The Degree of Completeness of Operation Report in Two Tertiary Institutions in Nigeria

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ABSTRACT

The operation report documents the intra- and post-operative surgical events; it easily communicates these events between clinicians. The quality of this report depends on its completeness and clarity. These reports serve as tools for further decision making, quality assurance, patient outcomes research and also have medico-legal implications. To assess the degree of completion of operation notes in two tertiary hospitals in Nigeria, we reviewed operative reports daily over twelve weeks, checking for degree of completion of individual fields. Twelve fields considered important were extracted from our report format and validated as essential by two general surgeons from both institutions and accepted by members in the study group. These fields were checked in each report to determine the degree of completion of the write-up. Data analysis was done with SPSS 17 for Windows (SPSS Inc. Chicago, Illinois) and reported as simple percentages. A total of 245operative reports were reviewed, involving 123 (50.2%) elective procedures; 11 (4.5%) did not specify the class of procedure (elective or emergency). Consultants undertook 50% of the procedures while trainees made the write-up in 212 (86.5%). No field was 100% complete. The drain (39%) and pack (47.8%) fields recorded the worst completion rate. Type of skin closure (60%), operations details (72.2%), blood loss (62.9%), and post-operative orders (73.9%) were low. There is compelling need for improving the technical quality of operative reports in our practice. Surgeons must teach and supervise their trainees on techniques of operations report writing to prevent avoidable litigations.

Keywords: Operative report, completeness, supervision, litigations

INTRODUCTION

The operative report is an important record which concisely documents surgical procedures and its content must closely reflect the actual operation performed. It serves as a medium for communicating the intra- and post-operative events between colleagues and other healthcare providers. It is also very important in making further decisions on patient care, measurement of operative outcome, quality assurance, practice patterns research and medico-legal practice[1,2]. It is considered good practice for the operating surgeon to record the operation notes as he does so with a better accuracy than his assistant[3].

Documentation of the operative report could be by either dictation or completing a prepared paper or electronic format. The electronic format is easier and preferred but the paper format applies in our practice and is routinely written immediately upon completion of the procedure and filed in the patient's case record. It contains instructions for patient care. The quality of an operation report strongly depends on its completeness, timeliness and consistency[1]; the proficiency of the recorder in the specified procedure is therefore very important in making a report meaningful in line with the functions earlier listed.

We have not audited the quality or completeness of the operations record in our practice but recent accounts within and without our institutions of poorly written, delayed or unwritten reports hours or days after a procedure prompted this audit which spans twelve weeks and involves all the surgical specialties and sub-specialties in our institutions. We hope to make our findings known to all surgeons and trainees in our institutions and we expect that it will lead to an improvement in our current practice of clinical records keeping.

MATERIALS AND METHODS

Settings: This study is conducted in two contiguous tertiary health facilities in South-South Nigeria.

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Inclusion criteria: The operation records of consecutive patients undergoing elective or emergency surgery in all surgical specialties or sub-specialties.

Exclusion criteria: The records from units where the authors work were excluded from the study.

Methods: Operative notes from both institutions were compared and were very similar in many fields. Twelve fields considered important were extracted and validated by two general surgeons from both institutions and same further evaluated and accepted by members in both study groups. The pre-operative diagnosis, operation performed (intra-operative diagnosis), operative findings and details, type of anaesthesia, estimated blood loss and post-operative orders were considered as very essential fields. A pilot study was conducted over one week to test the instrument used in recording our findings.

We concurrently reviewed patient's operations records daily for twelve week from March to June 2014, checking for entries made by the recorder in each of the selected fields. Fields left empty were recorded as incomplete even if the relevant information was documented elsewhere in the report or in the patient's case notes. All the surgeons, excepting members of the study group, were unaware of the study being conducted to eliminate bias.

Data Analysis: Analysis was done with SPSS 17 for Windows (SPSS Inc. Chicago, Illinois) and reported as simple percentages.

RESULTS

A total of 245 operations reports were analysed over twelve weeks, involving 123(50.2%) elective and 111 (45.3%) emergent procedures. Obstetric procedures 102 (41.6%) were most common. The class of procedure was not indicated in 11(4.5%). Consultants undertook 123 (50.2%) of the procedures while trainees entered the records in 212 (86.5%). No field was 100% complete. The drain (39%) and pack (47.8%) fields recorded the worst completion rate. Type of skin closure (60%), operations details (72.2%), blood loss (62.9%), and post-operative orders (73.9%) were low. Poor documentation spanned across all specialties/ sub-specialties as well as cadre of surgeon.

Table 1: Class of procedure including cadre of surgical staff involved in its execution and documentation.

Characteristic	Frequency (%)
Type of Operation	
Elective	123 (50.2)
Emergent	111 (45.3)
Unspecified	11 (4.5)
Surgeon	
Consultant	123 (50.2)
Senior registrar	98 (40.0)
Registrar	24 (9.8)
Operative Note Recorder	
Consultant	30 (12.2)
Senior registrar	104 (42.4)
Registrar	108 (44.1)
Unspecified	24 (9.8)

Table 2: Surgical sub-specialty including the number of procedures. Office procedures are not included.

Specialty	No. of cases (%)
Obstetrics	102 (41.60
General surgery	32 (13.1)
Urology	30 (12.2)
Paediatric surgery	24 (9.8)
Orthopaedics	17 (6.9)
Cardio-thoracic	14 (5.7)
Burns and plastics	13 (5.3)
ENT	4 (1.6)
Maxillo-facial	3 (1.2)
Neurosurgery	3 (1.2)
Ophthalmology	1 (0.4)

Table 3: Selected fields from the operative notes showing the percentage completion rate of different fields

Fields	Frequency (%)
Date of operation	242 (98.8)
Pre-operative diagnosis	244 (99.6)
Intra-operative diagnosis	243 (99.2)
Type of anaesthesia	239 (97.6)
Type of incision	224 (91.4)
Intra-operative findings	211 (86.1)
Full details of procedure	177 (72.2)
Use of packs	117 (47.8)
Swab count	122 (49.8)
Type of wound closure	147 (60.0)
Estimated blood loss	154 (62.9)
Post-operative orders	181 (73.9)

DISCUSSION

Accurate and complete documentation of patient's clinical information is an essential cognitive skill which forms part of good clinical practice and should be demonstrated by surgeons and taught to surgical trainees through the period of residency training. The operations report records the intra- and post-operative events and must be explicit and clear. The Royal College of Surgeons of England guidelines specifies that "Surgeons must ensure that accurate, comprehensive, legible and contemporaneous records are maintained of all their interactions with patients"[4]. The result of this study confirms fears that the skills at clinical records keeping, particularly the operation records, is unacceptably poor across all surgical specialty or sub-specialty irrespective of cadre of surgical staff.

