Applied Radiation and Isotopes 96 (2015) 71–82

Contents lists available at ScienceDirect

Applied Radiation and Isotopes

journal homepage: www.elsevier.com/locate/apradiso

Review

Blood volume analysis by radioisotopic dilution techniques: State of the art

Jesús Luis Gómez Perales *

Nuclear Medicine Service, Puerta del Mar University Hospital, Avenida Ana de Viya 21, 11009 Cádiz, Spain

HIGHLIGHTS

- Since the haematocrit reflects a proportion, it can be sometimes misleading.
- Blood volume analysis by radioisotopic dilution technique is still valid and very useful.
- The mean value of *f*-ratio (H_c/H_v) varies between 0.84 and 0.99, with a total range from 0.54 to 1.35.
- This variation of *f* could cause large errors when estimating RCV or PV once the other has been measured.

ARTICLE INFO

Article history:
Received 17 January 2014
Received in revised form
19 September 2014
Accepted 14 November 2014
Available online 20 November 2014

Keywords:
Blood volume
Plasma volume
Red cell volume
Radioisotopic dilution
Venous haematocrit
Body haematocrit

ABSTRACT

In the last years, there has been a growing recognition of the importance of blood volume abnormalities in the pathophysiology of several conditions and, consequently, a growing interest of accurate and rapid volume status assessment. Accordingly, there has been a surge of interest in blood volume analysis by radioisotopic dilution technique. However, there are still some controversies about this technique, such as the use of the *f*-cell ratio, the errors associated with the method and the reference values. This review aims to revise and discuss the theoretical and methodological aspects of this technique and also to discuss their controversies. Furthermore, it is questioned whether red cell volume or plasma volume can be accurately estimated once the other quantity has been measured or should red cell volume and plasma volume be directly measured.

As a conclusion, blood volume analysis by radioisotopic dilution technique is still valid and very useful.

Contents

Abbreviations: ; BV, blood volume; cpm, counts per minute; EV, erythrocytic volume; EVF, erythrocyte volume fraction; *f*-cell ratio or *f*-ratio or *f*, ratio between H_b and H_v ($f=H_b/H_v$); H_b, whole-body haematocrit; Hct: Ht or H, haematocrit; HSA, human serum albumin; H_v, venous haematocrit; ICSH, International Council for Standardization in Haematology; PCV, packed cell volume; PV, plasma volume; RBC, red blood cells; RCM, red cell mass; RCV, red cell volume; V_D, distribution volume

* Fax: +34 956 003 155.
E-mail addresses: jesuslgomez@hotmail.com, jesusl.gomez.sspa@juntadeandalucia.es

http://dx.doi.org/10.1016/j.apradiso.2014.11.014
0969-8043/

1. Introduction

Whole blood comprises a liquid phase (plasma) and a solid or cellular phase. The latter includes red blood cells (RBC), white blood cells and platelets. Platelets and white blood cells account for less than 0.1% of blood volume (BV). Thereby, the BV can be derived by summing the red cell volume (RCV) and the plasma volume (PV) inside the circulatory system. Nevertheless in some pathologies, such as leukaemia, the volume of leucocytes may constitute an appreciable fraction of the total circulating blood cells. In those cases, if the sum of the PV and RCV is used for its appraisal, the total BV would be underestimated.

Several normal and pathological conditions (e.g. posture, exercise, dehydration) affect the PV and many physiological mechanisms (e.g. hormonal, neural, renal, and cardiac) are involved in the regulation of the PV; whereas RCV is regulated by erythropoietin and growth factors. Deviations from normovolemia take place due to many pathological conditions, and these deviations of PV or RCV can be of significant importance for organ perfusion and blood pressure regulation by modifying vascular, cardiac, hepatic, renal, endocrine or immune endpoints.

Fluctuations in PV may result in either haemodilution or haemoconcentration, and can mask a genuine anaemia or can suggest polycythaemia where none exists (Dacic and Lewis, 1991). Hypervolemic or dilutional anaemia (normal RCV with increased BV and PV) and euvolemic or compensatory anaemia (normal BV with decreased RCV and increased PV) are not serious, but hypovolemic anaemia (decreased RCV, PV and BV) may be disastrous in conditions associated with augmented physiologic stress. Therefore, it is very important to differentiate between these kinds of anaemias.

