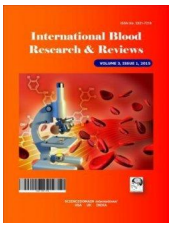

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Therapeutic Effects of Camel Milk to Sickle Cell Anaemia Patient

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Authors' contributions

This work was carried out in collaboration between all authors. Author YBR carried out the research and participated in writing the manuscript. Author SGI managed the literature searching and wrote the manuscript. Author MJL designed and supervised the study. Author RSUW co-supervisor I supervised the data interpretation. Author NMJ co-supervisor II supervised and reviewed the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

The therapeutic benefits of camel milk consumption are a supplement to routine sickle cell disease management. In maintaining hemolytic crises in sickle cell anaemia, patients were assessed during a six weeks study. Throughout the study, 20 patients were recruited for the study and divided into 4 groups, 5 patients per group. Group 2, 3 and 4 were treated with daily consumption of raw camel milk (100 ml, 50 ml + Folic acid + Paludrin and 100 ml + Folic acid + Paludrin respectively). In all groups, the foetal haemoglobin (Hb F), packed cell volume (PCV), platelet, red blood cell (RBC) and white blood cell (WBC) count were measured before initiation of the study and monitored at 2 weeks intervals for 6 weeks. In the group that took camel milk (50 ml in addition to Folic acid and Paludrin), there was a significant increase in WBC (8.16 ± 4.12 to 16.68 ± 3.53), a significant increase in PCV (21.28 ± 1.23 to 25.24 ± 1.11) with decrease in platelet (311.80 ± 61.93 to 260.40 ± 29.22) and significant increase in Hb F (7.06 ± 2.42 to 10.02 ± 2.41) compared to group 1 (control). However,

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there was no significant difference in the haematological parameters of group 2 and 4. The results implied that the consumption of camel milk in sickle cell patients resulted in an increase in foetal hemoglobin concentration which prevented crises in almost all the patients. Increase in foetal haemoglobin has been postulated to reduce hemolytic crises in sickle cell anaemia patients. Based on these findings, camel milk consumption may, therefore, be considered useful in the management of sickle cell diseases.

Keywords: Benefits; camel milk; foetal haemoglobin; red blood cells; sickle cell disease.

1. INTRODUCTION

Sickle cell anaemia (SCA) is a genetic disorder which affects the haemoglobin [1]; the molecule in red blood cells that delivers oxygen to cells throughout the body [1]. Sickle cell disease (SCD) is a common disease which plagues our communities in Africa and deserves cooperation from both medical practitioners and scientists in related areas to identify rational and sustainable strategies to manage this condition effectively.

Sickle cell is a heritable disease for which no cure has yet been found. Very often in our midst, we sadly experience the tremendous suffering and helplessness of parents managing children who have sickle cell disease (SCD). Children with SCD are characteristically thin, stunted in growth, pale because of chronic hemolysis and cell death, poor fat muscle and bone mass. These characteristics are associated with increased energy demand. Hydration maintains the integrity of red blood cell (RBC) membrane hydration. If the membrane becomes dehydrated, this impacts on its deformity which may lead to sickling. The red blood cell undergoes sickling when deoxygenated [2,3]. The existence of these abnormally shaped cells was first reported in 1910, when Herrick described their occurrence in a black dental student. The abnormality was subsequently identified as a result of an exchange of the amino acid valine for glutamate in the beta-globulin chain of the haemoglobin molecule [4]. This abnormal haemoglobin becomes polymerised causing the red blood cell to assume a sickle shape and making the cell both rigid and fragile [5,6]. People with this disorder have typical haemoglobin molecules called haemoglobin S, which can distort red blood cells into a sickle or crescent shape [7]. Hb S when deoxygenated will polymerise to form microfilaments and micro cables that distort RBC. The sickle forms of the RBC then occlude the microcirculation with subsequent infarction and necrosis [8]. The disease is characterised by chronic hemolytic anaemia and intermittent crises of variable frequency and severity. The latter include pain crises, other vaso-occlusive episodes such as pulmonary or central nervous system infarction, as well as aplastic crises. Signs and symptoms of sickle cell disease usually begin in early childhood; characteristic features of this disorder include a low number of red blood cells (anaemia), repeated infections and periodic episodes of pain in some parts of the body. The severity of symptoms varies from person to person. Some have mild pains while some have severe illnesses that need to be hospitalised [9]. Researchers are studying various drugs, as well as mineral supplements such as magnesium folate and zinc sulfate, that may help prevent potassium loss and red blood cell dehydration.

