Original Research Article

INCIDENCE OF NEONATAL CONVULSION/SEIZURES ASSOCIATED WITH PRIMARY DISTURBANCE OF CALCIUM, PHOSPHORUS, AND MAGNESIUM IN UNIVERSITY OF PORT HARCOURT TEACHING HOSPITAL (UPTH)

ABSTRACT

Neonatal seizures are abnormal electrical discharge in the neonates that usually manifest as stereotyped muscle activity of autonomic change. Seizure occur in up to 1.4% of mature infant and 20% of pre-mature infant. Neonate in university of Port Harcourt Teaching Hospital were used for the study, 86 blood samples were collected from the children department, the children include both male and female within the Age range of I day to 7 day. Out of the total of 86 sample analyzed for calcium, magnesium and Phosphorus from the results obtained from both calcium and magnesium failed below the reference value, that indicate that calcium and magnesium where the major causes of the neonatal seizures.

1.0 INTRODUCTION

Neonatal seizures are abnormal electrical discharge in the neonates that usually manifest as stereotyped muscle activity of autonomic change. The most common causes of Neonatal seizures may occur before delivery or after delivery. Seizure occur in up to 1.4% of mature infant and 20% of pre-mature infant, Neonatal seizure occur as a result of ischemic stroke in Neonate with polycythemia with thrombophiua, a genetic disorder or with severe hypotension., infections such as meningitis and sepsis may cause seizure. In such cases seizure is usually accompanied by

others symptoms and signs [1]. Group B streptococci and gram-negative bacteria are common causes of such infections in neonates. Encephalitis due to cytomegalovirus, herpes, simplex virus, rubella virus, treponema pallidum, or Toxoplasmgondii can also causes seizures.

Neonatal seizure are usually focal and be difficult to recognized, common manifestation include migratory clonic jerks of extremities, alternating hemi-seizures, and primitive subclonal seizure (which cause respiratory arrest, chewing movements, persistent eye dilation mystagmoid movements, and episodic changes in muscle (tone) [2].

Generalized tonic-clonic seizures are uncommon. Neonatal seizures have a vast number of possible aetiologies, common actiologics include neonatal encephalopathy (60%), intracranial infection (5-10%), intracranial hemorrhage, developmental malformations and correctable metabolic disturbances such as hypoglycemia and derangement of electrolytes (example, sodium, calcium and magnesium) [3].

This metabolic disturbances since they are correctable, early diagnosis is necessary for timely institution of appropriate treatment and important in diatomic clinical outcome this project is therefore aim that early determination of electrolyte that are associated with nernatal seizures**.**

Neonatal convulsion associated with primary disturbance of calcium, phosphorus, and magnesium metabolism f. Cockburn J.K Brown, N. R. BELTON, and J.O FORFAR (1947), from the department of child, life and Health, university of Edinburgh, Simpson Memoria maternity pavilion, and Royal Hospital for sick children, Edinburgh. Neonatal seizures associated with primary disturbance of calcium, phosphorus and magnesium metabolism have

been studied by Cockburn, F, Brown, J.K Betton N. R. and Forfar, J.O (1973). Hypocalcemia was present in 92% of cases, hypomagnesemia in 53% and hyperphosphataemia in 64%.

In nearly 80% of cases combinations of biochemical disturbance were present, the commonest being hypocalcaemia/hypomagnesaemia/hyperphophosphataemia. Isolated hypocalcaemia occurred in 19% of cases but isolated hypomagnesaemia in only 3%.

Neonatal convulsions may result from a variety of causes including primary disturbance of mineral metabolism (Schwartz, 1965, Mclnerney and Schubert, 1969, freeman, 1970, Rose and Lombroso, 1970).

2.0 MATERIALS AND METHODS

In this cross analytical study, 86 neonate diagnosed with seizure disorder were used as the subjects. 3mls of blood were collected into heparinized anti-coagulant bottles from the paediatric phlebotomy unit. Each batch collected were taken to the laboratory for analysis.

Inclusion: the study aim at neonates within the age range of 1-28 days after birth diagnosed with seizure disorder.

Exclusion: Neonates ranging within the age of 5 weeks and above and those without diagnosis of seizure

2.1. PHOSPHORUS

Materials and Equipments

Centrifuge, Hand glove, Anticoagulant free bottles, pipettes (Pasteur pipettes), Test tube racks, spectrophotometer, micro-pipettes (1000pI), phosphorus Reagent (ROT), phosphorus standard (STD), QC, Distilled water, cuvette.

