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Sickle Cell Anemia Therapeutic Approach Based on Drepanoalpha®: About 34 Cases

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Authors' contributions

This work was carried out in collaboration between all authors. Authors BZG and KNN designed the study. Author DSTT performed the statistical analysis. Author LTA wrote the protocol and author PTM wrote the first draft of the manuscript. Authors FMK and VBF managed the analyses of the study. Author GNB managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aim: The aim of this study is to evaluate clinical, biological, socio-economic and socio-demographic parameters on sickle cell patients before, during and after the administration of Drepanoalpha®, a nutraceutical used in the management of sickle cell disease in DR. Congo.
Methodology: The 34 selected cases were submitted to Drepanoalpha® for two months and the clinical (jaundice, pallor, physical asthenia, abdominal bloating, hepatomegaly, splenomegaly, sensitivity to infections, bone pain, anorexia), biological (hemoglobin and hematocrit) and socio-economic (cost per crisis, number and duration of hospitalization, number of transfusions) parameters were evaluated before, during and after administration.

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Results: The results reveal that the use of Drepanoalpha® could probably suppress the clinical expression of hyperhemolysis, as well as other sickle cell disease signs such as jaundice, pallor, splenomegaly and abdominal bloating and also decreased the physical asthenia and anorexia, preventing considered sickle cell disease patients from infections. Drepanoalpha® significantly increases the hemoglobin and hematocrit levels of all subjects. These results also indicate that considered subjects, mainly the males children with none education level, showed neither intolerance nor adverse effects when taking Drepanoalpha®. Treatment with this Nutraceutical is 13.64 times cheaper than hospitalization.
Conclusion: This could probably indicates that, this nutraceutical can be considered as safe potential candidate in the treatment of sickle cell anemia.

Keywords: Drepanoalpha®; nutraceutical; sickle cell anemia; hemoglobin; hematocrit.

1. INTRODUCTION

Sickle cell anemia is among tropical diseases responsible for high mortality. This chronic disease is due to the synthesis of hemoglobin S which comes from the substitution of a single amino-acid, glutamic acid by valine in sixth position of the β globin chain [1-4]. This substitution decreases the affinity of hemoglobin (Hb) for oxygen and significantly reduces the solubility of hemoglobin S (HbS) in its non-oxygenated form (deoxy HbS). Thus, when the partial pressure of oxygen decreases, hemoglobin S becomes very sparingly soluble and then polymerizes with other molecules of Hb S which crystallizes in the red blood cell then deforms into a sickle. Sickling predisposes erythrocytes to early hemolysis [5,6].

The mortality rate of sickle cell anemia is estimated at about five millions of people per year. In some African regions, the carriers of sickle cell feature account for up to 20% of the population with a prevalence between 25-30% in Central Africa [7,8]. Two per cent of the Congolese population is affected by this disease i.e. more than one million people [9]. From a genetic point of view, sickle cell anemia is a lethal disease because very few individuals reach the breeding age [1,10]. Indeed, 80% of anemic children not followed medically die before their fifth birthday [1,6,10]

Some treatment approaches have been developed in order to relieve sickle cell disease patients. These include bone marrow transplantation, repeated blood transfusion, use of hydroxyurea and so on. However, it turns out that these treatments are not only very expensive or cytotoxic but they may also constitute a certain risk of infection by HIV/AIDS while it is known that there are no specialized laboratories for the traceability of blood products in African rural areas [3,10-12].

So, phytotherapy is an alternative approach because natural products are a possible source of new types of drugs that can be used against several diseases in general and against sickle cell anemia in particular [10]. In this framework, our research team validated the antisickling activity of about 100 plants used in Congolese traditional medicine, isolated some bioactive molecules and developed a phytomedicine based on food plants called Drépanoalpha® [3,6,9-24]. Some studies on acute and subacute toxicity, nutrient composition, antisickling, anti-hemolytic, scavenging and antioxidant properties, the effect on the biochemical parameters of two animal models were carried out [25-27]. A preliminary study involving ten sickle cell patients was recently done [28].

The aim of this study is to evaluate the general status of sickle cell patients before, during and after the administration of Drepanoalpha® taking in account some parameters such as clinical, biological and socio-economic parameters.