Camel milk is a rich source of proteins with potential antimicrobial activities; these proteins are not found in cow milk or found only in a minor amount [10]. Camel milk is believed to modulate the immune system [11]. Camel milk used medicinally for centuries by nomadic is the closest to human mother's milk and contains 10 times more iron and three times more vitamin C than cow's milk [12]. Camel milk is rich in non-saturated fatty acids, iron, vitamin B and C [12].

Presently the healthcare cost in the management of patients with sickle cell disease is disproportionately high compared with the number of people afflicted by the disease. The group most affected by sickle cell disease is the rural people who belong to the low socio-economic class. Therefore, the use of alternative supplements has been on the increase in the management of sickle cell disease [13].

Camel milk has been widely used to treat diseases, but its therapeutic effect against sickle cell anaemia disease has not been studied. Camel milk contains iron and B vitamins which are essential for the synthesis of red blood cells, and camel milk contains phenylbutyrate, a compound found to be important in the production of phenylacetate which increases the production of fetal haemoglobin in sickle cell

anaemia patients. Foetal haemoglobin interferes with the polymerization of sickle haemoglobin, increased in foetal haemoglobin production could decrease the severity of disease in subjects with sickle cell anaemia. Most sickle cell anaemia patients of poor background cannot afford the treatments in the hospitals; this aroused the interest of the authors to investigate the effect of this milk against sickle cell disease.

2. MATERIALS AND METHODS

2.1 Sample Collection

Fresh camel milk was obtained in the evening from a herd of camels, from Kwalkwalawa village located in the vicinity of Usmanu Danfodiyo University Sokoto, Sokoto state. By using hand milking in sterile screw bottles and then transferred to an icebox transported to the laboratory and kept in a refrigerator at 4°C.

2.2 Chemicals and Reagents

All chemicals and reagents used in this study were of analytical grade. ERMA diluents, lysing and cleaning solutions were procured from AGD Biomedicals, Mumbai, India and the reagents were used for full blood count analyses. Cyanmethaemoglobin and Drabkins solution were procured from BDH chemical Ltd. Poole, England and were used for determination of foetal haemoglobin.

2.3 Sickle Cell Anemia Patients

The sickle cell anaemia (Hb SS) considered for this study were 20 (Male: 11 Female: 9) with in the age of 6 months to 16 years attending the sickle cell anaemic clinic of Usmanu Danfodiyo Teaching Hospital Sokoto. The blood samples collected from the patients were analysed for confirmation of sickle cell anaemia through haemoglobin electrophoresis using a modified method of Jain and Dar [14].

2.4 Informed Consent and Protection of Patients

Parental consent and that of authorities of Usmanu Danfodiyo Teaching Hospital Sokoto were obtained before the patients were recruited for the study. Ethical certificate was issued and the registration number is UDUTH/HREC/2015/380. All the patients and their parents were duly briefed of the nature of the study.

2.4.1 Inclusion criteria

Determination of malaria parasite and genotype of the patients was taken and only Hb SS were recruited and those with malaria were treated before the study.

2.4.2 Exclusion criteria

Excluded from the study were children with similar but non sickle cell disease and those with other globulin disorders.