Reagent Contents

RGT: 2 x 100ml Reogent

Animoniurnheptamolybdate	-	0.3mmol/L
Sulphuric acid (PHL1.0)	-	160mmol/l
Detergent	–	1%

Activators and stabilizers

STD: 1 x 5m1 standard 32

Phosphorus - 10mg/dl or 3.2mmolk

(Photometric UV test for the Determination of phosphorus)

Principle of the Test

Phosphate reacts with molybdate in strong acid medium to form a complex. The absorbance of this complex in the near UV is directly proportional to the phosphate concentration. Reaction principle (simplified).

$7H3P04 + 12\ (M070_{24})\ 6 + 1H^{+} \longrightarrow 7(PCMO12O4O) + 36H20$

Procedure

1. Four test tubes were arranged into the test tube rack and labeled as test (T), Blank (B) standard (s) and Qc (C)
2. $10\mu l$. of sample was pipetted into the sample tube 33
3. 10 μl. of standard was added to standard tube
4. 10 μl. of QC was added into the QC tube

5. l000pL (1.0l) of reagent (RGT) was added to each of the tubes

6. The tubes were mixed, incubated at Room temperature for 1 minute

Table 1: PROCEDURE TABLE

Tubes	Reagent Blank	Sample	STD	QC
Sample (s)		10 μl	-	-
Standard (STD)			10 μl.	
QC	-	-	-	10 μl
Reagent	1000 μl	1000 μl	1000 μl	1000 μl (1ml)

Calculation

Concentration C = 10 x $\frac{Asmple}{ASTD}$ mg/dl

C = 3.2 x $\frac{Asmple}{ASTD}$ $mmol/L$

Normal Values

Children 4.0 – 70mg/dl – 1.30 – 2.26mm 01/L

2.2 CALCIUM (CA)

Materials and Equipment

Spectrophotometer, test tubes, Distileld water, calcium kit, micro-pipette, test tube rack, 1ml pipettes

Reagent Composition

R_1 Buffer

2 – amino -2- methyl

Propan -1.01

-3.5m 01/L, PH 10.7

R2 Chromogen

0 - Cresolphthalein complexone -0.16mmol 35

8 - Hydroxyguinoline - 6.89mmol/L

Colorimetric Method

Principle of the Test: Calcium ions form a violet complex with 0- cresolphthalein complexone in alkaline medium

Procedure

1. Four test tubes were arranged in the test tube rack as Reagent Blank, standard, sample and Qc.
2. 25μl (0.025ml Jof Distilled water was added to the blank tube.
3. 25 μl of standard was added to the standard tube.
4. 25 μl of sample was added to the sample tube.
5. 25 μl of QC was added to Qc tube
6. 0.5ml of reagent (R_1) was added to each to each tubes
7. 0.5ml of R2 was added to each tubes.

8. Each tubes were mixed, the absorbance of the sample (A sample), standard (A Standard), QC was read against the reagent blank of 5 to 50 minutes at room temperature at a wavelength of (550-590nm).

Table 2: PROCEDURE TABLE

Tubes	Reagent Blank	Sample	STD	QC
Sample	-	-	25 $\mu l.$	-
DH_2^0	25 $\mu l.$	-	-	-
Std	-	25 $\mu l.$	-	-
QC	-	-	-	25 $\mu l.$
R_1	0.5ml	0.5ml	0.5ml	0.5ml
R_2	0.5ml	0.5ml	0.5ml	0.5ml

Calculation

Conc. (mmol/L) $= \frac{A\ sample \times Standard\ concentration}{A\ standard}$

Conc. (mg/dl) $= \frac{A\ sample \times Standard\ concentration}{A\ standard\ \ 37}$

Normal Values

Serum = 2.02 – 2.60mmol/l

(8.10 – 10.4mg/d).

2.3 MAGNESIUM

Materials And Equipment Used

Spectrophotometer micro pipette, 10ml pipette, test tubes, test tube rack, magnesium kit (standadrd and Reagent (A) and sample.

Contents And Composition Of Reagent

A. Reagent 4x50ml. calmagite 80μmol/L

EGTA 60μmol/L, diethylamine 0.2mo 1/h

S. Magnesium standard 1 x 5ml.

Magnesium 2mgld/(0.82mm0/k)

Colorimetric Method

Principles of the Test: Magnesium in the sample reacts with calmogite in alkaline medium formign a coloured complex that can be measured by spectrophotometer in the reagent to remove calcium interference.

Procedures

1. Four test tubes int eh test tue rack labelled blank, samle, standard and Q.C.
2. 10μl of standard was added into standard tube
3. 10μl of sample was added into sampel tube
4. 10μl of QC was added to QC tube.
5. 1ml off reagent (A) was added to each of the tubes.
6. The tubes were mixed and allowed to stand for 2 minutes at room temperature.
7. The absorbance of standard, sample and QC was read at 520nm against the reagent Blank.