Literature search on the topic of operative note writing or clinical documentation in Nigeria and Africa yielded little. This presupposes the topic is yet to be critically appraised by clinicians in the continent despite complaints of absent or inadequate documentation and maintenance of quality clinical records highlighted at conferences and accreditation or re-accreditation inspection of training facilities. It is indeed not unusual for parts or the entire patient records to be missing in our practice. This impedes adequate care, follow-up and clinical research. We fear that medical litigations arising from these cases will become rife as society becomes more enlightened.

Particular aspects of poor operative records keeping include omission of important fields[5], use of confusing abbreviations, and incomplete or illegible notes[6]. This study examined only the omission of fields. We observed that general fields such as date of operation and type of anaesthesia which are required in all operations but does not involve technical knowledge of an operation were more than 90% completed while fields specifically related to techniques of the procedures were poorly completed. We could not easily deduce reasons for this observation but we could reasonably assume that many trainees who wrote the notes in this study do not fully understand the details of the procedures they assisted in or performed. Although techniques of operative report writing or dictation is not taught trainees, they are often made to write or dictate the operative reports unsupervised; creating room for poor quality report. This situation is not only peculiar in low income countries. Human error, in particular illegible writing or unclear instructions, is often identified as a significant cause of failure in operation note audit.[7]Studies from the US evaluating the operation note as an insurance billing document revealed more than 60% of notes by trainees were incomplete and only 45% of the dictations made within 24hours after the procedure[8,9].

Most operations involve blood loss and this must be clearly documented as it determines the need for replacement therapy. Same goes for swab count, use of packs and tourniquets, wound length and closure technique as well as the post-operative orders. Failure to document these information in the appropriate fields provided for in the recording format, as revealed by this study, call to question the quality of care as the process of documentation consumes little time. We did not consider the practice of leaving blank a field and documenting same information in other sections of a patient's record an appropriate practice as it could be assumed the information was provided retrospectively.

There is an urgent need for surgeons in the continent to institute interventional measures aimed at correcting poor documentation of clinical information and improve on patient care and gain the confidence of colleagues and patients. One very effective intervention that is proven to bring about improvements in complete documentation is behavioural change. Cohen[10] and colleague observed an improvement in the practice of documentation in excess of 70% among trainees when completing operative notes after instituting behavioural changes. These changes must apply to both surgeons and trainees and requires frequent appraisals to become effective. We consider it mandatory for surgeons to routinely write their reports and only allow experienced trainees do so under direct supervision.

Every report should carry the clear identity of its writer at the end. Regulation on documentation in both institutions where this study was done expects all clinicians to write their names, designations and sign every report. This allows for such a person to be corrected or traced when issues pertaining to the operations record arise. Failure of a recorder to indicate his name at the end of the operation report is inappropriate practice. We observed that some reports did not bear the identity of the writer or a signature was so irregular to be traced to an individual. Also, failure to document the elective or emergent nature of a procedure falls short of good clinical practice.

A limitation with complete documentation in the operative note in our practice is the use of a universal recording format in writing operative notes irrespective of type of procedure or specialty involved; we did not consider this a major challenge though. Attention to details, legibility and promptness in documentation are of utmost importance. Specialty specific operative notes which list all the fields which are peculiar to a procedure have the advantage of ensuring that most of the important fields in an operation are fully documented.

We intend repeating this study after making our findings known to surgeons in our practices and discussing possible approaches to improving our practice of documentation. This we hope will produce a change in our attitude towards documenting patient's information and a commensurate improvement in the degree of completeness of records.

SUMMARY

There is compelling need for proper documentation of intra-operative events and improving the technical quality of records in surgical practice. Surgeons, particularly in low income countries, must teach and supervise their trainees on techniques of operations report writing to prevent avoidable litigations and increase the visibility of their practice through proper outcome research.

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Effects of *Malus Domestica* and *Moringa Oleifera* on Thyroid Status and some Enzyme Activities in Female Wistar Rats Fed with *Manihot Esculenta* Based-Diets

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ABSTRACT

The influence of Malus domestica (apple fruits) and Moringa oleifera (Moringa seeds) on the activities of thyroid hormones, thyroid peroxidase (TPO) and some antioxidant and organ enzymes in female wistar rats fed with Manihot esculenta (cassava)-based diets were investigated. Twenty four (24) animals were divided into 3 equal groups (with sub groups a and b). Group1a and 1b (Negative control) received standard diet for 14 and 28 days respectively, Group 2a and 2b (positive control) received cassava cyanide diet for 14 and 28 days respectively, while group 3a and 3b (treatment group) received apple and moringa preparations respectively for 14 days, following a 14-day cassava-cyanide diet. The animals were sacrificed and blood samples collected for hormonal and enzyme assay, using standard methods. Results showed that TPO activities(μL^{-1})3.63±0.08, and 3.52 ± 0.07of rats fed with apple and moringa diets were statistically higher ($p<0.05$) than the positive control group 2.64±0.07. There was no significant difference between activities of TPO in the two treatment diets ($p > 0.05$). The absence of significant difference between levels of thyroid hormones in the treatment and negative control rats on one hand and the positive correlation obtained between the glandular weight and feed type in each of the groups ($p < 0.05$) on the other hand, supported the ameliorative roles of the plant agents. In vitro antioxidant capacity of the plant agents followed the decreasing order, Duchess>Golden delicious >Moringa seeds >Northwest greening. CAT (catalase) and SOD (superoxide dismutase), obtained in the moringa treatment group (3b) were higher than in the apple-treatment group ($p < 0.05$). No significant difference was found between the former and the negative control (1a) ($p >0.05$). The moringa diet was more effective than the apple diet in liver toxicity management. Although the ratios of ALT/AST (De Ritis ratio) obtained were all below unitary (0.63- 0.8) - confirming the presence of hepatocellular injuries. Serum pancreatic amylase activity of the positive control rats administered cassava-based diet (group 2b) was statistically higher ($p < 0.05$) than those of the other groups. These results confirm the toxicity effects of cassava-cyanide on the thyroid gland and other organs and the ameliorative roles of the plant agents introduced.

