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Interventions on coronavirus disease (COVID-19): A case study of potassium supplementation in management of COVID-19

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Abstract

One of the complications of COVID-19 is its effect on electrolyte, mainly manifesting in hypokalaemia. Reversal of hypokalemic state in COVID-19 patients will be of beneficial effect to the patients. This study explored ways of improving the hypokalemic state in such patients. The fortification of potable water was actualized using palm bunch ash (PBA) derived from organic material, the empty palm fruit bunch (*Elaeis guineensis)* hereafter referred to as palm potash or palm potassium carbonate (PPC). Palm potassium carbonate (PPC) was obtained by complete combustion of empty palm fruit bunch to ashes. The resultant ash was allowed to cool for 24 hours and stored in a desiccator. This ash was used for potassium supplementation in potable water. The potassium fortified potable water was prepared using PPC (conc. approx. 20 g/l) and dispensed as 0.5 ml (10 drops) of PPC solution in 750 ml of potable water, Eva, premium table water TM. Ten volunteers of either sex were used for the study. At the commencement of the protocol, each volunteer had initial blood sample collected for electrolyte analysis so that each volunteer served as his or her own control. Thereafter, 3 liters of PPC fortified potable water was administered to each volunteer daily for 14 days. At the end of the first 7 days, blood samples were collected from the volunteers and further samples were collected on the 14th day. Results showed an increase in serum potassium level with a mean value of 3.6 ± 0.23 mmol/L at commencement of study (control) and a mean final value of 3.87± 0.15 mmol/L or 7.5% increase. This increase is statistically significant at $p \leq 0.01$. The rise in serum potassium following ingestion of PPC fortified potable water is sufficient to overcome the hypokalemic state of COVID-19 patients and other individuals with hypokalemia.

Keywords: Potassium; Palm bunch ash; Hypokalemia; COVID-19; Palm Potassium Carbonate

1. Introduction

Water is a universal solvent and one of the most important natural resources on earth. Good water quality is important to human existence and survival. Potable water meets certain clinical and physical conditions such as colour, taste, clinical and ionic composition, microbial contents etc. before it can be adjudged to be safe for drinking, hence potable.

Before water is designated potable, it must be free of contaminants, free of disease causing micro-organisms, harmful or toxic chemical substances. Water meant for consumption (potable) should be free from pollution, must be accessible, acceptable, available and affordable. The quality of water sources must be in tandem with WHO (2004) guideline on water [1].

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-COV-2) is the causative agent of the current pandemic, Coronavirus disease which manifested itself in 2019 and is referred to as COVID-19. Without doubt, one of the greatest humanitarian challenges that the world went through in recent times is the COVID-19 pandemic. This challenge has put the medical and scientific world into serious research and clinical trials resulting in the ongoing mitigation measures

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with vaccines developed by a number of pharmaceutical companies. Currently vaccine is known to be the greatest mitigation measure developed against COVID-19 since none of the treatments now in use has been found to give a better outcome (that has been found to be statistically significant). Researchers have explored many preventive and remedial measures such as development of antiviral drugs, antibody based therapies, water-clustered negative air ions (NAIs), vaccines and other non-pharmaceutical approaches such as use of face masks.

The purpose of this study is to investigate the use of potassium carbonate derived from palm bunch ash as potassium supplement and to fortify potable water with palm potassium carbonate (PPC) obtained from palm bunch ash (PBA) and use it as a therapeutic agent. This has become necessary in view of the hypokalemic episodes in hospitalised patients, and particularly COVID- 19 infested patients. Hypokalemia is a disturbing electrolyte disorder associated with severe complications of COVID-19 patients. Increasing experience in the care of COVID-19 patients showed that hypokalemia is a frequent manifestation observed among the patients [2]. The possible causes of hypokalemia in these cases have been attributed to the treatment regimen and failure of some organs in the body. However there still remain many unanswered clinical questions regarding the causes, prevalence and clinical outcomes of hypokalemia in COVID-19 patients.

From the study conducted by Alfano and his co-workers in 2021, it was found that out of the 290 COVID-19 patients studied, hypokalemia with mean serum potassium ranging from 2.4 to 3.5mmol/L was detected in 110 patients (41%) with mean serum potassium of 3.1 mmol/L during hospitalisation, while a majority of the patients (90.7%) experienced only a mild decrease in serum potassium level (3-3.4 mmol/L). The duration of this electrolyte imbalance ranged from 1 to 13 days and the mean time that elapsed between admission and onset of hypokalemia was on average of 3.6 days. One third (33.3%) of cases of hypokalemia was detected on admission and about half (50%) within one day after admission. In general, patients with hypokalemia had a longer follow-up compared to normokalemic patients and also showed significantly higher Sequential Organ Failure Assessment (SOFA). The overall report showed that although hypokalemia was not associated with mortality in the cohort of 290 patients investigated, it may be a life-threatening condition if it remains untreated.

