The Mean Platelet Volume, Platelet Size Deviation Width and Platelet to Large Cell Ratio as a Safe Method for Diagnosis of Idiopathic Thrombocytopenic Purpura

Thesis

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List of Abbreviations

BMI : Body mass index

CBC : Complete blood count

Hb : Hemoglobin concentration

HT : Hypoproductive thrombocytopenia

Ht : Height

ITP : Idiopathic thrombocytopenic purpura

MPV : Mean platelet volume

PDW : Platelet size distribution width

P-LCR : Platelet large cell ratio

ROC : Receiver operating characteristic curve

RPs : Reticulated platelets

WBC : White blood count

WT : Weight

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Introduction

Platelets were first described as distinct corpuscles and their role in coagulation and thrombosis recognized by the Italian pathologist Giulio Bizzozero (1882). It is now well recognized that platelets are a nucleated cell fragments derived from bone marrow megakaryocytes; that the platelet count in health is 150-400 X 10^9/1; that the mean platelet volume (MPV) in health ranges from 7.7 to 11.2 fl; and that the platelet life-span is 10 days. In the resting state some 30% of platelets are sequestered in the spleen **(Briggs et al., 2007).**

Two main mechanisms are involved in the pathogenesis of thrombocytopenia: (a) decreased platelet production in the bone marrow, as in the case of hypoproductive thrombocytopenia due to bone marrow suppression after chemotherapy for hematological malignancies, and (b) increased platelet destruction which is the case in idiopathic thrombocytopenic purpura (ITP) **(George et al., 2008).**

Since there is a significant risk of serious bleeding complications such as intracranial or gastrointestinal hemorrhage. Within a few hours, the diagnosis of ITP should be reached with the aid of medical history, physical examination, complete blood count and examination of peripheral blood smear **(George et al., 2008).**

There are reliable, positive diagnostic tests - namely mean platelet volume (MPV), platelet size deviation width (PDW) and, to a lesser extent, platelet-to-large-cell ratio (P-LCR)- for the differential diagnosis of ITP from hypoproductive thrombocytopenia (HT). These three tests are routinely generated by automated cell counters and are available within minutes after the examination of the patient **(Balduini et al., 1999).** These parameters relating to platelet size are derived from the impedance platelet size distribution curve, figure(7). Mean platelet volume (MPV) is calculated by dividing the platelet-crit (PCT), analogous to the red cell haematocrit, by the number of platelets, this is the same calculation as for the mean red cell volume (MCV), dividing haematocrit by the red cell count. Nearly all analysers report the MPV and some also report platelet size distribution width (PDW), which is the width of the size distribution curve in fl at the 20% level when the peak distribution curve is taken as 80% or 100%, depending on the analyser. The platelet large cell ratio (P-LCR), reported by the Sysmex XE-2100, is the number of cells falling above the 12-fl threshold divided by the total number of platelets **(Briggs et al., 2007).** These parameters have been previously found increased in patients with increased thrombopoiesis such as occurs in ITP due to the prevalence of young and large platelets. On the contrary, patients with hypoproductive thrombocytopenia (HT) have decreased values due to the prevalence of old and small platelets **(Balduini et al., 1999).**

The fact that MPV and PDW are increased in ITP was recognized already since 1983 **(Gardner, et al., 1983).** However, this knowledge gained very limited use in the daily Clinical practice. Recent studies reexamined the significance of platelet indices in ITP **(Kaito et al., 2005.**

Use of platelet indices can be of great help in clinical practice since they are routinely generated by automated cell counters. Moreover, invasive methods, like bone marrow aspiration could be avoided **(George et al., 2008).**

Aim of the work

Study the beneficial role of MPV, PDW, and P-LCR as a safe method for diagnosis of ITP and their role in differentiating hypoproductive from hyperdestructive thrombocytopenia.