Keywords: cassava-cyanide, toxicity, plant agents, TPO, thyroid, ameliorative

INTRODUCTION

Manihot esculenta cruntz popularly known as cassava in many African countries is also referred to as Mogo, Tapioca-root, or Mandioca. In the Philippines it is known as Yuga, Balinghoy or Kamoteng Kahoy; and in the India regions referred to as Tabolchu or Kappa[1]. In Nigeria cassava is known by different names in various ethnic groups; for example it is referred to as Anebo in Ogbia, Akpu in Igbo, Fufu in Yoruba and Rogo in Hausa. Its products include gari, edible starch, fufu, cassava flour, akpu paste and tapioca cakes. As a rich carbohydrate crop, cassava serves as a major staple food in the developing countries of the world, providing the basic diet for over half a billion people[2,3]. Nigeria had been rated as one of the world's largest producers of cassava[4].

Although cassava is rich in energy nutrient, it is implicated in the development of some adverse health conditions due to its hydrocyanic acid content. Prolonged and frequent intake of residual cyanide through improperly processed cassava foods had been linked with various types of toxicity syndromes including thyroid enlargement and other organ lesions such as thyroiditis, goiters, pancreatitis, renal and hepatic malfunctions in susceptible organisms[5,6].Toxicity syndromes includes Histotoxic ataxia ascribed to inactivation of the tissue enzyme - cytochrome oxidase by hydrogen cyanide which combines with the Fe^{3+} /Fe^{2+} component of the enzyme[6]. Others are respiratory problems resulting from inhibition of copper/zinc enzyme, carbonic anhydrase by the toxicant,

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hydrogen cyanide[7]. Hydrocyanide or its detoxification product, thiocyanate, (SCN), can inhibit iodide oxidation, that is, the conversion of iodide, I^-, to iodine radical, I_2, by inactivating the enzyme, thyroid peroxidase (TPO)[8]. At high concentration, SCN inhibits TPO and thereby reduces the incorporation of iodine radical into thyroglobulin [9] with subsequent reduction in thyroid hormone production. This gives rise to secretion of more TSH by the thyroid gland, resulting in the enlargement of the later by increase in both the number and size of its epithelial cells in a bid to maintain normal hormones secretion[10]. An enlarged thyroid gland with low hormone secretion is often referred to as simple goitre. Where there are numerous cases in a given environmental/geological area, simple goitre is called 'endemic goitre'[10], or IDD (Iodine Deficiency Disease).

Iodine Deficiency Disease has remained a nutritional problem in Nigeria and affects mostly women of child-bearing age (due to loss of iodine from the mother to the developing foetus during pregnancy), despite several intervention programmes such as salt iodination and mineral enrichment which targeted mostly women (the vulnerable population), particularly pregnant and lactating women and, by extension, the girl child[11]. The success of such programmes requires a thorough assessment of the root cause of the deficiency, without which they will only enjoy a short period of relief. Nutrient deficiency can arise when either the intake of a particular nutrient is subnormal or its metabolism in the body is compromised by some unresolved factors. Salt iodination would be a successful venture if it is meant to address the former. However, where the issue is a case of secondary mineral malnutrition involving metabolic problems, then it becomes necessary to address the underlying factor(s) antagonizing the utilization of the particular nutrient in the body [8].

Previous studies support the fact that IDD in Nigeria might not always be seen as an outcome of subnormal iodine intake or its lack in foods and diets but, more importantly, as a product of some underlying factors that antagonize iodine metabolism[5,12]. Toxicants and environmental stressors play an integral part in the issue of mineral availability in the body. Madukosiri[12] determined high iodine levels in the presence of high thiocyanate and low thyroid hormone values. According to that reference, a significantly higher level of thiocyanate was determined from the test group (subjects with visible goiter) compared to their corresponding control (with no visible evidence of goite). Those results support an implied role of thiocyanate in the incidence of goitre development in Bayelsa State, Nigeria, reports which were in line with other literature publications[6,13].

Subsequent studies using heat-treated cassava-cyanide showed various degrees of toxicity lesion in the affected organs/glands liver, kidney, pancrease, and thyroid gland[5]. Because organ lesions were observed, it became imperative to further confirm those observations by assaying the levels of the marker enzymes of the affected tissues; and this, in part, informed the present focus. Since cassava is a major energy source for the poor masses, there is no intention to advocate discontinuation of the use of cassava as foods, but find ways of toxicant detoxification and or amelioration of the symptoms of toxicity attributed to its hydrogen cyanide content. Already recent scientific reports have shown that some of the effects of toxicants and or free radicals in the body can be minimized, prevented or even cured by plant bioactive compounds (phytochemicals) [14,15,16,17]. The present study is therefore designed to ameliorate the toxicity effect of cassava-cyanide in the body in order to improve iodine nutriture/ metabolism. Since it targets the female population, only female rats were used.

MATERIALS AND METHODS

Collection and Preparation of Cassava Feeds:

Seven varieties of cassava traditionally known as Oguru, Yomugha, Janet, Accra, Agric sweet/bitter and Rowaina were used for the preparation of the rat feeds. The varieties were obtained from Okutukutu farms along Tombia-Yenagoa region of Bayelsa State. The taxonomist's identification had already been reported in an earlier study[18].

The tubers were washed with distilled water, outer brown peels manually removed and the pulp chopped into cube-sized pieces before subjection to heat treatment using dry air oven at 50°C (until total loss of moisture) and at 100°C for 30 minutes in order to mimic the usual effect of heat on toxicant level during processing. The dry cassava samples were milled and stored in a desiccator until required for use.