2. MATERIALS AND METHODS

2.1 Study Area and Sampling

This study was conducted at Centre de Médecine Mixte et Anémie SS (CMMASS) in Kinshasa, Democratic Republic of the Congo (DRC). Then, 34 cases were selected on the basis of the following criteria:

- Being a known sickle cell subject, registered and regularly followed up at the Centre de Médecine Mixte and Anemie SS and whose home addresses obtained are very clear and reliable;

- Having undergone one or more hospitalizations and consecutive transfusions due to haemolytic and vaso-occlusive crises between June 2013 and June 2014;
- Having accepted to take the product and to be subjected to the controls according to the protocol approved by the ethics committee of the department of biology of the faculty of sciences, University of Kinshasa.

There were no restrictions on age and sex. The selected subjects were also followed up at their respective homes during two months (60 days) once a week.

The daily dosage was given 2 to "times per day as follows (according age groups):

- 3 to 8 years : 1 tea spoonful
- 9 to 17 years : 1.5 tea spoonful
- Adults : 2 tea spoonfuls

2.2 Evaluated Parameters

The parameters evaluated in this study are:

1. Clinical: It was proceeded to the observation (jaundice, pallor, physical asthenia, abdominal bloating), palpation (hepatomegaly, splenomegaly) and the questioning the subject about his condition (sensitivity to infections, bone pain, anorexia).
2. Para clinical: Hemoglobin (Hb) and Hematocrit (Hct). Hb and Hct were determined as previously described [28].
3. Socio-economic (cost per crisis, number and duration of hospitalization, number of transfusions, education level).
4. Socio-demographic (age groups, gender and education level of the subjects).

2.3 Statistical Analysis

Differences between values before and after treatment with the drug were statistically compared using Windows Excel statistics tool at the significance of 95% confidence level.

3. RESULTS AND DISCUSSION

3.1 Results

3.1.1 Evaluation of socio-demographic characteristics

Figs. 1 and 2 provide information on the age groups, gender and education level of all subjects, respectively.

It appears from this figure that the majority of considered subjects are in the age range of 3-7 years followed by those of 26-29 years and 19-24 years, however those in the interval 15-19 years are less represented.

Fig. 2 shows that the sex male predominate on the female. Additionally, uneducated group constitute majority of subjects.

3.1.2 Evaluation of clinical parameters

The clinical parameters evaluated were grouped into clinical parameters 1 (i.e. parameters observable by naked eye or macroscopic parameters) and the clinical parameters 2 (i.e. parameters invisible to the naked eye or imperceptible or microscopic). These parameters were evaluated before, during and after treatment.

Clinical data (Table 1) show that before using Drepanoalpha®, 33 patients on 34 examined (97%) had signs of pallor, 88% had