Thrombocytopenia

Platelet physiology:

Platelets are small (2-μm-diameter), non-nucleated blood cells produced in the bone marrow from megakaryocytes. Platelets are activated rapidly after blood vessel injury or blood exposure to the artificial surfaces of implanted devices, and they are a crucial component of the primary hemostatic response. In their inactivated state, platelets are roughly discoid in shape and contain cytoplasmic organelles, cytoskeletal elements, invaginating open-canalicular membrane systems, and platelet-specific granules, called alpha and dense granules (**Kandice et al., 2001).**

Platelet function:

Platelets promote hemostasis by four interconnected mechanisms: (1) adhering to sites of vascular injury or artificial surfaces, (2) releasing compounds from their granules, (3) aggregating together to form a hemostatic platelet plug, and (4) providing a procoagulant surface for activated coagulation protein complexes on their phospholipid membranes **(Kandice et al., 2001).**

Platelets are essential to the maintenance of primary hemostasis, and a minimum number are required to ensure vascular integrity. Platelets gather and adhere to sites of vascular injury. After doing so, they initiate a hemostatic

process by releasing mediators that recruit more platelets to the site **(Kaplan et al., 2004).**

Platelets release a multitude of growth factors including platelet derived growth factor (PDGF), a potent chemotactic agent, and transforming growth factor-β, which stimulates the deposition of extracellular matrix. Both of these growth factors have been shown to play a significant role in the repair and regeneration of connective tissues **(Connell et al., 2008).**

Other healing associated growth factors produced by platelets include basic fibroblast growth factor, insulin-like growth factor-1(IGF-1), platelet-derived epidermal growth factor, and vascular endothelial growth factor. Local application of these factors in increased concentrations through platelet-rich plasma (PRP) has been used as an adjunct to wound healing for several decades **(Connell et al., 2008).**

Platelet regulation:

Thrombopoietin appears to play an important physiologic role in platelet homeostasis. With the use of a biologic assay, it has been shown that during the course of bone marrow transplantation, thrombopoietin levels are inversely related to the peripheral blood platelet count. Moreover, in a number of other thrombocytopenic disorders (including idiopathic thrombocytopenic purpura), plasma thrombopoietin levels are elevated **(Kaushansky , 1996).**

The precise inverse relationship between plasma level of thrombopoietin and the platelet count has led some investigators to propose that platelets regulate the levels of the hormone responsible for their production.Thrombopoietin is regulated by some of the same mechanisms proposed for the regulation of macrophage CSF, the cytokine responsible for monocyte and macrophage development **(Kaushansky, 1996).**

Thrombocytopenia

Thrombocytopenia (or-pania,or thrombopnia in short) is the presence of relatively few platelets in blood. Generally speaking, in humans, a normal platelet count ranges from 150,000 to 450,000 per mm. A common definition is a number less than 100,000 per mm **(Correia et al., 2008).**

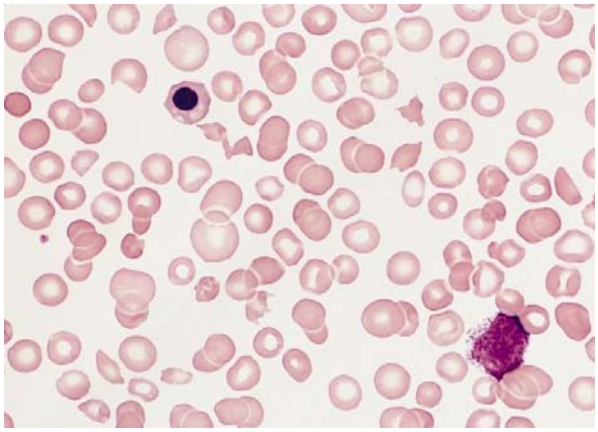

Figure (1): Thrombocytopenia

Causes and pathogenesis of thrombocytopenia:

Two main mechanisms are involved in the pathogenesis of thrombocytopenia: (a) decreased platelet production in the