Apples, *Malus domestica* cultivars (of the family Rosaceae)-Duchess, Golden delicious, and North-west greening were purchased from Opolo market, Bayelsa State; while for *Moringa oleifera Lam,* also referred to as the "Miracle Tree," "Horse radish-tree," or "Ben oil tree", the best known and most widely distributed species of the plant were purchased from Songhai-Amukpe, Sapele, Delta State. All plant agents were identified and authenticated by an expert in the Department of Crop Science, Faculty of Agriculture, Niger Delta University, Bayelsa. The apple samples (equal weight of cultivars) were similarly washed with distilled water, chopped into cube size and dried to constant weight in an oven (50^{o}C). On the other hand the seeds of *M. oleifera* were cracked, and dried as above. All samples were milled using Waring blender (Model No. BD0161DA-819FP, AKAI-TOKIO, JAPAN). Formulated cassava diets consisted of cassava flour, casein protein, sucrose, minerals, vitamins, non-nutritive cellulose, palm oil, and apple or moringa mills in the respective portions for groups 2 and 3 feeds (Table 1).The control diet was *Zea-maize*-based standard rat feed -Top Feeds, Eastern Premier Feed Mills Ltd, A subsidiary of Premier Feeds, Delta State.

Animals Treatment

Twenty four (24) adult female albino rats of the wistar strain (*Rattus norvegicus*) aged nine to twelve weeks and weighing 123.97g-194.3g were used for the present investigation. Rats were bred in animal farm at Famgbe, Yenegoa region of Bayelsa State. Animals were acclimatized at room temperature and diet for one week prior to experimental feeding. All animals (in the test and control groups) were fed *ad libitum* on diet and water. The clean metal cages housing the animals were placed in a well ventilated room and exposed to 12-hour day light and 12 hour-powered light at night with a relative humidity of 45-50$^{\%}$. Clean ceramic cups and plates were used; and as part of the measures taken to minimize contamination of feeds with urine and faeces, the cages were constructed to allow faecal pellets and urine to escape from the base of cages, while the food and water compartments provided limited access so as to avoid spilling of food materials during feeding. In addition, food and water were replaced twice daily- morning and evening. Cages were cleaned weekly while daily chart of weight gain or loss versus feeds consumed (after correction for feeds wasted) were kept throughout the experiment.

Animal Grouping

Animals were distributed randomly into three groups of eight rats each. Four out of the 8 rats in group 1 (that is control group 1a) were fed with standard diet for 14 days before sacrifice, while the remaining 4 rats (control group 1b) continued till 28 days before sacrifice. Group 2 (test group 2a) was fed cassava-cyanide diet for 2 weeks while 2b continued on same diet for 28days before sacrifice. Group 3 (a and b) consumed cassava-cyanide diet for 2 weeks, after which apple preparations were introduced into the feeds for group 3a and moringa preparations were introduced into the feeds for group 3b, for the remaining two weeks.

Sacrificing the Animals

At the end of the respective feeding periods the animals were anaesthetized under chloroform vapour and sacrificed. The blood was immediately withdrawn via cardiac puncture (with sterile syringe) and placed into labelled sample tubes - lithium heparinised tube (for plasma separation) and plain tubes (for serum collection).

Preparation of the Blood Samples

Blood specimen in the plain sample tubes was allowed to clot at room temperature after which a gentle ringing was carried out to dislodge the clot from the tube. The tube was centrifuged for ten minutes at 2,500rpm at the end of which a clean dry Pasteur pipette was used to transfer the supernatant (serum) from the centrifuge tube into a clean dry labelled sample bottle. The sample bottle was properly closed and kept at -20C till required for analysis. The plasma was obtained by centrifugation to separate the cells from the heparinised blood sample. Plasma sample was used for the determination of superoxide dismutase activity.

Thyroid Peroxidase Assay

Thyroid peroxidase activity was estimated using a spectrophotometer (UV-vis Spectrumlab 725s) at 353nm following triiodide (I_3^-) formation from iodide as described by Amar, *et al*[13] with modifications.

Extraction of Plant Samples

Plant samples were extracted using various preparations of water/alcohol solvents (30:70) and 100% water in a modified method as described by Zohra & Fawzia[19]. The extracts were kept in a refrigerator until used for phytochemical screening and determination of total phenol content.

Phytochemical Screening Test

Phytochemical screening test was done according to standard laboratory techniques of Trease and Evans[20,21] to determine the presence of: Flavonoids, Saponins, Terpenoids, Cardiac glycosides (Keller-Krillani test) and Anthraquinones (Borntrager's test). Quantification of total phenol content in mgGAE (Gallic Acid Equivalent) was performed as described by Zohra & Fawzia[19]. Determination of alkaloids was done by the gravimetric method of Harbone[22]. Folin-Denis Spectrophotometric method described in Pearson[23] was used for the determination of tannins.

Hydrocyanic acid

Alkaline picrate method as explained in Onwuka[24] was adopted for the determination of hydrocyanic acid.

Antioxidant Activity

The free radical scavenging activity of the extract was done using the stable free radical 1,1-diphenyl-2- picrylhydrazyl (DPPH)[25,26].

Thyroid Hormones

The levels of T_3, T_4 and THS were determined by use of automated testkit method of ELISA, according to the specification of the manufacturers (CLINNOTEC Diagnostics, and Pharmaceaticals, Horseshoe, Canada).

Antioxidant Enzymes:

Superoxide dismutase (SOD): Enzyme activity was determined by % inhibition of epinephrine oxidation to adenochrome in the blood[27].

Catalase (CAT): Determination of enzyme activity was carried out by enzyme-catalyzed decomposition of H_2O_2using potassium permanganate ($KMnO_4$)[28].

Serum Transaminases-ALT and AST:

Determination of serum transaminases were carried out by the kit (Cat. Nos. 100 and AS. 101 respectively) method of Randox Laboratory Limited, (Crumlin, BT29 4QY, United Kingdom).

Alkaline phosphatase (ALP): Enzyme activity was determined according to the kit (Cat. No. AP 542) method described by Randox Laboratories as above.

Pancreatic Amylase Assay: Alpha amylase was determined according to the Kit method explained by Agappe Diagnostics (Switzerland, GmbH).

Statistical Analysis

All data were statistically analyzed and presented in tables as mean ± S.D using Microsoft Excel Package. Paired Samples test and Correlation were done using the IBM statistical package for Social Sciences (SPSS) version 20.0. The level of significance was expressed at $p<0.05$.