2.5 Blood Sample Collection

Samples were collected by staff of Usmanu Danfodiyo Teaching Hospital Sokoto. Three (3) ml of venopuncture blood were collected from each of the patients using a plain plastic syringe. The blood was placed in a labeled vial containing EDTA. All blood samples collected were immediately analysed. Base line and serial hematological tests were performed after every two (2) weeks for a period of 6 weeks.

2.6 Experimental Design

The twenty (20) recruited patients of different age groups (6 months to 16 years) attending the sickle cell anemia clinic of Usmanu Danfodiyo University Teaching Hospital were randomly divided into four groups of five patients each as follows:

Group 1: Patients in this group serve as control; Hb SS with neither drug nor treatment with camel milk.
Group 2: Patients in this group were Hb SS treated with 100 ml of camel milk only.
Group 3: Patients in this group were Hb SS treated with 50 ml of camel milk in addition to Folic acid and Paludrin.
Group 4: Patients in this group were Hb SS treated with 100 ml of camel milk in addition to Folic acid and Paludrin.

All the patients in each group were properly supervised and monitored for strict compliance with the protocol. They are also not allowed to take any drug or formulation that may influence any of the hematological parameters to be analysed without the permission of their doctors.

2.7 Hematological Analysis

Foetal Hemoglobin (Hb F) was estimated using automated HPLC as described by Dacie and Lewis [15].

2.7.1 Determination of full blood count

Determination of packed cells volume (PCV), white blood cells (WBC), red blood cells (RBC) and Platelets were analysed using full automatic blood cell counter PCE-210 Version 5.4.

2.8 Data Analysis

The data were presented as mean ± standard error of the mean; the results were analyzed using Instant version 3.5. One-way analysis of variance (ANOVA) was used to compared between means and Tukey multiple comparison test was used to determine variation between means in all groups and values were considered statistically significant at (P<0.05).

3. RESULTS AND DISCUSSION

3.1 Results

The effect of camel milk on complete blood count of sickle cell anemia patients is presented in Table 1. There was no significant difference in white blood cells count (WBC) of sickle cell patients that were treated with 100 ml of camel milk only (group 2) to that of group 1 who were neither giving drugs nor treatment with milk. There was a significant increase (P<0.05) in WBC of group 3; patients treated with 50 ml of camel milk in addition to folic acid and paludrin throughout the 6 weeks period of treatment. There was a significant increase in WBC of group 4 after 2 weeks of treatment with 100 ml of camel milk in addition to folic acid and paludrin. There was no significant difference (P>0.05) in red blood cells count (RBC) of treated groups to that of control (group 1) except for group 3 which has a significant increase in RBC after 4 weeks of treatment with 50 ml of camel milk in addition to folic acid and paludrin. There was no significant difference (P>0.05) in packed cell volume (PCV) of group treated with 100 ml camel milk only (group 2) to that of untreated group (control) to that of control. There was a significant increase in PCV level of group 3 patients to that of groups 1, 2 and 4. Likewise, there was a significant increase in PCV of group 4 patient after 2 weeks administration of 100 ml camel milk in addition to normal drugs (folic acid and paludrin). There was no significant different (P>0.050) in platelet count of all groups to that of control except group 4 which has a significant increase in platelet after 6 weeks of treatment with 100 ml camel milk in addition to folic acid and paludrin.

Table 1. Effect of camel milk on complete blood count of sickle cell anemia patient

