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ISSN 0189-6016©2008EFFECTIVENESS AND SAFETY ASSESSMENT OF *MIST TONICA*, A HERBAL HAEMATINIC

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Abstract

Anaemia is a widespread public health problem, and in Ghana it is the fourth leading cause of hospital admissions and the second factor contributing to death. *Mist Tonica*, an herbal haematinic produced by the Centre for Scientific Research into Plant Medicine (CSRPM), Ghana, was assessed for its effectiveness and safety in humans after Ethics Committee approval. Clinically established anaemic-patients aged, 13 years and above, with haemoglobin levels less than 11.5 g/dl and 13.5g/dl for females and males respectively were treated with *Mist Tonica*, 8.96 g/ 40 mls three times daily for two weeks. The mean haemoglobin rise per week caused by *Mist Tonica* was 1.92 (0.76) g/dl, range (1.66 - 2.55) g/dl/week and over 88 % of the patients on *Mist Tonica* had their appetite for food improved. Haematological profile, liver and kidney functions were not adversely affected by *Mist Tonica*. Results of the study suggest that *Mist Tonica* is an effective and safe herbal haematinic.

Key words: Anaemia, haemoglobin, herbal, haematinic, safety, effectiveness

Introduction

Anaemia is defined as a state of haemoglobin concentration below an established cut-off level for age and sex of the individual. Quantitatively, in an adult female and male, it is less than 11.5 g/dl and 13.5 g/dl, respectively. It is associated with a decreased packed cell volume and or a decreased haemoglobin concentration.

WHO estimates for the number of anaemic people globally for the year 2004 was 2 billion, representing 30 % of the world's population (WHO, 2004). In Ghana, a review of the disease-profile and pathology reports of some selected hospitals, ranked anaemia as the fourth leading reason for hospital admissions and the second factor contributing to death. Fifty-nine percent (59 %) of pregnant women and lactating mothers were anaemic whilst 83.5 % of pre-school children and 71.3 % of school-age children were anaemic. Analysis of the economic impact of anaemia in Ghana indicated that from 2001 to 2005, Ghana's female workforce lost over one hundred and forty two billion cedis in economic productivity due to anaemia (Agble, 2004).

It is known that about 70 % of Ghanaians depend on herbal medicine for their primary health care needs. This is because they are most often cheaper, easily available and thought to have lesser side effects than allopathic medicines. Many of such herbal products have been used in Ghana for the management of anaemia. One of such products is *Mist Tonica*, produced and used at the CSRPM for the effective management of anaemia and loss of appetite. *Mist Tonica* is a decoction prepared from:

Khaya senegalensis (Desr.) A. Juss.; (Family: Meliaceae),

Mitragyna stipulosa(DC.) O. Ktze.; (Family: Rubiaceae)

Kigelia Africana (Lam.) Benth. ; (Family :Bignoniaceae).

K. senegalensis is commonly called Mahogany. It is a tree that grows up to about 20 metres high. It is distributed over all inter-tropical Africa. Traditionally, the stem-bark is used to treat convulsion, arthritis, haemorrhoids, malaria, boils, anaemia, helminthiasis and heat rash. The leaves are used to treat headache. The plant is used to treat loss of appetite (Mshana *et al*, 2002; Dalziel, 1948).

M. stipulosa is commonly called African Linden. It grows in forests or in thickets in Africa. Plants in this family are used to treat various ailments such as paralysis, loss of appetite, fever and malaria. The stem-bark of *Mitragyna stipulosa* is used to treat anaemia (Mshana *et al*, 2000; Ayensu, 1978).

The common name of *K. africana* is Sausage tree. It is distributed over all inter-tropical Africa. The leaves are used to treat wounds while the roots are used for constipation and tape worm infestation. The whole plant is used for haemorrhoids. The bark is used for otitis media, arthritis and anaemia. The fruits are used to treat constipation while the fruits and roots are for lumbago, snakebite and haemorrhoids (Mshana, *et al*, 2000; Ayensu, 1978).

