ECRONICON OPEN ACCESS

EC PAEDIATRICS
Research Article

Hypothesis of Iatrogenic Severe Hypothermia of Internal Organs in Extremely-Low Birthweight Infants during Bubble CPAP Intervention at Room-temperatures in Nigeria

Hippolite O Amadi[1]*, Amina G Abubakar[2], Amina L Abubakar[3], Hauwa Yusuf[2] and Maryam Usman[2]

[1]*Professor, Department of Bioengineering, Imperial College London, United Kingdom*

[2]*Special care baby unit, Jummai Babangida Maternal and Neonatal Hospital, Minna, Niger State, Nigeria*

[3]*Consultant Obstetrician/Gynecologist, Maternal Division, Jummai Babangida Maternal and Neonatal Hospital, Minna, Niger State, Nigeria*

***Corresponding Author:** Hippolite O Amadi, Professor, Department of Bioengineering, Imperial College London, United Kingdom.

Received: May 15, 2019; **Published:** May 29, 2019

Abstract

Background: Bubble continuous positive airway pressure (CPAP) application has become popular in Nigeria against the backdrop of very high incidence of respiratory distress syndrome among preterm neonates in the country. An estimated > 90% of interventions in Nigeria is carried out via an improvised technique or use of devices that deliver CPAP gas at room temperatures only. There is however, a high record of neonatal mortality amongst very- and extremely-low birthweight neonates that receive CPAP treatments using these devices. It is suspected that a possible dodgy severe hypothermia could be blamed; hence the need for a preliminary hypothesis.

Methods: The aetiology of CPAP iatrogenic hypothermia was studied via free-body modelling to formulate prevailing thermal interplay. Thirteen extremely-low birthweight neonates (BW: 600g - 1000g) were recruited to test the hypothesis. Four of these were treated with CPAP-temperature-controlled device, whereas the rest of the 13 were treated with disposable improvised CPAP devices that delivered air at room temperatures. A digital thermometer probe was inserted in the CPAPs' gas delivery tubes to measure the temperatures of the inspiratory gas just before the infant received this.

Results: Only four of the extremely-low birthweight infants were successfully weaned from the CPAP interventions. All four received pre-warmed CPAP gas but all nine unsuccessful infants received CPAP gas at room temperature. All 13 patients maintained physiological temperatures > 36.5°C, measured superficially via the axilla. Median inspiratory gas temperatures for all the deceased remained below 32°C throughout, whereas those of the successful infants remained above 35.5°C.

Conclusion: Acceptable axillary temperatures may be concealing dangerous internal iatrogenic hypothermia, perhaps at the lungs leading to organ failures and death. Internal organ temperatures below 33°C may be insufficient to guarantee neonatal survival. Bubble CPAP gas is therefore recommended to be pre-warmed and delivered at appropriate temperatures akin to incubator environment temperature when treating preterm neonates.

Keywords: *Neonate; RDS; Respiratory Support; Low-Income; Oxygen Therapy*

Abbreviations

bCPAP: Bubble Continuous Positive Airway Pressure; CPAP: Continuous Positive Airway Pressure; ELBW: Extremely Low Birthweight; IbCPAP: Improvised Bubble Continuous Positive Airway Pressure Device; LBW: Low Birthweight; politeCPAP: Temperature-Controlled Commercial bCPAP Machine; RDS: Respiratory Distress Syndrome; SCBU: Special Care Baby Unit

Introduction

Bubble continuous positive airway pressure (CPAP) intervention technique is common in Nigeria. This is a technique of generating a high volume flow of humidified and oxygenated air channelled through the neonate's nostrils to actualise gaseous exchange at the lungs. Properly designed CPAP machines have air-oxygen blending capability to ensure appropriately optimised oxygen ratio in the delivered gas. This capability helps to avoid high oxygen toxicity that could potentially lead to retinopathy of prematurity (ROP) [1]. Properly designed commercial models of bubble CPAP machines are not widely in use in Nigeria due to high costs of the devices, and unaffordable maintenance and high costs of consumables. These limitations have led to the popular use of a potentially unsafe application in Nigeria called 'Improvised bubble CPAP' (IbCPAP) setup [2]. It is estimated that over 90% of Nigeria neonates diagnosed with respiratory distress syndrome (RDS) or associated diseases would receive bubble CPAP intervention using the IbCPAP technique rather than appropriately designed models of the application.