Parameters		Group 1	Group 2	Group 3	Group 4
WBC ($X10^9$/L)	Before	7.03±1.13	11.68±1.29	8.16±4.12	10.24±3.25
	2WKS	6.23±0.63	11.28±0.62	14.10±2.69[a]	14.58±1.90[a]
	4WKS	6.40±0.40	11.92±0.87	16.44±3.27[a]	14.06±2.51
	6WKS	5.93±0.53	10.70±1.21	16.68±3.53[a]	13.86±1.87
RBC ($X10^{12}$/L)	Before	3.30±0.19	2.04±0.12[a]	2.77±0.42	2.65±0.14
	2WKS	3.31±0.20	2.65±0.09	3.18±0.10	3.82±0.48
	4WKS	3.17±0.23	2.25±0.12	3.73±0.44[b]	2.72±0.16
	6WKS	3.07±0.23	2.30±0.09	3.62±0.53	2.78±0.21
PCV (%)	Before	19.13±0.03	16.74±0.92	21.28±1.23[b]	19.96±0.94
	2WKS	18.70±0.30	18.86±0.53	25.20±1.41[abd]	23.06±0.39[a]
	4WKS	19.33±0.07	17.12±0.84	24.40±1.13[abd]	20.14±1.08
	6WKS	19.30±0.06	19.04±0.59	25.24±1.10[ab]	22.26±1.06
Platelet ($X10^9$/L)	Before	328.67±38.67	481.80±53.37	311.80±61.93	607.00±78.33[ac]
	2WKS	334.00±34.00	375.20±47.44	447.20±62.71	387.60±59.91
	4WKS	310.00±40.00	372.60±30.43	252.80±31.33	392.20±45.44
	6WKS	293.33±48.33	428.00±36.00	260.40±29.22	480.20±60.17[c]

Values are expressed as Mean±SEM. Values with the superscript "a" indicates statistically significant with group 1 at P<0.05, "b" implies significant with group 2 at P<0.05, "c" indicates significant with group 3 at P<0.05 and "d" indicates significant with group 4 at P<0.05. WBC: White blood cell; RBC: Red blood cells, PCV: Packed cells volume BF: Before Administration; WKS: Week's administration

Table 2. Effect of camel milk on Hb F count of sickle cell anemia patients

Groups	Hb F (%)			
	BF	2WKS	4WKS	6WKS
I	1.90±0.50	1.93±0.43	1.90±0.50	1.91±0.40
II	2.94±0.44	3.34±0.45	4.38±0.76	5.30±0.72
III	7.06±2.42	7.96±2.07[a]	9.26±2.30[a]	10.02±2.41[a]
IV	3.20±0.86	3.42±0.88	4.68±1.27	5.42±1.29

Values are expressed as Mean±SEM. values with superscript "a" indicates significant with control (group 1) at (P<0.05); Hb F: Foetal hemoglobin BF: Before Administration; WKS: Week's administration

The effect of camel milk on Hb F count of sickle cell anemia patients is presented in Table 2. There was no significant different ($P > 0.05$) in Hb F of all the treated groups as compared with control except for group 3 which has a significant increase ($P < 0.05$) in Hb F when compared with control.

3.2 Discussion

Treatment of sickle cell anemia (SCA) patients with camel milk and routine drugs (folic acid and paludrin) resulted in some hematological responses, throughout the period of study there was no any adverse effect by the camel milk in all the treatment groups. Sher et al. [16] defined hematological response as an increase in the Hb concentration of at least 2 g per deciliter in patients with thalassemia and a two fold increase in Hb F in patients with SCA. The short-term study duration was undertaken to assess the efficacy, safety and acceptability of camel milk as potential therapeutic agent for sickle cell anemia patients. It may be stated that camel milk may be safe and efficacious in improving hemolytic crises. The camel milk supplementation might have the ability to delay the hemolytic effects thereby allowing the synthesis of beneficial hematological parameter as was observed in groups treated with camel milk with or without routine drugs.

The effects of camel milk on hematological parameters were examined in camel milk and camel milk plus drugs treated groups of sickle cell patients. The significant increase in hematological parameters of group treated with 50 ml camel milk in addition to routing drugs might be due to positive actions of camel milk in the presence of folic acid and paludrin. Although, the abnormal increase in WBC count of group three might be due to other factors such as bacterial infections rather than adverse effect from camel milk supplementation as there was no any adverse reaction from consumption of camel milk.