RESULTS

Weight Gain/Loss versus Diet Consumed

At the end of the feeding, weight gain was from 1.17 to 89.17g (0.85 to 46.26% of body weight) and according to the decreasing order, 1 > 2 > 3a > 3b for rats in the negative control (standard feed), positive control (cassava-cyanide diet), apple-treatment diet and moringa-treatment diet respectively. Results showed that the rats administered the moringa treatment diet consumed the highest quantity (761.05g) of feed, but lost more weight (28.60g) than their counterparts that fed on apple diet (table 2). Contrarily, rats on the standard maize-diet consumed much less (475.04 to 489.37g) but recorded the highest weight gain, (17.43 to 46.26% of their body weight).

Among the organs, there was a significant reduction in the pancreatic weight of the cassava positive control and treatment groups (ranging from 0.28 to 0.77g) when compared to the negative control rats ($p < 0.05$), (table 2). In the same vein, a statistical significant reduction was observed in thyroid glands weight of the former (cassava positive control) compared to the control ($p < 0.05$). Contrarily there was no significant difference between the liver weights in the various groups, ($p > 0.05$).

There was a negative but significant correlation between the pancreatic weight and feed intake in the cassava-cyanide group, ($r = -0.957$); and between the pancreatic weight and feed intake in the negative control group (fed with maize-based diet), ($p < 0.05$); whereas a positive significant association (r = 0.954) was obtained between thyroid glands and feed intake in both the negative control (maize-based diet) and the apple-treatment groups, ($p < 0.05$).

Thyroid status/function

The negative control group had a significantly higher TPO activity ($5.06 \pm 0.12 \mu L^{-1}$) than those in the positive control ($2.64 \pm 0.07 \mu L^{-1}$) and the two treatment groups(ranging from 3.45 to $3.71 \mu L^{-1}$), ($p < 0.05$), (table 3). The TPO values in the various groups were according to the decreasing order, 1 >2a>3a>3b>2b. The magnitude of the activity changes on introduction of the respective diets therefore followed the same trend in a decreasing order 2b > 3b > 3a > 2a > 1b. Despite the above changes, the thyroid hormone showed no significant difference in T_3 or T_4 levels in the various groups, ($p > 0.05$). However a significantly higher TSH value was determined in cassava-cyanide groups 2b as against those of the control and treatment groups ($p < 0.05$) (Table 4).

Pancreatic Amylase

The values for pancreatic amylase followed a similar trend as those of TPO but in an increasing order 1a < 1b < 2a<3a<3b<2b. There was a significant increase in enzyme value in the cassava-cyanide group 2b when compared to that of the negative control, ($p < 0.05$), (table 3). Although the values obtained in the negative control 1 were lower than the levels determined for the treatment groups, there was no significant difference between them, ($p > 0.05$).

The Transaminases, and Antioxidant Enzymes

The AST value in control group 1b was significantly lower than those of the cassava-cyanide 2b and apple treatment 3a, ($p < 0.05$). Significant difference was also found between the two treatment values ($p < 0.05$), but the difference between the moringa treatment and the controls was not significant ($p > 0.05$). The levels of ALT followed the same pattern; while ALP values showed no significant difference between the various groups, ($p > 0.05$), (Table 5). The statistical comparison between the antioxidant enzyme values showed that rats fed on cassava-cyanide diet had a significantly lower value from those of the control and moringa treatment groups, ($p < 0.05$). Again the values in the treatment groups and the negative control were not statistically different ($p > 0.05$), (table 4).

The Antioxidant activity of Apple Cultivars / Moringa

The *in vitro* antioxidant activity (% DPPH inhibition) determined from the plant agents were all found to be higher than the standard vitamin C(0.2mg) and followed the decreasing order: Duchess (88.21±0.200) > Golden Delicious (85.19±0.195) > Moringa (76.38±0.470) > Northwest Greening (74.86±0.273)> Vitamin C (72.51±0.930).

Phytochemical Screening and Quantification of some Phytochemicals

Results of phytochemical screening showed the presence of alkaloids, flavonoids, tannins and saponins in almost all extract types compared to the secondary metabolites terpenoids, cardiac glycosides and anthraquinones which were not so distributed (Table 6). The ranking of positive tests was according to the decreasing order: alkaloids > flavonoids > tannins > saponins. Extracts of moringa showed more of the presence of alkaloids, flavonoids and saponins, whereas the apples were more positive for alkaloids, tannins and flavonoids, in that order.

Quantitative alkaloids values (%) obtained from various apple cultivars Duchess (DU), Golden delicious (GD), and Northwest greening (NG) were found to follow the decreasing order GD > NG > DU. Contrarily, the order for tannins was DU >NG > GD. The total phenol content was higher in apples than in moringa and ranged from 316.73 - 402.49 in Duchess (DU); 283.28 - 390.86 in Golden delicious (GD); 332.26 553.49 North-west greening (NG); and 89.45 - 243.98 (Mo), (mg GAE/100g, FW) (Table 7).

DISCUSSION

Body weight vs feed intake

Judging by weight gain (%), rats on the

Table 1. Composition of Formulated Cassava Diets (g/kg) Fed to the Various Rat Groups

Diet Components	Basal negative control diet (g/Kg) Group 1(a & b)	Test diet $_1$ (g/Kg) Group 2a	Test diet $_1$ (g/Kg) Group 2b	Test diet $_2$ (g/Kg) Group 3a	Test diet $_3$ (g/Kg) Group 3b
Standard Diet	1000	-	-	-	-
Sucrose	-	80	80	80	80
Vitamins	-	40	40	40	40
Mineral	-	20	20	20	20
Palm oil	-	40	40	40	40
Cellulose	-	20	20	-	-
Casein	-	40	40	40	40
Apple supplement	-	-	-	20	-
Moringa oleifera supplement	-	-	-	-	20
Heat –treated cassava flour	-	760	760	760	760
Total diet (kg)	1.0	1.0	1.0	1.0	1.0

The hydrocyanic acid content was found to be 53.70 ± 2.40 and 41.20 ±2.40 (mg / kg dry sample)in the control maiz-based feed and cassava diets respectively.

