means $\mp$ 1 SD.

Results

Plasma volumes which were determined using the ^{125}I RIHSA method on seven patients with nephrotic syndrome in relapse showed mean values of 1324 $\mp$ 368.56 on ml/m^2 basis, and 41.7 $\mp$ 13.78 on ml/kg basis. Control group values in the same order were 1427.66 $\mp$ 292.66 ml/m^2 and 57.9 $\mp$ 14.07 ml/kg. The mean values of plasma volumes which were measured with ^{51}Cr labeled erythrocytes in ten nephrotic children and in twelve controls were found to be very close to each other (1091.10 $\mp$ 293.2 ml/m^2 versus 1085 $\mp$ 196.85 ml/m^2 and 41.44 $\mp$ 10.25 ml/kg versus 43.01 $\mp$ 8.6 ml/kg).

The mean values for the nephrotics were lower than those of the controls when two different measurement and calculation methods were used, but the difference between nephrotics and controls was not statistically significant ($p>0.05$) except for the ml/kg basis determinations with the ^{125}I RIHSA method ($p<0.05$) (Figure 1).



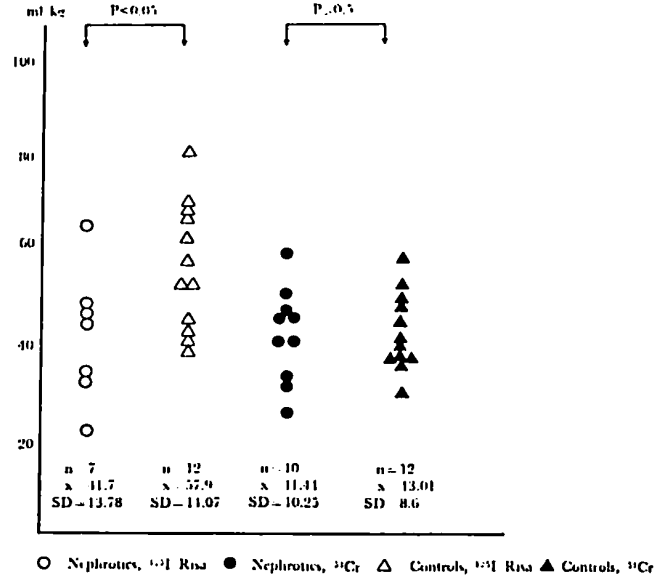


Figure 1
Comparison of the plasma volumes in nephrotic children and in controls.

Discussion

Commonly used and reliable methods of blood and plasma volume determinations in clinical practice are ^{125}I RIHSA and ^{51}Cr-labeled erythrocyte methods.[8, 9] Both methods have their advantages and disadvantages; the ^{51}Cr-labeled erythrocyte method can be applied in every laboratory; only one blood sample is needed, radiation dose is minimal, and the erythrocyte volume can be determined better than with other methods; the ^{125}I RIHSA method gives 18-23 % higher blood volume values than the ^{51}Cr method.[8, 10] There has been some controversy as to whether the venous Hct, arterial Hct, or the total body Hct. should be used in blood and plasma volume calculations.[5, 10, 11] However, use of venous Hct. is preferred by many because of the ease in calculations.[4] In this study we have used venous Hct. values.

During blood volume determinations the patient's position is important since plasma volumes which are measured in a prone position on patients in edematous and hypoalbuminemic states will be higher than those measured in the supine position.[4] The units used in expressing the volume are also important as ml/kg and ml/m^2 will give different results.[11, 12] Increase of the body weight of nephrotics during the edematous state will be misinterpreted as the dry body weight and results will be lower than they should be. In our study, only plasma volumes measured with the ^{125}I RIHSA method and expressed as ml/kg gave significantly decreased plasma volumes when compared to other calculation methods.