The experimental investigations carried out in this work surveyed the use of potassium carbonate derived from palm bunch ash as an alternative to potassium chloride or potassium iodide that are generally used as potassium supplement both for oral and intravenous administration. The potassium carbonate sourced from palm bunch ash has the added advantage that it contains other essential electrolytes such as magnesium, calcium, phosphate, though in small amounts. In the clinical trials conducted, the potassium carbonate was administered orally in the form of potassium fortified drinking water. The dosage requirements were explored in the course of the clinical investigations and a standardized dosage requirement was determined.

In this work a method for administering potassium to COVID-19 patients to prevent hypokalemia which had been identified as one of the complications from coronavirus disease was presented. The source of the potassium supplement is an organic matter, the palm bunch waste. Processes for production of the potassium concentrate and the dosage requirement were investigated. Clinical investigations using the potassium supplement for fortifying the drinking water to be administered to some selected volunteers were conducted in collaboration with Department of Pharmacology and Therapeutics, ESUT College of Medicine, Parklane-Enugu, Nigeria.

2. Material and methods

Production of Palm Potassium Carbonate: The main material used in this work is palm potassium carbonate (PPC) derived from burnt palm bunch waste. The amount of PPC required to produce potassium fortified drinking water was investigated and the dosage requirements were also studied. The process of production of refined palm potassium carbonate described in an earlier work [3] was investigated with a view to obtain a concentrated solution of potash (PPC) that can be used for fortifying drinking water with potassium at the point-of-use. The PPC was obtained by complete combustion of empty palm fruit bunch to produce palm bunch ash (PBA) from which a concentrated solution of PPC was obtained. The chemical composition of the (PPC) obtained from an earlier work [3] is presented in Table

Dosage requirements were investigated to determine the amount of (PPC) required to produce potassium fortified drinking water to be used for the clinical trials.

Table 1 Chemical Analysis of Palm Potassium Carbonate

Cation/Anion (mg/L)	Concentration (mg/L)
Potassium (K^+)	35420
Magnesium (Mg^{2+})	403
Calcium (Ca^{2+})	224
Sodium (Na^+)	101
Manganese (Mn^{2+})	0.06
Iron (Fe^{2+})	2.52
Chromium ($^{3+}$)	BDL
Nitrate (NO^{3-})	42
Nitrite (NO^{2-})	8.40
Phosphate (PO^{4-})	242
Chloride (Cl^-)	15176
Fluoride (F^-)	204
Sulphate (SO^{4-})	2072
Total Alkalinity	28840 mg/L as $CaC0_3$
Bicarbonate	4760 mg/L as $CaC0_3$
Carbonate	24080 mg/L as $CaC0_3$
Total Hardness	2240 mg/L as $CaC0_3$
Calcium Hardness	560 mg/L as $CaC0_3$
Magnesium Hardness	1680 mg/L as $CaC0_3$
Total Dissolved Solids (TDS)	94133

pH of stock solution = 12

PPC solution was found to contain the electrolytes which have been confirmed by epidemiological studies to have some health benefits. These electrolytes include potassium, magnesium, phosphate, etc. PPC solution was used to produce alkaline drinking water that has ionic composition comparable to those of some brands of bottled mineral drinking water [4]. The PPC alkaline water which is referred to in this work as Potassium fortified drinking water is however unique in that it contains potassium which most other mineral drinking water do not have. PPC is innocuous, safe and cost-effective.

Potash from PBA is used in Nigeria and some other African countries for a variety of purposes like soap making, as fertilizer and emulsifier in certain food preparations, etc. However, its potential as a material for fortifying the mineral content of drinking water and increasing its pH has not yet been harnessed.

Clinical-Trials: Experimental investigations involving clinical trials on the effect of administering PPC fortified drinking water as potassium supplement on some volunteers were conducted. Three liters per day of the potassium fortified drinking water containing 0.5 ml of PPC (conc. approximately 20 g/l) per 750 ml drinking water was administered to ten volunteers of either sex, body weight between 69 -70 kg, age 45-65 (mean 45 ± 0.5) years for a period of 14 days.