Even though *Mist Tonica* has been successfully used at the CSRPM for the effective management of anaemia and loss of appetite, there is no available empirical clinical data to support this assertion. The aim of this study was therefore to clinically evaluate the effectiveness and safety of *Mist Tonica* in anaemic patients with varying causes of anaemia.

Materials and Methods

Design of Study

The study design was based on an open, prospective, non-comparative clinical trial in 45 patients with clinically established anaemia, and confirmed by laboratory investigations. Study commenced after Ethics Committee approval.

Treatment and Duration of Study

A decoction of *Mist Tonica* is dispensed as 8.96 g/ 40 mls three times daily before meals for a period of 2 weeks.

Sample Selection Criteria

Inclusion Criteria

The selection criteria included male or female older than 13 years with haemoglobin levels of less than 11 g/dl or 13.5 g/dl for females and males respectively and the ability to provide written informed consent to participate in the study, and the ability to comply with the protocol. For those below 18 years, informed consent was provided by parents.

Exclusion Criteria

Patients on concurrent treatment with allopathic haematinics or other herbal medicines or with severe kidney or liver dysfunction or both and breastfeeding mothers were excluded. Also patients with both alcohol and drug abuse problems to such an extent that this will prevent compliance with dosing and evaluations were excluded from the study.

Patient Recruitment and Follow-up

During OPD consultations, patients who were clinically identified as anaemic were made to undergo laboratory tests to determine the packed cell volumes and haemoglobin levels and to confirm the cause of anaemia (where necessary). Blood was also taken for baseline kidney and liver function tests as well as other safety parameters such as fasting blood sugar and platelets, WBC and differential counts. *Mist Tonica* was then dispensed according to the recommended dosing for two weeks. Patients were to report for two follow –up visits; on days 7 and 14 after commencement of therapy. On day 7, full case history and examination were conducted. Patients were

assessed for drug compliance, possible adverse drug reactions and haemoglobin and packed cell volume. On day 14, clinical assessment of the patients, haemoglobin level and packed cell volumes, liver and kidney function tests as well as fasting blood sugar and platelets, WBC and differential counts were conducted and compared with baseline.

Analysis of Data

Data were statistically analysed using windows SPSS, 11.0 software. The mean rise in haemoglobin concentration per week due to *Mist Tonica* was computed. It was determined if it followed the normal distribution curve and was also tested statistically against the established rise in haemoglobin level of 1 gm/dl per week (Hope et al, 1998) at 95% confidence level using the allopathic haematinics (BNF, 2004). The effects of *Mist Tonica* on the liver and the kidneys as well as fasting blood sugar and haematological profile were also analysed statistically.

Results

Age-Sex Distribution

Twenty-five males and twenty females successfully took part in the test study. The modal age group of the study was 33-42 years. This constituted 33.3% of the test study. Twenty percent (20%) of the population was between 13-22 years and 28.9% between 23-32 years whilst 8.9% were 43-52 years. The test population presented with anaemia of varying underlying causes. 70 % of the population presented with anaemia due to malaria and 20 % presented with anaemia due to nutritional deficiency and other causes as shown in Table 1. The mean haemoglobin rise per week with *Mist Tonica* treatment revealed that the age group with the least haemoglobin rise of 1.66 g/dl/week was 23-32 years. This constituted 28.9% of the population and 43-52 years population group (8.9%) had the highest haemoglobin rise of 2.55 g/dl/week. The average haemoglobin rise with respect to the total population was 1.92 (0.76) g/dl/week.

A One-Sample t Test between *Mist Tonica* and allopathic haematinics

A one-sample t-test was performed to compare the mean haemoglobin rise with *Mist Tonica* and an established haemoglobin rise with allopathic haematinics of 1 g per week. The results showed that it was highly significant (p -value=0), two-tailed and the 95% confidence interval of the difference between the 1 g of allopathic haematinics and *Mist Tonica* is 0.6556 and 1.2083 for the lower and upper limits respectively. Hence, *Mist Tonica* is capable of raising the haemoglobin level above 1 g; the least level being 1.6556 g/dl/week and the upper value is 2.2083 g/dl/week (Table 2).

