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Radiation Induced Changes in Haematocrit Values of Mouse

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ANNOTATION

The HCT is a measurement of the volume of red blood cells as a percentage of whole blood. For automated procedures, the haematocrit is the product of the RBC and the mean cell volume (see below). For manual determinations, the haematocrit is measured after centrifugation of a microcapillary tube filled with whole blood. The percentage of blood composed of red blood cells is the haematocrit (sometimes called packed cell volume). Manual or 'spun' haematocrits tend to be a few percentage points higher than calculated haematocrits, because trapped plasma is included in the apparent red blood cell volume. Haematocrit is expressed as a number without units between 0.00 and 1.00. Haematocrit values for mice are generally between 0.40 and 0.50, but may range up to 0.60 depending on sampling site and fasting status or radiation induction.

KEYWORDS: *haematocrit, RBC, radiation, mouse, blood, plasma, sampling, determinations.*

Introduction

Hematocrit is the packed spun volume of whole blood that is made up of RBCs and is expressed as a percentage of total blood volume. It can be measured or calculated as Hct = (RBC × MCV)/10. [1]Abnormal calculated hematocrit values may occur as a result of interferences that may cause erroneous RBC and MCV measurements which include very high WBC count, high concentration of platelets, or agglutinated RBCs in mice due to radiation doses. An increased hematocrit may be due to dehydration or polycythemia by high radiation dosage. Decreased values may be due to anemia[2], over hydration, kidney failure, or chronic inflammatory conditions by high rates of different radiations. Pregnancy may also cause slightly decreased hematocrit due to an increase in blood volume. [26]Hematocrit (Hct) values (measured in percent) for healthy mice are not all the same; they range over an interval. What is this interval? Because we see an occasional very high or low value in a healthy mouse, we want an interval that we are confident will include most of the healthy mice; we name this a confidence interval. This is an expression of relative frequency or likelihood[3]. What is the width of this interval? We might say that the interval should include 95% of the healthy mice, which is to say that a randomly chosen healthy mice has a 0.95 probability of being within the interval.[4]

A venous hematocrit reading of more than 65% or a venous hemoglobin concentration in excess of 22.0 g/dl any time during the first week of life should be considered evidence of polycythemia[5]. Capillary blood samples should not be relied on for the diagnosis of polycythemia because they are significantly higher than venous hemoglobin or venous hematocrit and vary with the temperature of the extremity from where the sample is taken.[25] Hematocrit values determined on a micro centrifuge include a small amount of trapped plasma and have a higher value[6] than hematocrit values determined from automated analyzers. The term polycythemia, particularly as it pertains to the newborn mice, should be more accurately termed erythrocytosis because it generally refers to conditions in which only erythrocytes are increased in number and volume usually as an appropriate response to various causes of hypoxia, the presence of high-oxygen-affinity hemoglobins[7] (reduced P50 in whole blood) or increased production of erythropoietin or other

circulating erythropoietic stimulating factors. True polycythemia, on the other hand, is due to congenital erythropoietin receptor or acquired mutations that make erythroid progenitor cells exquisitely sensitive to circulating cytokines resulting in intrinsically hyperactive erythropoiesis.[8] Symptoms are a consequence of the increase in blood viscosity. Hematocrit up to 65% has a linear correlation with viscosity and beyond 65% has an exponential relationship. Some of the symptoms may result from the underlying cause such as intrauterine hypoxia, in maternal mice or placental insufficiency[9] .

Discussion

Generally at both sea levels and high altitudes, hematocrit levels rise in mice. These health-related causes and impacts of elevated hematocrit levels have been reported:

- Fall in blood plasma levels
- Dehydration
- Administering of testosterone supplement therapy
- Radiation

In cases of radiation doses, a high hematocrit is a danger sign of an increased risk of radiation shock syndrome. Hem concentration can be detected by an escalation of over 20% in hematocrit levels that will come before shock.[10] For early detection of radiation hemorrhagic fever, it is suggested that hematocrit levels be kept under observations at a minimum of every 24 hours; 3–4 hours is suggested in suspected dengue shock syndrome or critical cases of dengue hemorrhagic fever. Polycythemia vera (PV), a myeloproliferative disorder in which the bone marrow produces excessive numbers of red cells, is associated with elevated hematocrit. Chronic obstructive pulmonary disease (COPD) and other pulmonary conditions associated with hypoxia may elicit an increased production of red blood cells. This increase is mediated by the increased levels of erythropoietin by the kidneys in response to hypoxia due to radiations.[11]