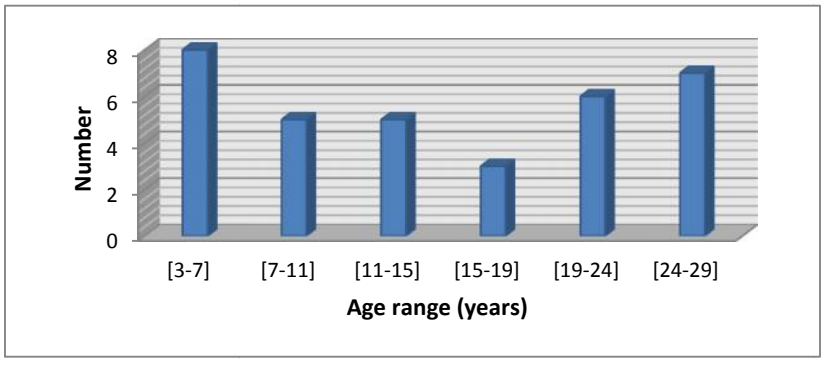

Fig. 1. Age of sickle cell disease subjects

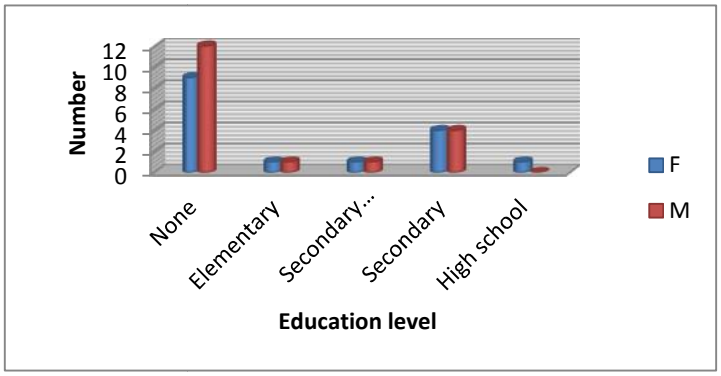

Fig. 2. Education level of sickle cell subjects

Table 1. Evaluation of clinical parameters 1

Subjects	Evaluated parameters														
	Jaundice			Pallor			A.B			Hepatomegaly			Splenomegaly		
	Be	Du	Aft	Be	Du	Aft	Be	Du	Aft	Be	Du	Aft	Be	Du	Aft
Number	33	9	1	25	1	0	18	10	0	2	0	0	30	5	0
%	97	27	3	74	3	0	53	29	0	6	0	0	88	14	0

Legend: Be: Before; Du: During (30 days); Aft: After (60 days); A.B: Abdominal bloating

splenomegaly, 73% had jaundice, 53% had belly ballooned but only 6% had hepatomegaly. After 60 days of treatment with Drepanoalpha®, it was found a positive change in all of considered subjects for all parameters. All the values obtained after treatment with Drepanoalpha® are significantly different ($p<0.05$) to that obtained before treatment. Indeed, no pallor, abdominal bloating, hepatomegaly and splenomegaly were found after treatment. However, it was found that 3% of subjects still had some signs of jaundice.

As it can be noticed from this table, 100% of subjects suffered from bone pain before treatment with Drepanoalpha®, 82% were very sensitive to infections, 79 % were suffering from abdominal pain, 70% were unable to eat and 74% had physical asthenia. But, after two months of treatment with Drepanoalpha®, radical changes ($p<0.05$) were noticed, sensibility to microbial strains has been observed to only 6% of subjects. However, for anorexia, abdominal or bone pains, none of them showed signs after the treatment.

3.1.3 Evaluation of para-clinical parameters during the treatment

Para-clinical parameters (hematocrit and hemoglobin levels) were assessed before, during and after Drepanoalpha® treatment. These results are shown in the Figs. 3 and 4.

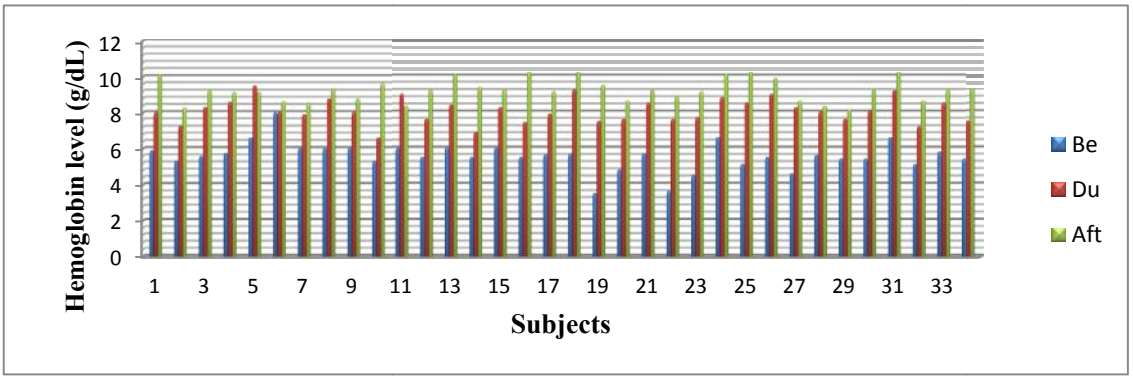

Fig. 3. Evaluation of hemoglobin level before (be), during (du) and after (aft) treatment with Drepanoalpha®