Table 3: Procedure Table

Tubes	Reagent Blank	Sample	STD	QC
Magnesium standard	-	10 μl.	-	-

Sample	-	-	10 μl.	-
QC	-	-	-	10 μl.
Reagent	1.0ml	1.0ml	1.0ml	1.0ml

Calculation

$\frac{A\ sample \times standard}{A\ standard}$ = (Sampel concentration)

$\frac{A\ sample \times 2}{A\ standard}$ = mg/dl

$\frac{A\ sample \times 0.82}{A\ standard}$ = mmol/dl

Reference Values

Serum and plasma 1.7 – 2.4mg/dl = 0.70 – 0.98mmol/140

Ethical Approval

The research was approved by the University of Port Harcourt teaching Hospital Research and ethics committee.

3.0 RESULTS AND DISCUSSION

Table 4: For Calcium

(x)	Freq. (f)	Mode	Mean (x)	Standard Deviation (δ)
1.4 – 1.6	13	`		
1.7 – 1.9	15	51		
2.0 – 2.3	22		1.82	
				1.12

Table 4 reveals the value of serum calcium of the neonates failed below the reference range of normal calcium 2.02-2.60mmol IL.

Table 5: Magnesium

	Ranking (x)		(x)		(x)
1	10	34	0.5	67	0.5
2	0.8	35	0.8	68	0.6
3	1.0	36	0.5	69	0.6
4	0.7	37	0.4	70	0.8
5	0.5	38	0.9	71	0.6
6	0.6	39	0.4	72	0.6
7	0.8	40	0.6	73	0.5
8	0.9	41	0.7	74	0.7
9	0.7	42	0.8	75	1.0

10	0.5	43	0.7	76	0.8
11	0.4	44	0.6	77	0.4
12	0.9	45	0.6	78	0.8
13	0.4	46	0.5	79	0.7
14	0.7	47	1.0	80	0.8
15	0.9	48	0.6	81	0.7
16	0.8	49	0.5	82	0.8
17	1.1	50	0.7	83	1.0
18	0.6	51	0.9	85	0.5
19	0.7	52	0.7	85	0.5
20	0.5	53	0.6	86	0.8
21	0.6	54	0.5		
22	0.6	55	0.8		
23	0.8	56	0.7		
24	0.6	57	0.6		
25	0.7	58	0.4		
26	0.8	59	1.0		
27	0.7	60	1.1		
28	1.2	61	0.8		
29	0.8	62	0.6		
30	0.6	63	0.8		
31	0.5	64	0.7		
32	0.4	65	0.6		

33	0.7	66	0.8	

$\sum x = 59.4$

Mean $\bar{x}$ $\frac{\sum}{n}$

$= \frac{59.4}{86}$

= **0.69**

Standard deviation

$\delta = Log\ x = \sum \frac{(10x - logx)^2}{n-1}$

$\sqrt{\frac{(2.023-1)^2}{86-1}}$

$\sqrt{\frac{(1.023)^3}{85}}$

$\sqrt{\frac{1.0465}{85}} = 0.012$

δ **= 0.046**

Table 6. Magnesium

(x)	Freq. (f)	Mode	Mean (x)	Standard Deviation (***δ***)
0.4 – 0.6	39			
0.7 – 0.9	38	39		
1.0 – 1.9	9			

			0.69e		0.012

Table 6 reveals that mean x of magnesium and standard deviation all failed below the normal range of magnesium which is 0.70 – 0.98mmol/L.

Table 7: Phosphorus

Ranking (x)		(x)		(x)	
1	1.9	34	2.4	68	2.4
2	1.8	35	2.9	69	1.8
3	3.0	36	3.2	70	2.4
4	2.1	37	2.4	71	3.1
5	1.8	38	2.8	72	2.7
6	2.1	39	3.1	73	2.6
7	2.4	40	2.6	74	2.3
8	1.9	41	2.8	75	2.4
9	2.3	42	2.3	76	3.1
10	3.0	43	2.6	77	2.5
11	1.8	44	3.0	78	2.5
12	2.5	45	2.6	79	2.5
13	2.9	46	3.0	80	1.8
14	1.7	47	2.5	81	2.0
15	2.4	48	2.9	82	1.7

16	2.4	49	2.5	83	1.6
17	2.4	50	2.5	84	2.4
18	2.3	51	1.6	85	2.8
19	24	52	1.6	86	2.7
20	2.0	53	2.9		
21	2.1	54	1.8		
22	1.8	55	2.0		
23	2.6	57	2.6		
24	2.4	57	2.6		
25	2.6	58	2.0		
26	2.3	59	2.3		
27	2.7	60	2.3		
28	1.8	61	1.6		
29	2.4	62	1.7		
30	2.9	63	2.3		
31	2.5	64	2.0		
32	1.6	65	2.1		
33	1.7	66	2.6		

