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The Biophysics and Flow Haemodynamics in Sickle Cell Patients: A Mathematical Model That Takes into Account Electochemical and Vascular Factors in the Genesis of Vaso-Occlusion

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Abstract
Sickle Cell Disease is inherited genetic disease. An autosomal recessive gene is responsible for the synthesis of Haemoglobin S. The disease manifests usually in Homozygous SS state. Synthesis of the Haemoglobin S is courtesy of beta globin gene mutation in chromosome number 11 within the nucleus of Erythroblast. Valine replaces Glutamic acid in position 6 of beta polypeptide chain of haemoglobin. But deoxygenation of Haemoglobin S results in polymerization of the Haemoglobin and the deformable discoid red cell changes to stiff sickle cell, and this is the hallmark of vaso-occlusion and crises. Intracellular concentration of both Magnesium ions and Potassium ions in red cells correlate positively with lower risk of sickling and crises in SCD according to studies. Introducing a hypothetical equation that determines Vaso-occlusion risk, shortened and christen VASOcclusity, a product of biochemical and biophysical considerations in SCD haemodynamics where the radius of the blood vessel and the Body Mass Index by extension are also considered strong factors and variables.
Keywords: Haemoglobin S, Polymerization, ions, Magnesium, Potassium, radius,

INTRODUCTION

Sickle Cell Disease is inherited genetic disease. An autosomal recessive gene is responsible for the synthesis of Haemoglobin S type of haemoglobin. The disease manifests usually in Homozygous SS state. Synthesis of the Haemoglobin S is courtesy of beta globin gene mutation in chromosome number 11 within the nucleus of Erythroblast. Valine replaces Glutamic acid in position 6 of beta polypeptide chain of haemoglobin and at the DNA level, this alteration is as results of single base change, from adenine to thymine within the sixth codon (Marotta et al 1977).

Deoxygenation of Haemoglobin S results in polymerization of the Haemoglobin and the normal deformable discoid red cell changes to stiff sickle cell, and this is the hallmark of vaso-occlusion and crises. Intracellular concentrations of Potassium ions $[K^+]$icf according to Lucia De Fracenschi et al 2005 and Magnesium ions $[Mg^{2+}]$icf in the red cells as reported by L De Fracenschi in 1997, do correlate positively with lower risk of sickling and crises in SCD. The intracellular concentration of these ions in the red blood cells inversely varies with the extent of red cell dehydration, an important concurrent event with haemoglobin polymerization and red cell sickling according to Bookchin and Lew(2002). Though drugs like clotrimazole are known to inhibit Gardos channel (Brugnara et al, 1997) thereby reducing red cell dehydration and protecting against sickling and vaso-occlusion, for the purpose of this study, a natural trace element Magnesium in its ionic form is taken as an important determinant of red cell Gardos channel inhibition. Inhibition of Gardos Channel reduces K^+ efflux and thus increasing [K+]icf. Introducing a hypothetical equations that determine Vaso-occlusion risk and it is shortened and christened VASOcclusity and its reciprocal derivative Vasopatency. The equation and its derivative are products of biochemical and biophysical considerations in SCD haemodynamics where the radius of the blood vessel is taken into consideration.

MATERIAL AND METHODS

Simple mathematical variation is used to establish relationships and constants in SCD cellular and vascular factors in the phenomenon of vaso-occlusion. The variables are first considered individually and the integrally.
The mathematical pattern in the derivation of Henderson-Hasselbach equation is considered along with Poiseuille-Hagen equation (Sutera and Skalak, 1993) assumption of laminar flow of incompreeible fluid in a hypothetical rigid tube.
The following points represent argument upon which the derivation is predicated:

- Entropy represents more ways in which things can be arranged or more ways that a given outcome can be achieved. It is increase in disorderliness.
- Entropy is directly proportional (α) to red cell deformability and directly proportional to vaso-patency and reduced risk of vaso-occlusion.
- It can also be said the risk of sickle cell crises from vaso-occlusion, referred to as VASocclusity, is

inversely proportional to red cell deformability and thus entropy.

- Red cell deformability is directly proportional (α) to Entropy α diameter or radius of the hypothetical rigid blood vessel under consideration.
- Risk of red cell sickling and vaso-occlusion (VASOcclusity) is inversely proportional to both the intracellular potassium ion concentration [K+]icf and that of Magnesium ion concentration $[Mg^{2+}]$icf.
- Assuming the number of sickle cell to discoid red cell ratio approximately 25% and the average size and surface area of red cell in both children and adults approximately the same.

$1/VASocclusity = K_1^I .r^4 .[Mg^{2+}]icf\,[K^+]icf$

$VASocclusity=1/K_1^I .1/ r^4 . 1/[Mg^{2+}]icf . 1/ [K^+]icf$…….equation (1)

An equation derivation that follows the pattern of Poiseuille-Hagen's equation.

Next, applying similar mathematical technique in deriving Henderson-Hasselbalch Equation

$-Log\ VASocclusity = - Log\ 1/K_1^I - Log\ \{1/ r^4.1/ [Mg^{2+}]icf.1/[K^+]icf\}$

let $- Log\ 1/ K_1^I$ be K_1 i.e.($- Log\ 1/ K_1^I = K_1$) and let's assume it to be SCD haemodynamic constant in this case.

- Log VASocclusity represents VASOpatency

Therefore

$VASOpatency = K_1 + Log\ r^4\,[Mg^{2+}]_{icf} .[K^+]_{icf}$ .....equation (2)

These two equations are so named Sabo 1st and 2nd equation and can at a glance reflect what factors determine flow and prevent vaso-occlusion in sickle cell haemodynamic model vasculature.

DISCUSSION

Patency is define as the degree of openness of a tube such as blood vessels or catheter, the relative absence of blockade and may be measured in percent. In Biological system, things rarely work in such a way as to predict events that are matter of mathematical certainty. This formula and its derivative appears useful in predicting the risk of Vaso-occlusion and sickle cell crises or possibly predicts the direction in which an event is skewed with varying degree of statistical probability. Reports have already shown that magnesium supplementation reduces risk of vaso-occlusion and crisis in similar way that Gardos channel inhibitor like clotrimazole in Human studies. On the other hand, the radius of any vessel, in this case the hypothetical rigid blood vessel with non compressible fluid (presumably blood) determines flow and thus patency. The size of nutrients arteries are known to vary with body size increase in growing age. Despite the fact that growth level of the human body does not significantly affect the size of the capillary beds, it does however affect the calibre (radius) of nutrient artery.

CONCLUSION

This formula, $VASocclusity = 1/K_1^I. 1/ r^4. 1/[Mg^{2+}]icf . 1/ [K^+]icf$, is hypothetical and a model. Along with its derivative $VASOpatency = K_1 + Log\ r^4\,[Mg^{2+}]_{icf} .[K^+]_{icf}$, here named Sabo's equations, may be useful in showing the direction of changes influencing the vaso-patency nay the risk of vaso-occlusion in the genesis of sickle cell crisis.

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