Table 2. Evaluation of clinical parameters 2

Subjects	Evaluated parameters														
	S.I			Anorexia			A.P			B.P			P.A		
	Be	Du	Aft	Be	Du	Aft	Be	Du	Aft	Be	Du	Aft	Be	Du	Aft
Number	28	9	2	24	1	0	27	6	0	34	10	0	25	1	0
%	82	26	6	71	3	0	79	18	0	100	29	0	73	3	0

Legend: Be: Before; Du: During (30 days); Aft: after (60 days); S.I.: Sensitivity to infections; A.D.: Abdominal pain; B.P.: Bone pain; P.A: Physical asthenia

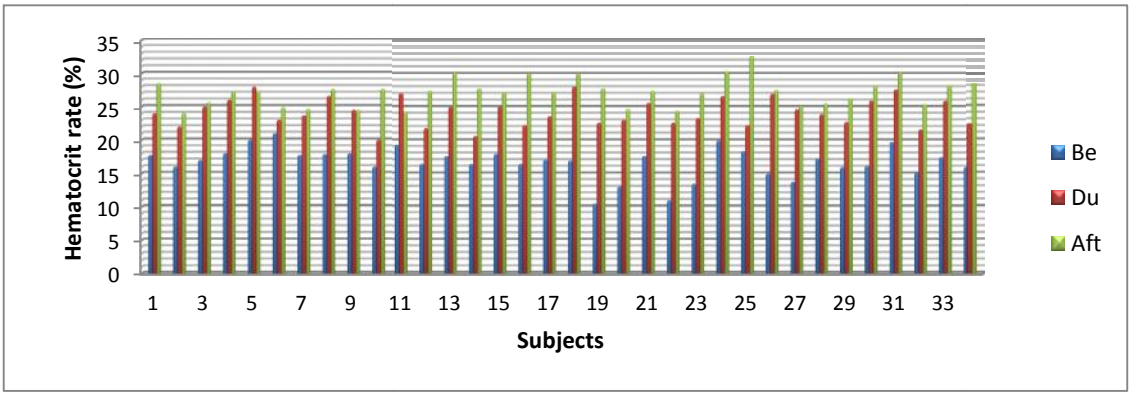

Fig. 4. Evaluation of hematocrit level before (be), during (du) and after (aft) treatment with Drepanoalpha®

These figures show clearly that Drepanoalpha® treatment increases the level of hemoglobin and these results in an increase of the hematocrit rate in all treated subjects. Before treatment hemoglobin level is in general under 6 g/100 mL (5.6 ±0.7 g/100 mL) of blood but after 60 days of treatment with Drepanoalpha® is higher than 8 g/100 mL (9.1±1.0 g/100 mL) and 20% of hemoglobin levels reach 10 g/100 mL indicating a significant difference ($p<0.05$) before and after treatment . It is the same for the hematocrit.

3.1.4 Evaluation of adverse effects of Drepanoalpha® treatment

Vomiting, pain and diarrhea were followed as side effects in all subjects during the 60 days of daily treatment with Drepanoalpha®. No side effect was noticed a part from one patient who indicated the occurrence of vomiting while taking medication.

3.1.5 Socio-economic evaluation

The cost of sickle cell anemia crises care and bimonthly blood transfusion were evaluated.

The bimonthly averages of crisis, hospitalization and transfusion are 2.82 ± 0.60 crisis, 24.56 ± 4.90 days and 1.65 ± 0.33 transfusions respectively. The average hospitalization cost is 226.32 ± 11.31 USD but Drepanoalpha® treatment cost only 30.88 ± 1.54 USD for the same period of time.

3.2 Discussion

3.2.1 Clinical parameters

It is well known that jaundice and/or pallor are the consequence of hyperhemolysis which is due to the sickling of the red blood cells. However, Ngbolua et al. [25] showed that Drepanoalpha® possess an antisickling activity which would justify this suppression of the clinical expression of hyperhemolysis expressed by jaundice as well as pallor.

The red blood cells of sickle-cell subjects are abnormal. They take a sickle form and are stopped by the filter represented by the spleen, where they are destroyed. This sequestration of abnormal red blood cells causes an increase in the volume of the spleen (splenomegaly) conducting to abdominal bloating. However, Drepanoalpha® with an antisickling effect gives the sickle cell red blood cells their circular biconcave shape [25], henceforth they will no longer be sequestered by the spleen. This justifies the absence of splenomegaly and abdominal bloating observed in all considered sickle cell subjects after treatment with Drepanoalpha®.