In the last sixty years, plasma volumes of nephrotic patients have been measured by various methods. In spite of normal or even increased values obtained the general opinion is that plasma volume is decreased.[1, 2, 4] Some cases of hypovolemic shock have been reported.[3] The etiology of nephrotic syndrome cases in which plasma and blood volumes were studied, differed, and most of the cases were in the adult age group.[4] In this study, when each of the 17 nephrotic relapse cases was interpreted individually, both normal and decreased plasma volumes were found. But on statistical analysis mean values of the ^{125}I RIHSA method were found to be lower than those of the controls; they were significantly decreased when ml/kg was used in calculations. when the ^{51}Cr-labeled erythrocyte method was used the control and study group's results were close to each other. The results of this study reinforce the need for accuracy in plasma volume determination in patients with nephrotic syndrome. The more accurate ^{125}I RIHSA method is superior to ^{51}Cr-labeled erythrocyte method because the ^{51}Cr-labeled erythrocyte method

gives lower plasma volumes. When the plasma volumes are expressed as ml/kg in the edematous state, the results will be found to be lower then they should be. Therefore calculation made on ml/m^2 basis will give more accurate results for plasma volume determinations.

Summary

Plasma volumes of seventeen patients with idiopathic nephrotic syndrome were measured. ^{125}I RIHSA method was used on seven patients and ^{51}Cr-labeled erythrocyte method was used on 10 patients for plasma volume determinations.

^{51}Cr-labeled erythrocyte method gave lower plasma volumes than ^{125}I RIHSA method, and the results expressed as ml/kg body weight gave lower values than the results expressed as ml/m^2 body surface area. These differences can be explained: ^{125}I RIHSA method specifically measures the plasma space, thus giving more reliable results than ^{51}Cr-labeled erythrocyte method; the differences between results expressed as ml/kg and ml/m^2 are due to the increased body weight in the edematous state, thus results expressed as ml/kg will be lower than the true values.

In conclusion, it is more accurate to perform plasma volume determination with ^{125}I RIHSA method and to avoid falsely low values the results should be expressed as ml/mg body surface area.

REFERENCES

1. Schreiner, G.E.: The nephrotic syndrome. In Disease of the Kidney. 2nd ed. Ed. Strauss, M.B., and Welt, L.G., Little, Brown and Co. Boston 1971, p. 502.
2. Squire, J. R.: The nephrotic syndrome. Advanc. Intern. Med. 7: 201, 1956.
3. Yamauchi, H., an Hoper, J. Jr.: Hypovolemic shock and hypotension as a complication in the nephrotic syndrome. Ann. Intern. Med 60: 242, 1964.
4. Eisenberg, S.: Blood volume in persons with the nephrotic syndrome. Am. J. Med. Sci. 225: 220, 1968.
5. Kirsch, K. A., Johnson, R. F., and Gorthen, R. J.: The significance of the total-body hematocrit in measurement of blood compartments. J. Nucl. Med. 12 17, 1971.
6. Wintrobe, M. M.: Clinical Hematology. 6th ed. W. Lea and Febiger, Philadelphia, 1967, p. 345.
7. Chase, G. D. and Rabinowitz, J. L.: Principles of Radioisotope Methodology Burgess publishing Co. Minn. 1968. p. 530.
8. Underwood, P.S., Boyan, C.P., Howland, W.S.: Appraisal of RIHSA blood volume for clinical use. Anesthesia and Analgesia. 45: 1, 1966.
9. Sukarochana, K., Parenzan, L., Thakurdas, N., and Kiesewetter, W. B.: Red cell mass determinations in infancy and childhood, with the use of radioactive chromium. J. Pediat, 59: 903, 1961.

10. Swan, H., Nelson, W.: Blood volume I Critique Spun v.s. Isotope hematocrit ^{125}RIHSA v.s. ^{51}Cr RBC. Ann. Surg. 173: 481, 1971.

11. Gross, S. and Godel, J. C.: Comparative studies of height and weight as a blood volume reference standard in normal children and children with Sickle Cell anemia. Am.J.Clin. Path. 55: 662, 1971.

12. Russel, S. J. M.: Blood volume studies in healthy children Arch. Dis. Child. 24: 88, 1949.