Initial blood samples were collected from volunteers for initial assessment of potassium level so that each individual would serve as his or her own control. Thereafter, each volunteer was made to take 3 L per day of potable water fortified with the stock solution of PPC for the 1st week and blood sample collected for further analysis. During the 2nd week of the study, the cycle was repeated and third round of blood sample was collected at the end of the 14th day. The results were arranged in tabular form for comparative analysis (Table 3).Hypokalemia was defined as a serum potassium <3.5 mmol/L and the normal level of serum potassium ranges from 3.5 -5.3 mmol/L.

Statistical analysis using students t-test was done to determine the statistical significance of the increment of serum potassium due to administration of potassium fortified drinking water.

3. Results

Table 2 Dosage requirements for producing PPC drinking water using PPC of concentration approx. 20 g/l potassium and the expected Potassium contents

Dosage of Stock solution	0.5 ml (10 drops)	1 ml (20 drops)	1.5 ml (30 drops)
Volume of water to be treated	1 litre	1litre	1 litre
Potassium content	10 mg/L	20 mg/L	30 mg/L

Computation of amount of potassium administered to be administered to volunteers: 0.5 ml (10 drop) of PPC solution (conc. approx. 20 g/l) in 750 ml of drinking water is equivalent to 10 mg potassium, hence 3 liters of the potassium fortified drinking water contains 40 mg potassium. Each volunteer was therefore administered 40 mg potassium per day through 3 liters of potassium fortified drinking water.

Table 3 Electrolyte distribution of volunteers before and after PPC fortified potable water administration

Volunteers	Base line values of electrolytes (mmol/L)			1st week electrolytes (mmol/L)			2nd week electrolytes (mmol/L)		
	Na^+	K^+	Cl^-	Na^+	K^+	Cl^-	Na^+	K^+	Cl^-
OK	143	3.4	104	143	3.5	108	142	3.9	107
NS	141	3.5	104	141	3.7	100	143	3.8	105
NC	143	3.4	106	142	3.5	101	142	3.5	109
AS	143	4.1	99	143	4.2	98	144	4.2	98
ME	144	3.8	95	144	3.9	99	142	3.9	100
EG	143	3.6	105	141	3.8	100	143	3.8	98
NO	142	3.5	105	142	3.6	109	141	3.7	101
PA	145	3.7	100	145	3.8	100	144	3.9	105
UN	144	3.6	99	143	3.8	100	142	4.1	103
JS	141	3.5	102	140	3.7	103	140	3.8	105

4. Discussion

The effect of potassium supplements in the management of COVID-19 patients is the main focus of this work. Hypokalemia, a deficiency in potassium, is defined as a potassium level less than 3.3 mmol/L while the normal range is from 3.5 to 5.5 mmol/L. Potassium is one of the body's major electrolytes. It has been observed that patients presenting with COVID-19 experience multiple clinical conditions that may cause electrolyte imbalance and hypokalemia has been found to be one of such conditions that is capable of causing severe complications in COVID- 19 patients [2].

Potassium supplements are usually administered to correct hypokalemia. Salts of potassium (potassium chloride or potassium iodide) are used and administered orally or intravenously. Intravenous magnesium sulphate is also administered in the case of hypomagnesemia. In the clinical trials conducted by Alfano and co-workers in 2021, during the whole period of hospitalisation of the patients under study, each potassium chloride treated patient received a mean of 128.5 and 109.7 mmol of potassium chloride intravenously or orally respectively as potassium supplement. Potassium sparing diuretics were administered among the hypokalemic patients since long term administration of the normal diuretics are widely known to cause hypokalemia and other electrolyte imbalance. These interventions were found to be helpful in the management of the COVID-19 patients. Hypokalemia is one of the most frequent electrolyte disorders in hospitalised patients and severe hypokalemia is associated with potential life threatening complications [5]. Potassium is essential for transmission of nerve impulses, contraction of cardiac muscles, maintenance of intracellular tonicity, skeletal and smooth muscles and maintenance of normal renal functions. Electrolytes like potassium, magnesium, sodium etc are important ions in the body. Potassium is one of the major ions in the body. Nearly 98% of the body's potassium is intracellular. The ratio of intracellular to extracellular potassium is important in determining the cellular membrane potential. Small changes in the extracellular potassium level can have profound effects on the function of the cardiovascular and neuromuscular systems [6, 7]. The kidney determines potassium homeostasis, and excess potassium is excreted in the urine. The reference range for serum potassium level is 3.5 – 5 mmol/l, with total body potassium stores of approximately 50 mmol/kg (i.e approximately 3500 mmol in a 70-kg person). 1 mmol/l drop in potassium correlates to a loss of 100 – 200 mmol of total body potassium. Hypokalemia may result from the movement of potassium into cells without loss of potassium from the body. Causes of hypokalemia include renal losses, gastrointestinal losses, medication effects, transcellular shift, malnutrition or decreased dietary intake, parenteral nutrition [8].