Table 2: Mean Body Weight Change and Relative Organ Weight Pre and Post-Treatment Feeding in Wistar Rats

Rat Groups	Mean Initial Weight (g)	Mean Final Weight (g)	Total Feed Intake (g)	Mean Weight Gain (g) (% body weight)	Mean Weight Loss (g), (% body weight)	Net Weight Gain/Loss (g) (% body weight)	Pancreas (g)	. Liver (g) -	Thyroid Gland (g)
Negative Control									
1a	163.172±1.56	191.62± 1.48	475.04	28.45, (17.43)	0	28.45, (17.43)	0.42±^{a} 0.10	2.17±0.75	1.01±0.31^{abcd}
1b	192.75±1.58	281.92±0.47	489.37	89.17, (46.26)	0	89.17, (46.26)	0.76^{abcd} 0.11	2.97±1.47	0.38±0.16^{a}
Positive Control									
2a	146.50±2.65	131.07±2.7	356.3	15.43, (10.53)	-20.75, (14.16)	-5.32, (3.63)	0.53± 0.24	1.82±0.72	0.63±0.37
2b	153.27±0.37	139.52±2.15	758.09	13.75, (8.97)	-35.36, (23.07)	-21.61, (14.1)	0.54±^{b} 0.09	1.94±1.09	0.30±0.11^{b}
Treatment Groups									
3a	126.05±2.08	119.56±3.38	676.9	6.49, (5.15)	-26.49, (21.02)	-20.00, (15.87)	0.34±^{c} 0.06	4.00±0.35	0.38±0.11^{c}
3b	138.25±1.58	137.08±1.39	761.05	1.17, (0.85)	-28.60, (21.53)	-27.43, (19.84)	0.45±^{d} 0.10	3.67±0.26	0.36±0.09^{d}

N=8 for each group,(N=4 for sub-group) ; groups 1 & 2 ate the standard and cassava-cyanide diets respectively; sub-groups a & b ate the respective diets for 2 & 4 weeks, in that order. Group 3 ate cassava diet for two weeks followed by the treatment diets made with apples (a) & moringa (b) for the rest 2 weeks. Net weight gain was calculated as the difference between mean body weight gain and body weight loss. Figures with the same superscripts in each column are significant at p< 0.05.

Table 3. Serum Thyroid Peroxidase and Pancreatic Amylase Activities versus Diet Type.

Experimental Grouping	Diet Type & duration of Feeding	Thyriod Peroxidase Activity (μL^{-1})	Activity Change (%)	Pancreatic Amylase Activity (μL^{-1})	Activity Change (%)
Negative Control. Group					
1a	(Standard Diet) 14 Days.	4.89 ± 0.18	-	109.5±2.08	-
1b	(Standard Diet) 28 Days.	5.06 ± 0.12[abc]	3.36	110.76±1.50[a]	1.14
Positive Control Group					
2a	Formulated Cassava Feed. 14 Days	4.30 ± 0.07	12.07	116.25±2.22	6.16
2b	Formulated Cassava Feed. 28 Days	2.64 ± 0.07[a]	47.83	122.50±3.00[a]	11.81
Treatment. Group					
3a	Formulated Cassava Feed And Apple. 28 Days.	3.63 ± 0.08[b]	28.26	117.75±2.06	7.53
3b	Formulated Cassava Feed And *Moringa Oleifera* . 28 Days.	3.52 ± 0.067[c]	30.43	120.0±2.16	9

Data were expressed as mean ± SD. Values with the same superscripts in each column are significant ($p<0.05$).

Table 4.Thyroid Hormone Levels Determined in Wistar rats Fed Cassava-cyanide Diets

Rat Group	T3(ng/ml)	T4 (ng/ml)	TSH (μ/L)
Group 1a	2.18±0.19	4.6±0.40	0.98±0.83[a]
Group 1b	2.58±0.42	6.20±0.18	2.05±1.44
Group 2a	2.18±0.62	4.85±0.78	1.05±0.57
Group 2b	2.80±0.24	4.25±0.42	4.73±0.75[ab]
Group 3a	2.24±0.62	5.33±0.54	3.53±0.43
Group 3b	2.20±0.64	5.18±0.76	1.66± 0.63[b]

T3, T4, and TSH; triiodothyronine, tetraiodothyronine, and thyroid stimulating hormone respectively. Values with same superscripts in each column are significant ($p < 0.05$). Groups 1, 2, & 3 (a & b), standard feed, cassava-based feed, and treatment diets (apple & moringa) respectively.

Table 5. Levels of some Serum Enzymes in Wistar Rats Feed with various Cassava- cyanide Feeds (**Mean**SD).

Group	AST (μ/L)	ALT (μ/L)	ALP (μ/L)	CAT	SOD
Group 1a	67.23 ±0.25	49.47±0.1528^{a}	60.47±0.45	ND	ND
Group 1b	66.87±0.31a^{ab}	42.03±0.0643^{b}	61.23±0.18	119.67±0.00^{a}	54.3±0.00^{a}
Group 2a	87.33±0.81	56.67±0.5859	82.47±0.45	104.88± 0.00	69.3±0.00^{b}
Group 2b	96.93±0.42^{ad}	65.53±0.3780^{abc}	90.13±0.70	90.84± 0.00^{ab}	80.5±0.00^{abc}
Group 3a	90.83±0.70^{bc}	57.47±0.3786	82.47±0.15	98.18± 0.00	89.6±0.00
Group 3b	69.6±0.07^{cd}	44.23±3.45^{c}	62.93±0.15	117.26±0.00	57.1±0.00^{c}

AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; ALP, Alkaline Phosphatase; CAT, Catalase; SOD, Superoxide dismutase; and ND, not determined. Values with same superscripts in each column are significant ($p < 0.05$).Groups 1, 2, & 3 (a & b), standard feed, cassava-based feed, and treatment diets (apple & moringa) respectively. ND- sample not available.

Table 6. Phytochemical Screening Test For extracts of Apple cultivars and *Moringa oleifera* Seeds.