The increasing degradation of red blood cells leads to anemia which conducted to physical asthenia as well as anorexia in many sickle cell subjects. Drepanoalpha® has been shown to contain micronutrients (particularly iron with 9.0 mg/100 g), vitamins and also a high energy value [28]. This could justify the vigor and the appetite observed in sickle cell subjects understudy.

Apart from its antisickling properties due to polyphenols (mainly anthocyanins), Drepanoalpha® would prevent sickle-cell subjects from current infections such as malaria and bacterial infections. In addition, the richness of Drepanoalpha® in secondary metabolites such as alkaloids and triterpenoids is an added value because these compounds are known for their antimicrobial properties [29].

3.2.2 Para-clinical parameters

Anemia occurs when the hemoglobin rate is less than 14 g/dL or 12 g/dL for respectively men and women. The main causes of anemia are deficiencies of iron and folate or vitamin B12, the excess destruction of red blood cells or hemolysis [30]. Drepanoalpha® have already showed an increase of Hb and red blood cells number in animal models [24-26]. Our research team previous work [25] also showed that Drepanoalpha® had a high iron content which is a haematopoietic factor that would prevent anemia in sickle cell subject.

For the considered subject the mean value of Hb level was 5.3±1.9 g/dL before treatment, 7.9±2.2 g/dL after 30 days and 8.9±0.8 g/dL after 60 days. For Hct, before the treatment the mean value was 16.0±0.1 %, 24.0±4.2% after 30 days of treatment and 27.0±3.2 after 60 days of treatment. By comparing the mean values of hematocrit and/or hemoglobin before and after treatment with Drepanoalpha®, it was found that there is a very significant difference ($p < 0.05$). This indicates that Drepanoalpha® increases significantly the hemoglobin level and thus prevents the anemia. This confirms results obtain for ten cases which were recently submitted to Drepanoalpha® treatment [28]. It can be proposed that this treatment be used for a time longer than 60 days in order to permit the patient to recover the normal hemoglobin level.

The possibility of a selection bias was estimated, following the situation at the individual pathological level of each patient. A definition of the diagnostic criteria was taken into account and the clinical and Para-clinical parameters of different groups were compared.

3.2.3 Cost of care in sickle cell crises

It is well established that in sickle-cell subjects, the sickling of red blood cells causes vascular obstruction, which is the basis of many crises. Taking care of these crises require a financial and social contribution. Obtained results show that sickle cell disease management with Drepanoalpha®, considerably reduces the crises number and the hospital cost. In fact, mean number of crises determined was 2.82 ± 0.60 and the hospitalization duration of 24.56 ± 4.90 with at least two transfusions that cost about 226.32 ± 11.31 $. However, during the treatment with Drepanoalpha® no crisis and no hospitalization was noticed for all considered subjects for a cost about 30.88 ± 1.54 $. These values clearly show that the Drepanoalpha® treatment allows families to be socially stable saving about 196 $ for two months.

4. CONCLUSION

The aim of this study was to assess the general condition of 34 sickle cell disease patients treated with Drepanoalpha® considering some clinical, biological, socio-demographic and socio-economic parameters. Obtained results showed that Drepanoalpha® has significantly suppressed apparent sickle cell disease characteristics such as jaundice, pallor, splenomegaly and abdominal bloating known as consequence of hyperhemolysis and sickling of blood red cells. This nutraceutical decreased physical asthenia and anorexia, prevented sickle cell subject infections and increased hemoglobin and hematocrit levels. The number of crises in all subjects was also reduced conducting to the decrease of treatment cost. This study completes previous works done with Drepanoalpha® *in vitro* and on animal models about antisickling activity, chemical composition and acute and sub-acute toxicity. It can be concluded that Drepanoalpha® is potential safe drug that can be used in the management of sickle cell disease. However, a study with an important number of patients have to be done and chromatographic profile of the phytomedicine to be done.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this manuscript.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the ethics committee of the department of biology, sciences faculty, university of Kinshasa and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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