

Semen Abnormality And Nigerian Herbal Remedies: A Preliminary Investigation.

H Enuh, C Oragwu, C Okeke, E Elu, O Orisakwe

Citation

H Enuh, C Oragwu, C Okeke, E Elu, O Orisakwe. *Semen Abnormality And Nigerian Herbal Remedies: A Preliminary Investigation.* The Internet Journal of Toxicology. 2012 Volume 8 Number 2.

Abstract

The uses of herbal products are not regulated in Nigeria and in many low-income countries and are freely available to everyone. The safety of these herbal medicines is poorly understood. Commonly used herbal remedies can interfere with reproductive health. This is a prospective study that investigated the possible effects of Nigerian herbal remedies on semen quality involving 218 patients who attended the fertility unit of Nnamdi Azikiwe University Teaching Hospital, Nnewi, Southeastern, Nigeria. Questionnaire was administered by an interviewer and a seminal fluid analysis with respect to motility, concentration, and volume were carried using WHO standard. The result showed that 83.97% of the patients with history of herbal intake had abnormal seminal fluid analysis while only 16.03% of subjects with no history of herbal intake had abnormal result. This gives a clue of the possibility of male infertility from Nigerian herbal remedies. The reproductive health damage from consumption of Nigerian herbal remedies should be identified with indepth risk assessment.

INTRODUCTION

The use of homeopathic and herbal medicines has increased in recent years. This has probably arisen as a result of a number of factors including disillusionment with conventional drugs, growing confidence in complementary medicine, and a belief that the products are safe, often on the grounds that 'natural' equates to safe^[1-4]. A review of literature has shown a range of favourable and unfavourable effects for a range of natural substances^[5]. Patients often turn to complementary medicines, including homeopathic and herbal remedies, for chronic and inflammatory conditions, and those refractory to the beneficial effects of conventional products^[6-10]. In Nigeria socio-economic deprivation, poverty and ignorance have led to trust and reliance on traditional herbal preparations for health reasons. The use of herbal products are not regulated in Nigeria and in many low income countries and are freely available to everyone. Cases of organ (kidney, liver, heart, testis, etc) failure after prolonged intake of herbal preparations have been anecdotally reported in Nigeria and other African countries. An increasing number of cases remain undocumented due to poor record keeping in the developing world^[11].

Nigeria has about twelve million infertile persons^[12]. Although there is a general documented belief that the most common cause of infertility in Nigeria is infection^[13], cases

abound where infection have been treated without correction of infertility^[12]. In Nigeria there are higher rates of irreversible oligospermia or azoospermia than most other causes of infertility and less resources for the management of infertility^[14]. Of adult couples in African countries, it is estimated that 10–25% are subfertile and of these subfertile couples female factors account for about 55% and male factors for about 30–40% of causes, while 5–15% of causes are unexplained^[12]. According to investigation on classification of infertility by Ikechebelu and coworkers based in Southeastern Nigeria, there is higher prevalence of male infertility in southeastern Nigeria. About 65.0% of them had primary infertility while 35% had secondary infertility^[15].

In view of these alarming statistics, our laboratory set out to investigate if there is a relationship between the intake of Nigerian herbal remedies (NHR) and semen quality and by extrapolation male reproductive health amongst men who reported to the infertility clinic of Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, Nigeria.

METHODOLOGY

STUDY SUBJECTS RECRUITMENT

Two hundred and eighteen male volunteers of infertile couples attending the infertility clinics of the Department of

Obstetrics and Gynaecology and Urology Clinic of Surgical Outpatient, Department of Surgery, Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria, who conformed to the selection criteria (Table. 1) were recruited into this prospective study. Their wives had no anatomic disorder and/or infection and the men shared the common complaint of difficulty to impregnate their wives after 1 year effort of normal sexual activity with the intention to become pregnant.

Figure 1

Table 1. Criteria for inclusion and exclusion of subjects

| Inclusion Criteria | Exclusion Criteria |
|---|--|
| <ul style="list-style-type: none"> • men within the reproductive age of 20–45 years; • male partners of couples in good marital harmony, living together and having regular unprotected coitus for two or more years; • normal descended testes. | <ul style="list-style-type: none"> • male contraceptive users; • testicular varicocele; • genital infections; • long term medications; • previous groin/scrotal surgery; • known HIV positive men; • smoking/chronic alcohol intake (other than occasional alcohol intake); • chronic and serious systemic illness; • men currently on fertility drugs or steroid preparations. |

DATA COLLECTION

With informed consent, a standard questionnaire was administered to each study subject in person to obtain information on age, occupation, lifestyle, education, exposure to passive smoke etc. Clinical students interviewed the infertile participants.