One of the goals of this research was to come up with a strategy for treating certain ailments, especially hypokalemia, using potassium supplement derived from an organic material. The starting point was therefore to survey the literature for the recommended medical practice for potassium supplementation. According to a publication from Medscape authored by Garth (2005) it was stated that emergency department management of hypokalemia include the following [9].

- Patients in whom severe hypokalemia is suspected should be placed on a cardiac monitor; establish intravenous access and assess respiratory status.
- Direct potassium replacement therapy by symptomatology and the potassium level. Begin therapy after laboratory confirmation of the diagnosis.
- Patients who have mild or moderate hypokalemia (potassium level of 2.5 – 3.5 mmol/l) are usually asymptomatic; If these patients have only minor symptoms, they may need only oral potassium replacement therapy. Patients with mild hypokalemia whose underlying cause of hypokalemia can be corrected may not need potassium replacement, such as those with vomiting successfully treated with antiemetic. If cardiac arrhythmias or significant symptoms are present, then more aggressive therapy is warranted. This treatment is similar to the treatment of severe hypokalemia.
- If the potassium level is less than 2.5 mmol/l, intravenous potassium should be given. Admission or Emergency Department (ED) observation is indicated; replacement therapy takes more than a few hours.
- The serum potassium level is difficult to replenish if the serum magnesium level is also low. Look to replace both.

Potassium supplements are available in liquid, powder or tablet form. Any form may irritate the gastrointestinal tract and cause vomiting. Should be taken with food or after meals to minimize gastro-intestinal discomfort. Oral potassium preparations include 8mmol KCl slow-release tablets, 20 mmol KCl elixir, 20 mmol KCl powder, 25 mmol KCl tablet. Many institutions have policies that limit maximum amount of potassium that can be given per hour.

Complications: Replacing potassium too quickly can cause a rapid rise in the blood potassium level, leading to a relative hyperkalemia with subsequent cardiac complications. If hypokalemia is not corrected easily with replacement therapy, search for other co-existing metabolic abnormalities (eg, hypomagnesemia). It has been reported that hypokalemia may be refractory to treatment until hypomagnesemia is corrected. The presence of magnesium in the palm potassium carbonate may enhance the efficacy of the compound in the treatment of hypokalemia.

In the present study, potassium carbonate derived from organic palm bunch waste was investigated as a potential source for potassium, magnesium and phosphate. These electrolytes are very essential for the body's metabolism. Clinical studies were therefore carried out to investigate the effects of administering palm potassium carbonate fortified drinking water as a means of potassium supplement on the serum potassium levels of some volunteers.

5. Conclusion

One of the challenges confronting COVID-19 patients generally is potassium depletion which can be corrected with PPC fortified potable water which has advantage of being easily procured. This product (PPC) did not cause any adverse effect on the subjects and can be recommended for use in patients with established hypokalemia such as COVID-19 patients. Regular consumption of such fortified water would serve as prophylactic measure against hypokalemia in under reported population. The asymptomatic hypokalemic patients will also be protected. The meanpotassium level of patients before the study was 3.7 mmo/L and after ingestion of 3 L/day of PPC fortified drinking water for 14 days.

The m potassium level in the blood became 3.8 mmol/L, ie 2.7% rise. This value is sufficient to raise the serum potassium level in hypokalaemic individuals. Using student's t-test the increase in serum potassiumwithin the 14-day period was significant even at $p \leq 0.01$.

It can therefore be projected that PPC fortification of drinking water will be of tremendous value and benefit in the management of COVID-19 patients in order to avert the incidences of hypokalemia often presented by such patients during hospitalisation.

More clinical trials will be required to further investigate the therapeutic properties of palm potassium carbonate (PPC) concentrate as indicated by this study.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no conflict of interests.

Statement of ethical approval

The approval of the Enugu State University Teaching Hospital was gotten before undertaking the study

Statement of informed consent

Written Informed consent was obtained from all individual participants included in the study.

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