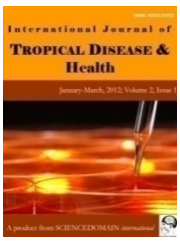

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Biochemical Parameters of Umbilical Cord Blood in Niger Delta, Nigeria: Towards Ensuring Efficient Cord Blood Stem Cell Transplantation

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Authors' contributions

There was equal contribution of all the authors to this study. All the authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aim: The aim of this study was to determine the levels of basic biochemical parameters like uric acid, potassium, sodium, bicarbonate and chloride in umbilical cord blood with a view to assess its suitability for stem cell transplantation.
Study Design: This is a cross-sectional prospective study.
Place and Duration of the Study: The study was carried out at the Departments of Obstetrics and Gynaecology, and Chemical Pathology University of Benin Teaching Hospital, Benin City Nigeria between July 2010 and March 2011.
Methodology: Cord blood from a total of 164 pregnant women (HIV, hepatitis B and C negative) who delivered in University of Benin Teaching Hospital from July 2010 to March 2011 were analyzed for some basic biochemical parameters.
Results: The levels of the biochemical parameters were sodium 135.4±6.1mmol/L (128 to 150mmol/L), potassium 7.08±1.9mmol/L (4.5 to 14.7mmol/L), bicarbonate 19.6±2.4mmol/L(14-25mmol/L), chloride 101.7±3.8mmol/L (90-109mmol/L) and uric acid 1.63±0.9mmol/L (0.19-3.09mmol/L) chloride was the most stable with a CV of 3.71% while uric acid was the least stable with a CV of 12.63%.
Conclusion: Umbilical cord blood could become an important source of stem cell in sub-

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sahara Africa especially with the large number of deliveries. However careful selection of quality cord blood must be enforced to avoid contaminants and haemolysis which may be responsible for the hyperkalaemia as seen in this study.

Keywords: Haematopoietic stem cells; umbilical cord blood; biochemical parameters; hyperkalaemia.

1. INTRODUCTION

Cord blood has been shown to be a source of stem cells for transplantation. The first cord blood transplantation was performed for a 5year old child with fanconi's anaemia, by Dr. Gluckman and colleagues in October 1988 [1]. Also the first cord blood transplant for haemoglobinopathy was in 1995 by Issaragris et al. [2]. As at 2007, at least 350,000 to 400,000 Umbilical cord blood (UCB) units have been banked with over 6000 UCB transplant performed worldwide [3]. UCB has become a fully established source of stem cell for transplanting malignant and non malignant disorders with reduced incidence of graft versus host disease [4,5].

Cord blood mononuclear cells are comprised of a heterogenous population of haematopoietic and mesenchymal stem cell, endothelial progenitor cells and immature immunological cells [6,7]. The conventional medical use of cord blood is limited to haematopoietic reconstitution [8], with clinical trials ongoing in type 1 diabetes mellitus [9], and cerebral palsy [10].

Preclinical studies have demonstrated efficacy of cord blood in diverse conditions ranging from heat stroke [11,12], to amyotrophic lateral sclerosis [13], to post infarct regeneration [14], to liver failure [15].

In haematopoietic stem cell transplants ablation of recipient marrow is required to eradicate the endogenous stem cell compartment, and HLA matching with post transplant immune support is used to prevent graft versus host disease (GVHD) [8]. For non-haematopoietic applications such as cardiovascular or neurological indications, the therapeutic activities of the cord blood are believed to be mediated in many cases by growth factor secretion [16,17].

Tumor lysis syndrome describes the metabolic complications of either rapid tumor cell turnover or chemotherapy induced tumor cell lysis. The syndrome is characterized by hyperuricaemia, hyperphosphataemia, hypocalcaemia, hyperkalaemia and acute renal failure [18,19]. The acute renal failure is associated with large increase in plasma uric acid level. The pathophysiology of uric acid nephropathy includes intratubular precipitation of uric acid causing mechanical obstruction, direct toxicity to epithelial and endothelial cells and potential activation of the innate immune system [20,21,22,23]. Occasionally, patients will develop tumor lysis syndrome spontaneously, but the majority of cases are associated with chemotherapy before the widespread adoption of prophylaxis, most cases of acute renal failure in tumor lysis syndrome were due to uric acid nephropathy [24].

Since chemotherapy is a very important process in stem cell transplantation especially in ensuring marrow ablation, which can result to tumor lysis syndrome and its complications such as electrolyte derangement. In this study, we analyzed some biochemical parameters of cord blood as a way of ensuring the quality of cord blood collected for stem cell

transplantation in order to minimize post transplant complications that may arise from derangement of these analytes.