LABORATORY INVESTIGATION

Semen was obtained by masturbation after at least 3 days of sexual abstinence. The samples were analyzed within 2 to 4 hours of ejaculation using WHO 1999^[16] guideline (volume 2.0 ml or more, sperm concentration, 20×10^6 spermatozoa/ml or more, total sperm 40×10^6 spermatozoa per ejaculate or more, motility 50% or more with forward progression(categories a and b) or 25% or more with rapid progression(category a)within 60 minutes of ejaculation. Sperm counts were classified as follows: $<1 \times 10^6 \text{ ml}^{-1}$ azoospermia (AS), $1\text{--}20 \times 10^6 \text{ ml}^{-1}$ oligospermia (OS) and $>20 \times 10^6 \text{ ml}^{-1}$ normospermia (NS).

STATISTICS

Statistical analysis was performed using chi-square test. A p value <0.05 was considered statistically significant.

RESULTS

Figure 2

Fig 1a: Effect of Nigerian herbal remedy NHR on motility, count and volume of semen of the patients.

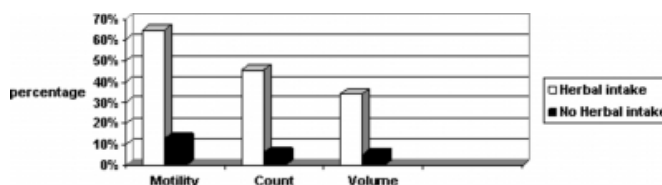


Figure 1a shows the effect of the herbal intake on motility, count and volume of semen of the patients. Herbal intake affected these parameters with the most profound effect on sperm motility in more than 60% of the patients. Among subjects with abnormal parameters 84% took NHR whereas 16% did not take NHR Fig 1b.

Figure 3

Figure 1b



Fig 2 shows the effect of herbal remedies on the type of infertility. Herbal intake tended to affect both primary and secondary infertility with primary infertility with a higher percentage (51%)

Figure 4

Fig 2: Effect of Nigerian herbal remedy on primary and secondary infertility

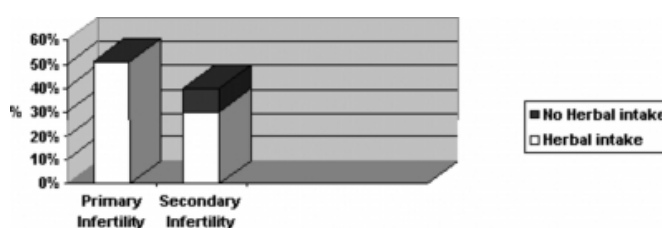
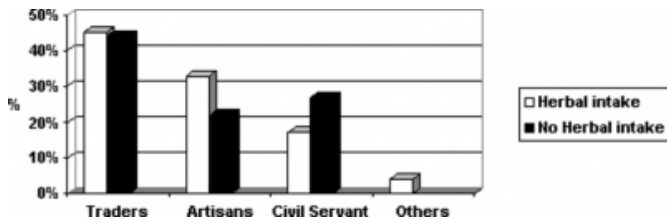


Figure 5

Fig 3: Socioeconomic status and education affected the peoples attitude to accepting Nigerian herbal remedy as an alternative care as can be seen on Fig 3. Uneducated traders and artisans showed more patronage of NHR than the educated civil servants.



