

Reduction of frequency of pain in clinical trial with association of arginine and hydroxyurea in sickle cell anemia's patients in Brazil

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Accepted on 11 March, 2020

Commentary

Arginine is a substrate for NO production, which is a cofactor of the enzyme guanylate cyclase (GC), responsible for the reaction that makes the conversion of guanosine triphosphate (GTP) into cyclic guanine monophosphate (cGMP), causing relaxation of smooth muscles and vascular and, consequently, vasodilation. This would be the mechanism that can assist in the adjuvant activity of arginine in the treatment of patients with SCA who use hydroxyurea, since, with the increased bioavailability of circulating arginine, which is found in a reduced form in SCA patients, there is the possibility of supplying the demand for the NO formation reaction, and also the formation of cGMP, thus improving microcirculation due to vasodilation. Thus, there would be a reduction in pain, facilitate circulation and avoid more important complications, such as stroke and leg ulcers that are difficult to treat, and which can be a gateway for important infections. It is also an objective to reduce the number of hospitalization of these patients, facilitating their personal and professional life[1-4].

The association hydroxyurea and L-arginine is described in studies that demonstrate that hydroxyurea increases the use of arginine for the production of circulating NO, reducing pain and hospitalizations. A deregulation of arginine metabolism contributes to endothelial dysfunction in patients with sickle cell anemia, and is strongly associated with the patient's prospective mortality. New treatments aimed at improving the bioavailability of arginine and NO through the inhibition of arginase, suppression of the hemolytic rate, supplementation of oral arginine or use of NO donors represent possible therapeutic strategies for complications of hemolytic disorders[5-12].

Thus, we conducted a double blind randomized clinical trial in patients in the city of Fortaleza-CE, Brazil, who used hydroxyurea, to study the efficacy of arginine as a therapeutic adjuvant. We observed an increase in nitric oxide in patients belonging to the study group, which converges with a reduction in the frequency of pain. We believe that in cases of patients who do not evolve the clinic only with the use of hydroxyurea, they can use arginine as an adjunct, since it is a genetic disease that has a varied clinic, and throughout the patient's life. In the hematological analysis, it was observed that there was an increase in the concentration of total Hb in the study group, even if not significant. Likewise, there was a gradual increase in hematocrit, which can probably be attributed to a decrease in hemolysis. Also noteworthy is a decrease in the reticulocyte count, which can also be attributed to reduced hemolysis. Arginine is cheap and has had no adverse effects on our work, and its supplementation is a good option for public policies in Brazil. The clinical trial brings a new possibility to be used in

the treatment of SCA, even in those patients who are not responsive, so that NO can help the action of HU, which is also a NO donor, enhancing its action. And in the case of responsive patients, new studies in which the dose reduction is performed may demonstrate the potential of L-arginine in SCA. As well as, its use in children, even in other pharmaceutical forms more suitable for this age group[13].

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Citation: Eleutério R. Reduction of frequency of pain in clinical trial with association of arginine and hydroxyurea in sickle cell anemia's patients in Brazil *Hematol Blood Disord* 2020;3(1):23-24.

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