$\sum x = 200.6$

Mean $\bar{x} = \frac{\sum x}{n}$

$= \frac{200.6}{86} = 2.33$

Standard deviation δ

$$\boldsymbol{\delta = Log\ x\ } = \sum \frac{(10x - logx)^2}{n-1}$$

$$\sqrt{\frac{(2.30 - 0.37)^2}{85}}$$

$$\sqrt{\frac{3.75}{85}}$$

$$\sqrt{\frac{12,64}{85}} = 0.03$$

Table 8: For Phosphorus

(x)	Freq. (f)	Mode	Mean (x)	Standard Deviation ($\boldsymbol{\delta}$)
1.6 – 1.9	19			
2.0 – 2.5	42	42		
2.6 – 2.9	18			
3.0 – 3.3	7		2.33	
				0.03

Table 8 reveals that the mean (x) and standard deviation of phosphorus the mean ( ) shows the value above the reference range but the standard deviation felled below the reference range of 1.30 – 2.26mmol/L.

DISCUSSION

The results obtained from the study shows that, the seizure diagnosed by the pediatrician resulted from low level of calcium and magnesium concentration in the neonate's plasma.

Therefore, the results revealed that neonatal seizure is mainly caused by hypocalcemia and hypormagnesernia. This is consistent with the work of Mcinerney et al, 2008 [4] [5].

Also the study show that increase in phosphorus may lead to decrease in calcium and magnesium as the mean value of phosphorus above the reference value.

Electrolyte imbalance in neonatal seizure: acute or severe electrolyte imbalance rapidly progressive neurologic symptoms or seizures which is the major reason for neonatal seizure.

Seizure are more frequently observed in patients within hypocalcemia and hypomagnesaemia and hyponetremia

Investigation have shown that magnesium, calcium,sodium depletion causes a marked irritability of the nervous system, eventually resulting to seizures [6].

Symptoms and Signs

Neonatal seizures are focal and may be difficult to recognize. Common manifestation include migratory clonic jerks of extremities, alternating hemiseizures, and primitive subclonic seizures (which cause respiratory arrest, chewing movements, persistent eye deviations nystagmoid movements, and episodic changes in muscle tone). Generalized toniccdonic seizures are, uncommon.

Clinically silent electrical seizure activity is often present after a hypoxic-ischemic result prenatal asphyxia or stroke) and in neonates with CNS infections, especially after initial

treatment, which is more likely to stop clinical manifestations than electrical seizure activity (Burke, (1954).

Zimmet, P; Breidah.i, H.D., and Nayler, W.G. (1968) reported that Hypomagnesaenxia is a rare cause of seizures, which may occur when the serum mg level 1.4m Eg/l/L 0.7mmo/L). Hypomagnesemia often occurs with hypocalcemia and should be considered in neonates with hypocalcemia if seizures continue after adequate Ca therapy.

Blood Plasma calcium concentrations in the convulsing infants had significantly lower plasma calcium concentrations based on mean ± /SD). The mean and ± SD of magnesium in some infants with convulsions were low but. As observed in this study, Mcinerney and Schubert a (1969), rose and lombroso (1970), and keen (1969) found the outcome satisfactory in the majority of neonatal convulsions due to primary hypocalcemia and hypomagnesaemia.

Hypocalcaemia and hypomagncsacmia infants who convulsed frequently showed a clinical pattern compounded of hypertonicity, jitteriness, increased muscle response to stimulation, increased tendon reflexes, a hyperalert state between fits, and transient

hemisyndrom, these are not always present, nor are they specific for primary hypocalcaemia/hypomagnesaemia they may also occur in brain damaged infants probably due to the secondaryl8 disturbances of mineral metabolism which accompany brain damage (Brown et al; 1972).

4.0 CONCLUSION

This work revealed a significant low level in calcium and magnesium.

There is an exceptionally important role for patient education pregnant mothers on diet support, electrolytes screening, culture and sensitivity, blood Glucose should be a routing test for all pregnant mothers.

Also the neonates diagnosed of seizure should be treated for hypocalcema and hypomagnesemia by the paediatrician.

It can be safely concluded that pregnant mothers should develop the habit of attending antenatal clinic, so that the baby state of health can be closely monitored within this period

RECOMMENDATION

Enlightenment campaign on neonatals seizure associated with electrolytes disturbance should be done using various information media as Television, Newspaper, Radio and seminars. Further work may be necessary on neonatals seizures such as glucose test, neurocranial x-ray, sodium determination etc.

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