DISCUSSION

Reproductive disorders are important health issues. The World Health Organization estimates that approximately 8% of couples, or 50–80 million people worldwide, have some forms of infertility^[17]. Although both exogenous exposures and endogenous pathological disorders have been associated with infertility, a significant proportion of infertility remains unexplained. In young generation, infertility is now affecting one couple in six^[18-19]. This may be due to the decrease in sperm quality as described previously^[20]. The most frequent factors implicated in male infertility are occupational exposure to heavy metals, such as Cd, Pb, Mn and Hg, to pesticides and solvents, smoking (exposure to Cd, Pb, Hg, Ni, Ar, Mn) and diet rich in sea food (exposure to methylmercury)^[21-22]. One of the major neglected source of these substances is herbal remedies. Hence the need to evaluate male infertility with respect to herbal remedies ingestion. We have investigated the possible effects of Nigerian herbal remedies on semen quality with respect to motility, concentration and volume of patients who attended the fertility unit of Nnamdi Azikiwe University Teaching Hospital, Nnewi, Southeastern, Nigeria.

In this study, sperm motility was mostly affected parameter among patients with history of ingestion of Nigerian herbal remedies. About 65% showed abnormal motility. Concentration and volume of the semen were also reduced in patients who admitted that they have been taken one form of herbal remedy or the other.

Although infertility may be due to endocrine, genetic, anatomical, immunological or psychogenic problem, it is well known that one of the immunological infertility may be caused by decreased mobility of spermatozoa induced by various physical and biochemical factors. The external sperm membrane consists of soluble antigenic components

and in some cases can induce the production of auto-(iso-)antibodies^[23]. In this study, sperm motility was mostly affected parameter among patients with history of ingestion of Nigerian herbal remedies.

Heavy metals are biologically active substances and may in susceptible individuals affect the immune system and cause health disturbances. Heavy metals are known to induce so called cellular hypersensitivity (delayed type or type 4 reaction) but humoral responses may be affected as well. An association between undesirable reaction to metals and presence of autoantibodies has been suggested by several authors^[24-26]. Changes in cytokine production were reported by others^[27-29]. Since metals such as mercury, cadmium and lead are toxic in relatively low concentrations^[30], undesirable reactions caused by metal antigens may further complicate the health status of the patient. Patients with autoimmune and allergic diseases may be particularly vulnerable^[31]. Metal-induced reactions are influenced by genetic background in experimental animals^[32] and

associated with certain HLA antigens in man^[33]. Association between the exposure to organic and inorganic mercury and male infertility has been described by Choy and Hanf with coworkers^[34-35]. The exposition to lead and cadmium resulted in the decrease of fertility and in lower quality of sperm^[36-37].

Herbal preparations are often aggressively advertised as “soft medicine or pure natural remedies”, as a variable alternative to pharmaceutical drugs called “chemical clubs”. However, as Ernst wrote, “the notion that natural can be equated with harmless is as prevalent as it is misleading”^[38]. The study of Obi et al 2006^[39] revealed that the Nigerian herbal remedies NHR contained high levels of iron, nickel, cadmium, copper, lead, selenium, and zinc sufficient to cause adverse health effect when regularly taken as recommended. These are usually ingested intermittently and in some cases for years^[40]. Exposures will be expected to vary from high doses to sub-acute doses. The lead content of these remedies may increase the blood lead levels. This remedy-induced fluctuation may increase the risk of lead toxicity depending on existing blood lead levels^[41] and the duration of remedy use. Prolonged use may significantly increase body lead burdens.

Because these heavy metals are usually not identified as being present or associated with traditional and herbal remedies, the clinical identification of metal toxicity is unlikely during a clinical evaluation, especially if the patient

hides the use of the NHR because of perceived embarrassment. The metal constituents of NHR may be the silent etiologic agents of a variety of ailments. Several possibilities exist to explain the presence of heavy metals in NHR, heavy metals could be included intentionally for alleged medicinal properties, the presence of heavy metal may be the result of accidental contamination during manufacture, for instance, from grinding weights or lead-releasing containers or other manufacturing utensils^[42]. Medicinal herbs may contain heavy metals when grown in seriously polluted soil^[43]. In this context, it is relevant to know that NHR may contain animal and mineral products which may also be contaminated with heavy metals^[44]. In Nigeria and most developing countries, pharmacovigilance is very nascent. In an ethnographic survey of the use of herbal medicines in Nigeria, 39% of the people used herbal medicines for cough, 62% for measles, 38% for ear infections and 24% used topical creams and soaps for skin infections^[45]. In Nigeria, the first line of treatment for 60% of children with high fever resulting from malaria is the use of herbal medicines at home^[46]. It is feared that the use of herbal medicines in adult may even be higher with the high growth of herbal market and its great commercial benefit. There are no documentations on the likely side effects or health effects of these herbal remedies.