Safety Assessment of *Mist Tonica*

Total white cell and differential counts, fasting blood sugar, liver enzymes and kidney function tests showed no comparable statistical differences between baseline and the end of therapy values (Table 3).

Discussion

This study sought to validate the claim for the clinical effectiveness and safety of *Mist Tonica* in the management of anaemia. The sampling distribution of the mean haemoglobin rise of the test population with *Mist Tonica* follows the normal curve distribution. The least haemoglobin rise with *Mist Tonica* on the population per week was 1.66 g/dl, the highest was 2.55 g. Statistical tests using a one sample t test confirmed that at 95% confidence level, the least value of haemoglobin rise (1.66 g/dl/week) was even above the established rise with allopathic haematinics treatment of 1 g/dl/week (Hope et al, 1998).

Table 1: Causes of anaemia during the study.

Diseases	Percentage (%) of anaemia-related diseases
1. Malaria with Anaemia	70
2. Sepsis With Anaemia a. Tuberculosis b. Pneumonia c. Urinary tract Infection	3
3. Sickle-cell Disease with Anaemia	0.5
4. Helminthiasis	1
5. Nutritional a. Iron deficiency anaemia b. Folate and Vit BCo deficiency	20
6. Burns with Anaemia	0.5
7. Post Surgery with Anaemia a. Ruptured ectopic gestation b. Typhoid perforation c. Prostatectomy	5

Table 2: One-sample t-test

	Test Value = 1					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Mean haemoglobin rise/week/mist tonica	6.847	35	.000	.9319	.6556	1.2083

Table 3: Details of Safety variables- Haematological and Biochemical Investigations in Patients (n=45) with Anaemia on *Mist Tonica* therapy.

Safety Variable	Normal range	Baseline value Mean ± SD	Value At Follow-Up-2 (2 weeks) Mean ± SD
WBC×10 ⁹ /L	4.0-11	5 ± 1.05	6.2 ± 1.03
Neutrophils (%)	40-75	60.80 ± 5.65	59.80 ± 4.72
Eosinophils (%)	1-6	1.47 ± 1.22	1.23 ± 0.50
Basophils (%)	0-1	0	0
Lymphocytes (%)	20-45	27.23 ± 4.54	27.93 ± 5.07
Monocytes (%)	2-10	2.57 ± 0.94	0.70 ± 1.70
SGPT/ALT (iu/L)	5-35	16.03 ± 6.97	15.45 ± 6.45
SGOT/AST(iu/L)	5-35	17.04 ± 5.65	16.25 ± 6.05
Creatinine (umol/L)	M: 53-97	60 ± 2.7	59 ± 1.5
	F: 44-80	51 ± 1.9	48 ± 1.2
Urea(umol/L)	1.7 -9.1	3.4 ± 1.05	3.3 ± 1.03
Platelets×10 ⁹ /L	150 - 400	197 ± 20.5	202 ± 15.7
Fasting Blood Sugar (mmol/L)	3.5 - 5.5	4.07 ± 0.1	4.05 ± 0.2

The uniqueness of *Mist Tonica* stems from the fact that it acts as both a haematinic and an appetite enhancer. Even though phytochemical screening on *Mist Tonica* revealed the presence of saponins, tannins and flavonoids, the active principle responsible for the haematinic activity of the formulation is not known. Improvement in appetite may be due to the presence of *Khaya senegalensis* which is known to be an appetite stimulator (Mshana *et al.*, 2000; Dalziel, 1948)

These findings/observations are very significant as *Mist Tonica*, like many herbal haematinics could serve as potential substitute for blood transfusion (Erah *et al.*, 2003).

Conclusion

Mist Tonica appears to be an effective herbal treatment for the management of anaemia in humans. Its ability to raise haemoglobin levels by at least 1.66 g/dl per week makes it a potential useful haematinic agent. Results of the study also show that *Mist Tonica* has no adverse effect on renal and liver function or bone marrow of patients. This study validates the use of *Mist Tonica* as an herbal medicine in the management of anaemia.

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