Samples	Metabolite	Water – Extract	Water- Ethanol Extract	Water- Methanol Extract	Water- Acetone Extract
Duchess (red apple)	Flavonoids	-	-	+	+
	Saponins	+	-	+	+
	Tannins	+	+	+	-
	Alkaloids	+	+	+	+
	Anthraquinone		+	-	
	Terpenoids		+	-	
	Cardiac glycoside		-	-	
Golden Delicious (yellow apple)	Flavonoids	+	+	+	+
	Saponins	-	-	+	_
	Tannins	+	+	+	+
	Alkaloids	+	+	+	+
	Anthraquinone		-	+	
	Terpenoids		-	+	
	Cardiac glycoside		-	-	
Northwest-Greening (green apple)	Flavonoids	+	-	+	+
	Saponins	-	+	-	+
	Tannins	+	+	+	+
	Alkaloids	+	+	+	+
	Anthraquinone		-	+	
	Terpenoids		+	-	
	Cardiac glycoside		+	+	
Moringa oleifera	Flavonoids	+	+	+	+
	Saponins	+	-	+	+
	Tannins	+	-	-	-
	Alkaloids	+	+	+	+
	Anthraquinone		-	-	
	Terpenoids		+	-	
	Cardiac glycoside		-	-	

(+, -, *presence and absence of phytochemical, respectively).*

Table 7. Quantitative Determination of Total phenol, Alkaloids and Tannins content of extracts from *Malus domestica* cultivars and *Moringa oleifera* seeds *(mean±SD)*.

M. Domestica *(GAE)*	**Duchess**	**Golden Delicious**	**Northwest-Greening**	**Moringa oleifera**
Total Phenol (mg GAE/100G, FW)				
Aq.E.E	300.8±3.10	328±2.43	308±1.35	092±2.55
Aq.M.E	400±2.49	389±1.86	330±2.26	180±3.03
Aq.A.E	318±1.27	310±1.50	155±1.51	119±1.37
Aq.E	320±2.52	285±1.72	287±3.32	243±0.98
Alkaloids (%), Aq.Eueous				
Tannins (mg/100g	16±0.024	21±0.004	19±0.003	9±0.006
DW)Aq.M.E	21.9±0.002	14.6±0.001	17.7±0.001	10.9±0.001
Aq.E.E	21.4±0.001	12.6±0.001	15.9±0.001	4.59±0.001

GAE - Gallic Acid Equivalent; FW - fresh weight; Aq.E.E aqueous ethanol extract; Aq.M.E aqueous methanol extract; Aq.A.E aqueous acetone extract; and Aq.A.E aqueous extract.

treatment diets had the least weight gain. Moringa treatment group, in turn, consumed more feeds, but lost more weight than the apple treatment counterparts. This trend was attributed to a number of factors including sensory and biochemical factors. Organoleptic properties of a diet are known to affect palatability and food intake. Phytochemicals can, through biochemical signalling, increase oxidative processes and cause weight reduction. Therefore the weight loss observed in the present study was attributed to organoleptic and biochemical properties of the constituent phytochemicals. This fact is consistent with the report of various scholars[14,29,30]. According to them, polyphenols could suppress or lower weight gain and reduce fat deposit in rats by increasing fatty acid oxidation through the stimulation of AMPK (AMP kinase) activation via its phosphorylation. From our phytochemical screening, the results posit and link the presence of flavonoids and saponins to such functions.

Another factor which could give rise to weight reduction is the metabolic process of hydrogen cyanide detoxification in the body which requires the break-down of an essential sulphur-containing amino acid, preferably methionine[5,31,32]. However in the present study, an additional protein (in form of casein, 40g/kg) was introduced into the feeds in order to minimize such weight losses. Despite that precaution, cassava-cyanide positive control rats recorded the highest weight reduction compared to the remaining groups.

Thyroid Status

Thyroid peroxidase (PTO) activity is linked with thyroid hormone metabolism both in hyperthyroidism and in hypothyroidism[8,33]. As a result, TPO activity can serve as a thyroid hormone (T_3, T_4, or TSH) marker. The present study obtained TPO levels within the published literature ranges[34]. However introduction of cassava diets significantly inhibited the TPO activity by 47.83%, when compared to those of control rats. This inhibition was ameliorated or reduced to 28.26% and 30.43% when apple and moringa -cassava diets, (in that order), were separately administered during the last two weeks of the feeding. Apples were therefore considered more effective than moringa in activation or restoration of TPO activity to or near control levels. The observed effect was linked to the levels of total phenol determined in apples and to a lesser extent in moringa an observation in-line with literature reports[35]. Phenolic compounds having powerful antioxidant properties could accomplish those functions in several ways including: direct activation of the respective enzyme, scavenging and suppression of radical species or inhibition of respective enzymes involved in free radical production, thereby up-regulating or protecting antioxidant defence[36].

Several phenolic compounds had been demonstrated to be capable of causing significant changes in the activation of peroxidases. The phenolics were considered as co-substrates for peroxidase enzymes and through their (the former's) functional groups affect the enzyme activity in various ways[37,38]. Although the apples (particularly the DS) were found to have higher values of total phenol content and hence higher *in vitro* antioxidant activity and *in vivo* TPO effects than the moringa, there was no significant difference between their values. When compared to standard ascorbic acid, the plant samples showed higher levels of antioxidant activity and exhibited over 74% DPPH inhibition which was found to be in consonant with literature reports[35].

Besides, moringa had also been shown to reduce the consummation or utilization of antioxidant enzymes thereby up-regulating and protecting antioxidant defence[35,39]. The lack of statistical difference between the enzymatic antioxidant components (catalase and superoxide dismutase) measured in moringa treatment rats and their counterpart control 1b,supported its (moringa's) antioxidant protective function and highlighted the amelioration effect on rats that consumed it. In the light of the present phytochemical study, those functions were attributed to the flavonoids and saponins presence in the various extracts of moringa.