Male infertility can also be classed as primary or secondary. Primary is seen in couples who has never conceived for the first time while in secondary, they have conceived in the past. In our work, we found 60.09% cases of primary infertility. This finding tend to be in agreement Ikechebelu and coworkers that reported high prevalence of male infertility in southeastern Nigeria with 65 and 35% primary infertility and secondary infertility respectively. In our work, we found 60.09% cases of primary infertility amongst the patients on Nigerian herbal remedies. NHR like B-success^[47], Operation Sweep^[48-49], and Rinbacin^[50] that were recommended for management of male infertility have been found to have deleterious effects on the testis of male albino rats. Orisakwe et al 2004^[51] demonstrated that consumption of Hibiscus Sabdarifa HS calyx extract a popular local red wine in Nigeria by growing rats reduced sperm counts and spermatogenesis with evidence of marked degenerative histological changes. It is feared that the uninformed local population must have been involved in the sterilization of their males by the habitual consumption of a local beverage of HS calyx extract. If HS is consumed throughout gestation and neonatal life, male reproductive function might be impaired by disruption of the development of sex organs

because the male reproductive system may be particularly vulnerable to toxic insult during gestation as has been observed with other substances. In a study performed to evaluate the effect of some these widely used herbs on sperm DNA, high concentrations of St John's Wort, Ginkgo biloba and Echinacea purpurea were found to damage the reproductive cells and were even mutagenic to sperm cells. Commonly used herbal remedies can interfere with sperm motility. Many should be avoided by couples experiencing fertility problems^[52].

Uneducated traders and artisans showed more patronage of NHR than the educated civil servants. Education perhaps rather than economic wellbeing may have contributed to choice of NHR.

Enlightenment and awareness creation may be useful in checking the untoward effect of complimentary alternative medicine in Nigeria in an addition to regulation. Since majority of Nigerians both in rural and urban areas consume these remedies, the Nigerian public should be alerted on the inherent danger in consuming some of these herbal remedies. The reproductive health damage from consumption of Nigerian herbal remedies should be identified with indepth risk assessment.

References

1. Gee BC, Wilson P, Morris AD, Emerson RM. Herbal is not synonymous with safe. *Arch Dermatol* 2002; 138: 1613.
2. Capasso R, Izzo AA, Pinto L, Bifulco T, Vitobello, Mascolo N. Phytotherapy and quality of herbal medicines. *Fitoterapia* 2000; 71: S58_/65.
3. Goldman P. Herbal medicines today and the roots of modern pharmacology. *Ann Intern Med* 2001; 135: 594_/600.
4. Cohen MH. Regulation, religious experience, and epilepsy: a lens on complementary therapies. *Epilepsy Behav* 2003; 4: 602_/606.
5. Topliss JG, Clark AM, Ernst E, Hufford CD, Johnson GAR, Rimoldi JM, Weimann BJ. Natural and synthetic substances related to human health. IUPAC Technical Report. *Pure Appl Chem* 2002; 74: 1957_/85.
6. Zini A, Fishcher MA, Nam RK, Jarvi K. Use of alternative and hormonal therapies in male infertility. *Urology* 2004; 63: 141_/43.
7. Van Wassenhoven M, Ives G. An observational study of patients receiving homeopathic treatment. *Homeopathy* 2004; 93: 2_/11.
8. Brunelli B, Gorson KC. The use of complementary and alternative medicines by patients with peripheral neuropathy. *J Neurol Sci* 2004; 218: 59_/66.
9. Sharples FMC, van Haselen R, Fisher P. NHS patients' perspective on complementary medicine: a survey. *Complement Ther Med* 2003; 11: 243_/48.
10. Smith JR, Spurrier NJ, Travis Martin J, Rosenbaum JT. Prevalent use of complementary and alternative medicine by patients with inflammatory eye disease. *Ocul Immunol Inflamm* 2004; 12: 203_/14.
11. Orisakwe O.E., Dioka C. E., and Ofoefule S.I., (1996). A