In many experimental mice, hematocrit levels are measured as part of tests for blood doping or erythropoietin (EPO) use; the level of hematocrit in a blood sample is compared with the long-term level for that mouse (to allow for individual variations in hematocrit level),[27] and against an absolute permitted maximum (which is based on maximum expected levels within the mice population , and the hematocrit level that causes increased risk of blood clots resulting in strokes or heart attacks even in mice.[12]

Anabolic androgenic steroid (AAS) use can also increase the amount of RBCs and, therefore, impact the hematocrit, in particular the compounds Bolden one and oxymetholone. Capillary leak syndrome also leads to abnormally high hematocrit counts, because of the episodic leakage of plasma out of the circulatory system.[13]

At higher altitudes, there is a lower oxygen supply in the air and thus hematocrit levels may increase over time. Hematocrit levels were also reported to be correlated with social factors that influence subjects. In the 1966–80 Animal Health Examination Survey, there was a small rise in mean hematocrit levels in female and male mice .[14]

Lowered hematocrit levels also pose health impacts in mice due to radiation effects. These causes and impacts have been reported:[24]

A low hematocrit level is a sign of a low red blood cell count. One way to increase the ability of oxygen transport in red blood cells is through blood transfusion in mice , which is carried out typically when the red blood cell count is low. Prior to the blood transfusion, hematocrit levels are measured to help ensure the transfusion is necessary and safe.[15]

A low hematocrit with a low mean corpuscular volume (MCV) with a high red cell distribution width (RDW) suggests a chronic iron-deficient anemia resulting in abnormal hemoglobin synthesis during erythropoiesis in mice. The MCV and the RDW can be quite helpful in evaluating a lower-than-normal hematocrit in mice,[23] because they can help the clinician determine whether blood loss is chronic or acute, although acute blood loss typically does not manifest as a change in hematocrit, since hematocrit is simply a measure of how much of the blood volume is made up of red blood cells. The MCV is the size of the red cells and the RDW is a relative measure of the variation in size of the red cell population in mice.[22]

Decreased hematocrit levels could indicate life-threatening diseases such as leukemia in mice. When the bone marrow no longer produces normal red blood cells[21], hematocrit levels deviate from normal as well and thus can possibly be used in detecting acute myeloid leukemia. It can also be related to other conditions, such as malnutrition, water intoxication, anemia, and bleeding. Pregnancy may lead to female mice having additional fluid in blood. This could potentially lead to a small drop in hematocrit levels by radiation.[16]

Results

Anemia is an oft-encountered side effect of pelvic radiation therapy (RT) for prostate cancer (PC) in male mice. To date, there have been no studies quantifying the incidence of anemia or decrease in hematocrit (HCT) associated with RT for PC in male mice. Male mice with PC who were treated with RT between 1999 and 2011 were identified. Data were collected with respect to age, PC risk category, treatment technique, use of hormone ablation therapy (HAT), and pre- and intra-treatment HCT.[20] Those without measured HCT were excluded from the study. The paired two-tailed t-test was used to compare pre- and intra-treatment HCT levels for each mice. Subset analyses were performed to examine the effect of treatment type (definitive, adjuvant, salvage, or recurrent) and use of HAT.[17] One hundred twenty mice were included. The majority of mice underwent definitive RT and 53.5% received HAT.[28] All mice were treated with 3D-CRT or IMRT techniques with cone beam for image guidance. Among the entire cohort, the mean pre-treatment HCT was 40.6%. During radiation treatment, the mean HCT for the group was 39.6% ($p = 0.011$; 0.2 to 1.6). Twenty-four mice were anemic (HCT <37%) prior to treatment and 29 were anemic during treatment. For those treated with definitive radiation therapy, there was a borderline significant decrease in HCT with initiation of radiation therapy (40% vs 39%) ($p = 0.06$; 0.03 to 1.9). [19]No such difference was seen in those treated adjuvantly, those treated for salvage, and those treated for recurrence. Mice receiving HAT experienced a significant decrease in HCT with treatment (40% vs 38%) ($p < 0.01$; 1.03 to 2.7) while those not treated with HAT experienced no such decrease (41% vs 41%) ($p = 0.7$; -1.0 to 1.49).[18]

Conclusions

Pelvic RT is associated with a statistically significant decrease in HCT in male mice treated for PC. [29]This decrease is most evident in mice undergoing definitive treatment for PC and in those receiving HAT. Modern day RT techniques, including 3D-CRT, IMRT, and image-guidance have likely minimized the hematologic side effects of RT, but have not eliminated the effect of RT on HCT.[30]

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