Effect of hydrocyanide on thyroid peroxidase

One toxicant known to be capable of deactivating TPO is hydrogen cyanide (HCN) (product of linamarine hydrolysis during cassava processing). Hydrogen cyanide can form a stable complex with the active site related residues of TPO which are shown to include a heam and the carbonyl group with the sulphur of a methionyl amino acid residue selenocystein[40]. As already mentioned, HCN can interact with the haem iron at the active site and deactivate the enzyme. The hydrogen cyanide content of the control (maize-based) diet was even higher than those of the treatment feeds and therefore was expected to have given rise to reduced activity of TPO in control rats. Contrarily the activity of TPO in the control animals was higher than those in the test groups, implying that the hydrocyanide load of the cassava diet was neither the sole nor the major anti-thyroid agent present. The present thinking is in consonant with the report of Amar, *et al*[13] who demonstrated the role of thiocyanate in TPO inhibition and hypothyroidism. They showed that thiocyanate could play such major role in cassava toxicity since its level of content and toxicity were unaffected by heat processing. Their observation was also in line with a previous investigation which determined higher thiocyanate levels in subjects with iodine deficiency goitre[12] Thiocyanate, together with other related compounds are the hydrolytic product of HCN-metabolizing enzymes such as glucosidases, sulphur transferase enzymes, and myrosinase present in plants and animal tissues[40]. These and other factors such as the nature and the capacity of antioxidant factors (as already highlighted) and other substances present in the body (or consumed along with the toxicant) determine the extent to which the consuming organism handles its toxicant load.

Thyroid hormone levels

The present finding determined higher TSH level from cassava-cyanide positive control 2b, when compared to the counterpart negative control 1b and treatment groups an observation which was also in agreement with the cited literature[13]. Consistent with that report, the TSH level declined after two weeks of consumption of the apple and Mo treatment diets. The lack of significant difference between the treatment groups showed that the two treatment diets were somewhat equally effective in their ameliorative function. That fact was supported by a significant positive correlation (representing a positive association / relationship) between them. High output of TSH is a known characteristic of goitres arising from iodine deficiency[33]. Hypothyroidism could mean a low total T_4 or T_3 level along with an elevated TSH; or high TSH and a low Free T_4 but normal T_3[8,33]. Going by that classification, the case at hand depicts an early hypothyroidism. In early hormone deficiency, serum TSH and T_3 can increase while T_4 decreases[33]. However those authors equally pointed out that sometimes all of those tests might remain within normal limits even in the face of iodine deficiency and therefore were deemed insufficiently sensitive to gauge hormone levels unless in severe cases. The present case depicts an early secondary iodine deficiency mediated through inactivation of TPO with subsequent reduction in T_4, normal T_3 and raised TSH; but of which the introduction of plants' phytochemicals successfully ameliorated. Functional abnormality in cassava consuming rats is confirmed but further investigations are necessary to adequately determine the state of thyroid pathology during cassava-cyanide consumption and the particular phytochemical compounds posited to have ameliorated the toxicity symptoms. Amar *et al*[13] in their report noted that iodide supplementation reduced the potency of cassava toxicity but failed to cancel it. The present study has therefore made further contribution by providing ways of treating or preventing cassava toxicity and restoring many of the affected biochemical parameters to control levels.

The Transaminases and other Enzymes

Activities of serum transaminases AST and ALT as well as ALP were found to increase following feeding with the cassava-cyanide diets but declined after administration of the treatment diets. The liver weight of cassava-cyanide group was lower than those of the treatment and controls but there were no significant differences between them, an observation contrary to the report of Amar *et al*[13]. However, increased level of AST is a sensitive index of active hepatic parenchymal damage and can represent the onset of early hepatic or latent liver cell damage. The calculated ALT / AST ratio (De Rittis ratio) of less than 1, together with the decrease/increase in organ weight support the presence of hepatocellular injury[42]; while the observed decline in transaminase levels following feeding with the treatment diets was taken as the ameliorative effect of the plant agents. The levels of the transaminases determined for both the controls and the moringa treatment rats were comparable. This supported the ameliorative effect of the plant agents and agreed with other published values[43]. Similarly increased level of serum pancreatic amylase activity determined was taken as a measure of pancreatic damage and confirmed the observation of other scholars[6,32] on the toxicity of cassava-cyanide on pancreatic tissue. According to Tulsawani *et al*[6], the toxicity of HCN on the pancreatic tissue was mediated through its inhibition of antioxidant enzymes and consequent lipid peroxidation. In the light of that report, the low CAT value in group 2b was in line with the correspondingly raised a-amylase level in that group. Following the introduction of the apple treatment diet, the a-amylase level declined. That effect was attributed to the alkaloids and tannins content of apples. This time the apple diet was found more effective than that of moringa in amelioration of pancreatic toxicity. Our values were lower than those reported by Adeniyi *et al*[44]. A significant but negative correlation obtained between the pancreatic weight and feed intake in control group 1b and in cassava-cyanide group 2b depicted an antagonistic relationship and agreed with the above cited reference on the adverse or toxicity effect of cassava-cyanide diet on pancreatic tissue.

CONCLUSION

The activity of TPO was inhibited after two weeks of cassava-cyanide consumption but re-feeding with apple and moringa-treated feeds restored the levels to near control values. This effect was rated higher with apples than moringa diet but the difference was not significant. Also the apple diet was found more effective than that of moringa in amelioration of pancreatic toxicity. The phenol content and the *in vitro* antioxidant/free radical scavenging activity of agents in apples were rated higher than that of moringa. On the other hand, the *in vivo* ameliorative effect, judging by the levels of the biochemical parameters such as those of transaminases, ALP, and the antioxidant enzymes (SOD and CAT) levels determined, was more in favour of Moringa than the apple-treated feed. Introduction of *M. oleifera* into the feeds ameliorated the levels of the antioxidant enzymes (CAT and SOD) and, on the other hand, lowered the serum levels of the organ enzymes the transaminases (AST, ALT) and ALP *in vivo.* The results did posit that the flavonoids and saponins content might play an important role to that effect. Although the high level of TSH and low to normal values of T_3 and T_4 in cassava-cyanide group suggested early hypothyroidism, further investigations would be necessary to adequately access the implication of that phenomenon in thyroid function of cassava-consuming animals. These findings were proof that intake of those plant agents could ameliorate the toxicity of cassava-cyanide and therefore should be encouraged, particularly in regions with high consumption of cassava-cyanide-containing foodstuff, so as to counter toxicity and thyroid associated diseases. Also worthy of note is the observed weight loss in the moringa diet group, despite increased meal consumption. This lends credence to the various moringa-based weight loss supplement currently abounding in the market. The results of the present investigation has therefore contributed to available information by providing further ways of treating or preventing cassava toxicity and restoring many of the affected biochemical parameters to control levels. Further studies are however necessary to confirm the combined effect of both supplements in a diet. The effect of individual phytochemical compound and the mechanism of their actions in thyroid function should be determined.

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