- comparative review of poisoning in Nigeria. *J. W. Afr. Pharm.* 10 (2): 53-55.
12. Giwa-Osagie OO. Nigeria has twelve million infertile persons. *Pharmanews* 2003;25(7):48-49.
13. Cates W, Farley TMM, Rowe PJ. Worldwide patterns of infertility, is Africa different? *Lancet* 1985;2:596-598
14. Osegbe DN, Amaku EO. The causes of male infertility in 504 consecutive Nigeria patients. *Int Urol Nephrol* 1985;17:349.
15. Ikechebelu JI, Adinma JI, Orie EF, Ikegwuonu SO, 2003. High prevalence of male infertility in southeastern Nigeria *Journal of Obstetrics and Gynaecology*, 23(6):657-659.
16. WHO laboratory manual for the examination of human semen and sperm cervical mucus interaction, 4th edition, Cambridge university press, Cambridge.
17. World Health Organization, 1987. Infections, pregnancies, and infertility: perspectives on prevention. *Fertil. Steril.* 47, 964-968.
18. Brugo-Olmedo S, Chillik C, Kopelman S. Definition and causes of infertility. *Reprod Biomed Online* 2001; 2(1):41-53.
19. Sundby J. Methodological considerations in the study of frequency, risk factors and outcome of reduced fertility. *Scand J Soc Med* 1989; 17(2):135-140.
20. International workshop on the Impact of the Environment on Reproductive Health (1991: Copenhagen). Impact of the environment on reproductive health. *Prog Hum Reprod Res* 1991; 20:1-11.
21. Gerhard I, Monga B, Waldbrenner A, Runnebaum B. Heavy metals and fertility. *J Toxicol Environ Health* 1998; 54(8):593-611.
22. Oliva A, Spira A, Multigner L. Contribution of environmental factors to the risk of male infertility. *Hum Reprod* 2001; 16(8):1768-1776.
23. Ulcova-Galova Z. Diagnosis- infertility. Attack of antibodies. Praha: Petrklíč; 1999. (In Czech)
24. Frank I, Bieger WP. Autoimmunität bei Patienten mit zellulärer Sensibilisierung gegenüber Dentalmetallen. *Immun Infekt* 1997; 2:70-76. (In German)
25. Kosuda LL, Greiner DL, Bigazzi PE. Effects of HgCl₂ on the expression of autoimmune responses and disease in diabetes-prone BB rats. *Autoimmunity* 1997; 26(3):173-187.
26. Pusey CD, Bowman C, Morgan A, Weetman AP, Hartley B, Lockwood CM. Kinetics and pathogenicity of autoantibodies induced by mercuric chloride in the brown Norway rat. *Clin Exp Immunol* 1990; 81(1):76-82.
27. Kaminska T, Filar J, Madej E, Szuster-Ciesielska A, Kandefer-Szerszen M. Modification of bovine interferon and tumor necrosis factor production by lead in vivo and in vitro. *Arch Immunol Ther Exp (Warsz.)* 1998; 46(5):323-328.
28. O'Brian-Ladner AR, Nelson SR, Murphy WJ, Blumer BM, Wesselius LJ. Iron is a regulatory component of human IL-1 beta production. Support for regional variability in the lung. *Am J Respir Cell Mol Biol* 2000; 23(1):112-119.
29. Bostofte E, Serup J, Rebbe H. Has the fertility of Danish men declined through the years in terms of semen quality? A comparison of semen qualities between 1952 and 1972. *Int J Fertil* 1983; 28(2):91-95.
30. Lawrence DA. Posited mechanisms of metal immunotoxicity. *Hum Exp Toxicol.* 1995; 14:114-116.
31. Bartova J, Prochazkova J, Kratka Z, Benetkova K, Vencliková Z, Sterzl I. Dental amalgam as a risk factor in autoimmune diseases. *Neuroendocrinol Lett* 2003; 24(1-2):65-67.
32. Bigazzi PE. Autoimmunity induced with metals. In : Chang LW, ed. *Toxicology of metals*. The USA: CRC Press, Inc 1996; 835-853.
33. Prochazkova J, Bartova J, Ivaskova E, Kupkova L, Sterzl I, Stejskal VDM. HLA - association in patients with intolerance to mercury and other metals in dental materials. *Disease Markers* 2000; 16:135-138.