2. PATIENTS AND METHOD

Cord blood from a total of 164 HIV, hepatitis B and C negative pregnant women who delivered in University Of Benin Teaching Hospital, Benin City, Nigeria between July 2010 and March 2011 were collected. The pregnant women were properly briefed about the study and informed consents where obtained from them before umbilical cord blood was collected, 4.5mL of the umbilical cord blood was collected in a 5mL specimen collection tube containing 0.5mL lithium heparin as anticoagulant; this was in keeping with blood to anticoagulant ratio of 9:1. After collection, the tube was immediately inverted 8-10times to ensure adequate anticoagulation of the specimen. The specimens were centrifuged for 5minutes at 3,000rpm. The plasma were separated into clean covered plain tubes and stored in an ultrafridzer at -80^{o}c within 30minutes of collection.

The plasma sodium, potassium, bicarbonate and chloride were analyzed using the ion selective electrode system (ISE 4000) while the uric acid was analyzed using uricase method.

3. STATISTICAL ANALYSIS

Statistical package for scientific solutions (SPSS), version 16 was used for the statistical analysis. All values were reported as mean ± standard error of mean (SEM).

4. RESULTS

The levels of the biochemical parameters were; sodium 135.4± 6.1mmol/L (128 - 159 mmol/L), potassium 7.08± 1.9 mmol/L (4.5 - 14.7), bicarbonate 19.6± 2.4 mmol/L (14 – 25mmol/L), chloride 101.7± 3.8 mmol/L (90 – 109mmol/L) and uric acid 1.63± 0.9 mmol/L (0.19 – 3.09 mmol/L) (Table 1). Chloride was the most stable of all the analytes with a coefficient of variation (C V) of 3.71%, followed by sodium with a CV of 4.49%. uric acid was the least stable analyte with a coefficient of variation of 12.63% (Table 2).

Table 1. The levels of the various biochemical parameters in cord blood

Biochemical analyte	Minimum (mmol/L)	Maximum (mmol/L)	Mean (mmol/L)	Standard deviation
Na+	128	150	135.44	6.088
K	4.5	14.7	7.08	1.875
HCO	14	25	19.60	2.356
Cl	90	109	101.74	3.773
Uric acid	0.19	3.09	1.63	0.857

There was a significant positive correlation between sodium and chloride with a p-value of 0.01 (r=0.362), sodium and bicarbonate with a *P-value of 0.002*. There was a positive correlation between sodium and uric acid acid ,(r=0.121) bicarbonate and chloride (r= 0.165) bicarbonate and uric acid (r=0.063) chloride and but the correlation was not significant with a *P-value* greater than 0.05. However, there was a negative correlation between sodium and potassium (r=-0.37) potassium and bicarbonate, (r=-0.045) potassium and chloride, (r=-

0.0146) potassium and uric acid (r=-0.163) but the correlation was not significant with a *P-value* greater than 0.05 (Table 3).

Table 2. Coefficient of variation of the various biochemical parameters

Biochemical Analyte	Coefficient of Variation (%)	Comment
Na+	4.49	
K	6.48	
HCO	5.02	
Cl	3.71	Most stable measurement
Uric acid	12.63	Least stable measurement

Table 3. Correlation studies for the various analytes

Association	Correlation (r)	P-value	Comment
Na vs K	0.37	.80	No sig. correlation
Na vs HCO	0.42	.002	Sig. correlation
Na vs Cl	0.362	.01	Sig. correlation
Na vs Uric acid	0.121	.40	No sig. correlation
k vs HCO	0.045	.76	No sig. correlation
K vs Cl	0.146	.31	No sig. correlation
K vs Uric acid	0.163	.26	No sig. correlation
HCO vs Cl	0.165	.25	No sig. correlation
K vs Uric acid	0.063	.66	No sig. correlation
Cl vs Uric acid	0.035	.81	No sig. correlation

Fig. 1 is a histogram showing plasma potassium level in umbilical cord blood compared with the high normal reference value in the University of Benin Teaching Hospital.