Camel immune system is stronger than that of humans' and the small immunoglobulins may likely pass from the camel milk into the human blood. As immunoglobulins are found in camel milk throughout lactation, drinking milk would provide a tool for combating autoimmune diseases by rehabilitating the immune system rather than its depression. Immunoglobulins (Igs) are large long and short-chained domains, having difficulties reaching and penetrating antigens. Camel immunoglobulins have no short chains and small so are active against antigens. The camel immunoglobulins present in camel milk might serve as a tool for combating autoimmune diseases. The most pertinent factor is that conventional management of autoimmune diseases are based on immune-suppression Goldberg et al. [17], while camel milk Igs enhance the immune system, revitalizing immune integrity [18]. Camel milk was first mentioned in the Holy Qur'an as being a remedy for sicknesses [Verse 2:136-154]. This claim was valid in this study today and, therefore, can be considered a natural and historical management. Camel milk has being reported to have a high level of iron [19] this might be the reason for the increased level of RBC and Hb F in group III. Prophet Muhammad (SAW) considered camel milk as medicine [Bukhari 7:71 Medicine#589 and #590]. Camel milk contains various protective proteins such as lysozymes, immunoglobulins, lactoperoxidase, lactoferin [20], mainly enzymes which exert antibacteria and immunological properties [20]. The presence of these proteins helps explain some of the natural healing properties of the milk. The known immunological action of some protective proteins present in camel milk such as Lysozymes which Participates in primary immune system and is based on targeting of structures common to invading pathogens. Immunoglobulins give protection to the body against infections [21].

The groups supplemented with a combination of routing drugs and camel milk has the highest percentage increase in Hb F. The antisickling

agents present in camel milk are known to increase the Hb F level in patients with SCA. Rodgers et al. [22] reported that hydroxyurea increase the level of Hb F in patients with SCA. Similarly Sher et al. [16] reported an increase in Hb F in SCA patients treated with an infusion of arginine butyrate. Noguchi et al. [23] reports that an increase in the level of Hb F in sufficient quantities can ameliorate sickle cell disorder. Hb F contains gamma globin chains instead of beta chains. Hence, it is not affected by the genetic defect that causes SCA. Increase levels of Hb F decreases the tendency towards intracellular polymerization of sickle Hb that characterizes the disease [24].

The insignificant changes in platelet levels of the treatment groups is of advantageous as an increase platelet count would lead to high reactivity and hyper-coagulation and changes in the levels and turnover of clotting factors have been associated with sickle cell anemia [25].

Patients with SCA are known to have a reduced RBC and WBC levels. This is as a result of the increase hemolysis resulting from vaso-occlusion phenomena that is common in patients with SCA [26]. Although, camel milk supplementation with or without routine drugs have no any changes in the levels of both the RBC and WBC. Hydroxyurea is known to increase the levels of Hb F, which in turn decrease the tendency towards intracellular polymerization of sickle Hb that characterizes the SCD. A decrease in the polymerization of Hb S will reduce vaso-occlusion and hemolytic processes. Goldberg et al. [17] reported an increase in the level of Hb F and a reduction of the rate of hemolysis and intracellular polymerization of Hb S in patients with SCA. Treatment of SCA patients with camel milk resulted in an increase Hb F production which may inhibit polymerization and hemolysis. The therapeutic benefits of camel milk, as supplement to sickle cell anemia patients, appear to be safe and efficacious in improving hematological parameters. Camel milk was well tolerated with no adverse effect in all the treatment groups and its use was not associated with an increase in hemolytic crises episode.

4. CONCLUSION

The results obtained in this study suggest that group treated with 50 ml camel milk in addition to Folic acid and Paludrin displayed a significant increase in Hb F, WBC, PCV throughout the period of treatments and a significant increase in RBC count after 4 weeks of treatment. 50 ml camel milk plus routine drugs might be good dosage that could reduce hemolytic crises in sickle cell anemia patients.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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