34. Choy CM, Lam CW, Cheung LT, Briton-Jones CM, Cheung LP, Haines CJ. Infertility, blood mercury concentrations and dietary seafood consumption. *BJOG* 2002; 109(10):1121-1125.
35. Hanf V, Forstmann A, Costea JE, Schieferstein G, Fischer I, Schweinsberg F. Mercury in urine and ejaculate in husbands of barren couples. *Toxicol Lett* 1996; 1-3:227-231.
36. Omu AE, Dashti H, Mohamed AT, Mattappallil AB. Significance of trace elements in seminal plasma of infertile men. *Nutrition* 1995; 11(5 Suppl):502-505.
37. Telisman S, Cvitkovic P, Jurasovic J, Pizent A, Gavella M, Rocic B. Semen quality and reproductive endocrine function in relation to biomarkers of lead, cadmium, zinc and copper in men. *Environ Health Perspect* 2000; 108(1):45-53.
38. Bogusz MJ. (Ed). 2008. Forensic science. Hand book of Analytical separation, vol 6 Elsevier BV pg 589
39. Obi E., Akunyili D.N., Ekpo B.O., Orisakwe O.E. (2006). Heavy metals hazards of Nigerian Herbal Remedies. *Sci Total Environ.* 2006; 369(1-3): 35-41.
40. Davis LE, Wands JR, Weiss SA. Central nervous system intoxication from mercurous chloride laxatives. *Arch Neurol* 1974;30: 428-31.
41. Garvey JG, Gary H, Richard VL, Raymond DHC. Heavy metal hazards of Asian traditional remedies. *Int J Environ Health Res* 2001;11:63-71.
42. Koh HL, Woo SO. Chinese proprietary medicine in Singapore regulatory control of toxic heavy metals and undeclared drugs. *Drug Safety* 2000;23:351-62.
43. Schicher H. Contamination of natural products with pesticides and heavy metals. In: Breimer DD, Speiser P, editors. *Topics in Pharmaceuticals Sciences*. Amsterdam: Elsevier Science; 1983. p. 417-23.
44. Chaung IC, Chen KS, Huang YL, Lee PN, Lin TH. Determination of trace elements in some natural drugs by atomic absorption spectrometry. *Biol Trace Elem Res* 2000;76:235-44.
45. Oyejide CO, Oke ES. An ethnographic study of acute respiratory infections in four local government areas of Nigeria. *Afr J Med Med Sci* 1995;4(1):85-91.
46. WHO. Traditional medicine; 2003.
47. Obi, E., Heavy metal hazards of Nigerian herbal supplements: investigations into testicular toxicity in albino rats. Ph.D dissertation. Abia State University, Uturu, Abia State, Nigeria 2006.
48. Debem, H., Testicular toxicity of Operation Sweep M.Sc. dissertation. Usmanu Dan Fodio University Sokoto, Nigeria 2006.
49. Orisakwe OE, Debem HC, Etuk EU, Elsa AT (2010) Spermatotoxic effects of operation sweep herbal supplement in male albino rats *J Basic Clin Physiol Pharmacol.*;21(2):147-56
50. Orisakwe OE, Afonne OJ, Dioka EC, Agbasi PU, Azikiwe C, Obi E. Testicular toxicity of rinbacin in rats. *Biol Pharm Bull* 2002;25 (2):206-8.
51. Orisakwe O E, Husaini D C, Afonne O J (2004) Testicular effects of sub-chronic administration of Hibiscus sabdariffa calyx aqueous extract in rats
52. Ondrizek RR, Chan PJ, Patton WC, King A. Inhibition of human sperm motility by specific herbs used in alternative medicine. *J Assist Reprod Genet* 1999;16:87-91.

53. Ondrizek RR, Chan PJ, Patton WC, King A. An alternative medicine study of herbal. Fertil Steril

1999;71:517-22. Marks L, Partin AW, Epstein JI, et

Author Information

Hilary Enuh

Department of Medicine, Richmond University Medical Center

Chikelue Ifeanyi Oragwu

Africa Education Initiative Research Group, Nnamdi Azikiwe University

Chinedu Okeke

Africa Education Initiative Research Group, Nnamdi Azikiwe University

Emmanuel Elu

Africa Education Initiative Research Group, Nnamdi Azikiwe University

Orish Ebere Orisakwe

Department of Clinical Pharmacy, Toxicology Unit, University of Port Harcourt