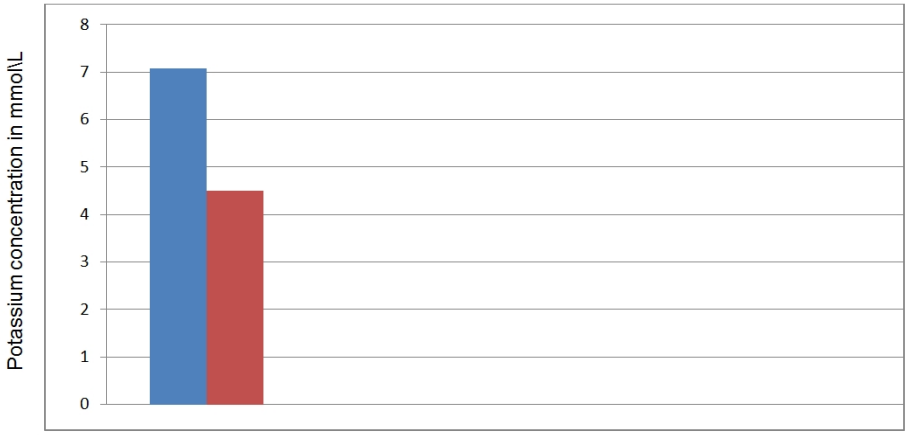

Fig. 1. This is a histogram showing plasma potassium levels in umbilical cord blood Vs high normal reference value in the University of Benin Teaching Hospital

Key:

Umbilical cord blood

High normal reference value in the University of Benin Teaching Hospital

5. DISCUSSION

In this study, we demonstrated that umbilical cord blood has low normal sodium level and hyperkalaemia, although results from previous studies reported high levels of aldosterone in neonates [25] compared to their mothers [26], aldosterone has been previously shown to cross the placental barrier from the mother to the foetus [27] and highest aldosterone levels detected in cord blood are consistent with de novo synthesis in the fetal adrenal gland given the very early expression of the aldosterone synthase gene starting from the 13 gestational weeks [28]. The reason for the low normal sodium and hyperkalaemia could be the result of the inability of the fetal kidneys to appropriately control sodium and water reabsorption as a result of the impaired ability of nephronic segments to adequately respond to aldosterone action. The neonatal weight loss related to extracellular fluid loss [29], which occurs during the first week after birth, is likely to be the consequence of this tubular insensitivity. Yet, the physiological trigger and the role of this transient sodium and water negative balance in newborn infants are still unclear.

From a pathophysiological perspective, it has been reported that plasma aldosterone levels and potassium concentration levels are higher in low birth weight infant [30], similarly, preterm infants have higher aldosterone levels and hyperkalaemia than full term infants [31,32]. Given that low birth weight infants have greater risk of developing adult hypertension [33], high levels of plasma aldosterone and hyperkalaemia may thus serve as important biochemical parameters and represent risk factors for dysregulated renin-angiotensin aldosterone system and early onset of a high blood pressure. It is very likely that neonatal insensitivity to aldosterone action varies with birth weight and could be a predictive factor of future chronic disease with a possible involvement of gene development programming as recently described for glucocorticoids sensitivity [34].

The umbilical cord blood bicarbonate level was low normal which is in agreement with previous studies that defined fetal metabolic acidaemia as an umbilical vessels pH of less than 7.20 and base excess of less than -8 [35,36]. The uric acid and chloride levels were within normal range [37].

Considering the fact that most of the patients for stem cell transplantation are prone to developing tumor lysis syndrome either as a result of rapid tumor cell turnover or chemotherapy. The syndrome is characterized by hyperuricaemia, hyperphosphataemia, hypocalcaemia and acute renal failure [18,19]. The acute renal failure is associated with large increase in plasma uric acid level. The pathophysiology of uric acid nephropathy includes intratubular precipitation of uric acid causing mechanical obstruction, direct toxicity to epithelial and endothelial cells, and potential activation of the innate immune system [20,21,22]. There is every need to ensure that the umbilical cord is devoid of any form of electrolyte and uric acid derangement.

Umbilical cord blood could become an important source of stem cell in sub-sahara Africa especially with the large number of deliveries, Shahrokri et al. [38] highlighted the importance of umbilical cord blood stem cell transplantation as a potential cure for blood diseases. However, careful selection of quality cord blood must be enforced, avoiding haemolysis which may be partly responsible for the hyperkalaemia as noted in this study in order to minimize post transplant complications that may arise from derangement of these biochemical analytes.

6. CONCLUSION

Umbilical cord blood could become an important source of stem cell in sub-sahara africa especially with the large number of deliveries. However careful selection of quality cord blood must be enforced to avoid contaminants and haemolysis which may be responsible for the hyperkalaemia as seen in this study.

CONSENT

The pregnant women were properly briefed about the study and an informed consent was obtained from them before the umbilical cord blood was collected.

ETHICAL APPROVAL

The study was approved by the ethical committee of the University of Benin Teaching Hospital, Benin City, Nigeria.

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COMPETING INTEREST

Apart from non availability of equipment/reagents to carryout immune-genetic analysis of the samples which would have extend the scope of this study, no other competing interest exist.

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