Erythrocytosis or polycythaemia consists of an augmented proportion of RBC in the circulating blood. In polycythaemia vera (absolute polycythaemia) there is a true augmentation of the RCV with normal PV. By contrast, in apparent polycythaemia (pseudopolycythemia or Gaisböck syndrome) there is decreased PV and increased or normal RCV. In order to select the right treatment it is necessary to discriminate between these two kinds of polycythaemias. The laboratory parameters such as haemoglobin, red cell count, and haematocrit may not always reflect the total RCV because of variations in PV.

For all the above it follows that the assessment of RCV and PV is an important tool in clinical medicine for the evaluation of several disorders or diseases. The measurements of RCV and PV are well-established techniques performed routinely in nuclear medicine departments, and the development of these measurement techniques has a long history. They were first described in the early 20th century and have become more refined during time and evolved to use radiolabelled tracers. The measurement of PV in humans by a dilution method, using a red dye (Vital red), was first described in 1915 (Keith et al., 1915). Since then, the development of radiolabelled biological tracers has further refined these techniques. Other techniques, such as pulse-dye and exhaled carboxyhaemoglobin dilution, have also been described with variable success (Sawano et al., 2006; Imai et al., 2000).

2. Haematocrit and *f*-cell ratio

The haematocrit is a necessary parameter in the measurement of RCV, while *f*-cell ratio is an empirical factor very important when estimating RCV or PV once the other quantity has been measured. For this reason it is important to deepen the analysis of these parameters. The haematocrit (Hct, Ht or H), also known as erythrocyte volume fraction (EVF) or packed cell volume (PCV), is the proportion by volume of the BV that consists of RBC. Although typically the haematocrit is expressed in percentage (%), henceforth in this text, when this parameter appears into any equation, we will refer to it in terms of proportion, in order to simplify these equations.

The venous haematocrit (H_v) is a routine blood test that is available as a part of a complete automated blood count. The reference ranges for H_v are 37–43% in women and 42–47% in men, although these values may slightly change considering the different laboratories and the equipment used for the test. Haematocrit has also been traditionally measured by spinning down a tube of blood and then comparing the height of the column of RBC with the height of the entire sample. However, a centrifuged haematocrit value must be corrected, because it introduces a significant non-rectilinear error due to variability in the plasma trapping between packed erythrocytes. Furthermore, several factors will affect the H_v value. Firstly, it is the practice of some authors to include the white cell layer in their reading of the observed packed cell volume. Secondly, although most authors agree that the observed packed cell volume must be corrected for trapped plasma, there is considerable variation in the applied correction factor (Chaplin and Mollison, 1952; Maizels, 1945). Therefore, H_v has been measured by Coulter counter over more than 30 years, rather than by centrifugation, in view of the much better linearity of the former.

It is believed that there is normally a sufficient correlation between the RCV and certain peripheral blood values, such as total erythrocyte counts, haematocrit and haemoglobin content. Thus, H_v is often used clinically as a surrogate measure for RCV, although this assumes a normal PV, which is not always the case. Discrepancies occur when the PV becomes disproportionately reduced or increased. In such cases there is poor correlation between RCV and haematocrit, so that H_v is an imprecise estimate of actual RCV (Takanishi et al., 2008). Therefore, the H_v values may falsely reflect a low RCV in states of excess PV (dilutional anaemia), or it may falsely reflect a high RCV when PV is low (Hurley, 1974; Bentley and Lewis, 1976; Lorberboym et al., 2005). For example, the H_v values in hypovolemic anaemic patients are elevated because the PV does not increase to achieve the normovolemic anaemic state (Valeri et al., 2006).

Since the haematocrit reflects a proportion, this parameter can sometimes lead to errors of interpretation. Fig. 1 shows an example of two samples (A and B) with the same haematocrit. Compared with sample A, sample B shows a balanced reduction in both RCV and PV with a preserved ratio between these two parameters. Despite the two samples having the same