A study in Malawi presented a debilitating persistent hypothermia during application of a CPAP model (Pumani system®. Hadleigh Health Technologies, San Rafael, CA, USA) [3]; hence, recommending the use of 'aggressive warming' as the solution to counteract the effect. The IbCPAP and other respiratory support techniques that deliver gas at room temperatures have also been associated with neonatal hypothermia especially among low birthweight infants (LBW). These systems might have been fairly successful with bigger neonates; however, these score very poor success rates among extremely-low birthweight (ELBW) neonates in Nigeria. It is understood that some designs of CPAP machines incorporate the capability of post-process warming of the blended gas to a desired temperature before delivery to the neonate. This capability can potentially eliminate or drastically reduce the chances of the neonate presenting with iatrogenic hypothermia. Lack of this capability in any application - commercially branded system or the disposable IbCPAP - is therefore a significant deficiency against risks of death and neonatal mortality reduction owing to RDS.

It is presently not well-understood amongst Nigerian clinicians whether hypothermia would be blamed for many of the unsuccessful ELBW interventions using IbCPAP and the other systems that deliver gas at room temperatures. Earlier study has demonstrated that room temperatures of Nigeria nurseries could fall as low as 26°C during late hours of the night and early hours of the morning [4]. It is, hence intuitively expected that a sustained rush of cold air into a neonate's lungs at room temperatures could potentially instigate cold stress deep in the internal organs of the body. It is also not well-understood if the superficial warming of incubator or overhead warmer that normally aim to sustain a skin temperature of approximately 37°C, is adequate enough to permeate the body to neutralise any damages being done by the continuous streaming cold gas during CPAP application. An ELBW neonate, owing to extreme prematurity, could be worse-off in such a situation as this class of neonate is unable to autonomously generate or regulate its own body heat for thermal compensation by shivering for example, but rely absolutely on external warming [5]. There might therefore be more thermal events going-on deep in the body than the axillary probe of body temperature could reveal. Literature has revealed that a difference normally exists between body temperatures measured superficially via the axilla and the actual physiological core-temperature in humans, the latter being consistently higher than the former [6]. This could physiologically represent the temperature drop against the lagging activities of the skin surface and its immediate deep tissues. This might not necessarily hold in a non-physiological situation such as continuous streaming of external cold air concentrated in the lungs [2,3,7].

This study was therefore aimed at examining the theory of a possible interplay between the superficial warmth from the incubator, the streaming cold inspiratory gas of a CPAP device and any possible autonomous contributory warmth from the neonate; and also the validation of the theory via clinical measurements.

Methodology

Physio-thermal modelling

The ideal physiological thermal coordination of a healthy baby could be modelled as a system that monitors and regulates its functional temperature against possible external interferences. The autonomous system operates various body mechanisms in the presence

of adverse external cold or heat, all in the attempt to maintain the physiologically allowable body temperature, preventing organ failure and hence sustenance of life. However, the efficiency of these mechanisms reduces in cases of prematurity and could become completely ineffective for extremely-preterm or extremely-low birthweight neonates; hence, requiring intervention of the warm microenvironment of an incubator or radiant warmer, for example. The elevated temperature of the microenvironment warms the neonates' superficial skin and the deeper internal organs as the warm air also goes in and out of the lungs during respiration. The neonate essentially receives both superficial and internal organ warming simultaneously, a process that helps to maintain normotherm and neonatal thermoneutrality. However, when the internal organ warming as implemented by warm incubator environment at > 36°C is replaced with organ cooling as represented by streaming bubble CPAP air at below 32°C, there could be alteration of expected thermoneutrality and a dodgy catastrophic consequence could result. This can be represented as modelled in figures 1 and 2. The World Health Organisation (WHO) defined neonatal severe hypothermia as temperatures below 32°C [8]; however, a more recent study of Nigerian preterm neonates demonstrated that some deacesed infants were already dead from hypothermia before the WHO's severe-hypothermic threshhold of 32°C [9]. The continuous cooling of the internal organ exclussively triggered by the bubble CPAP air was capable of rapid lowering of internal temperatures far below this threshhold whilst the superficial axilla temperatures remained normotherm.

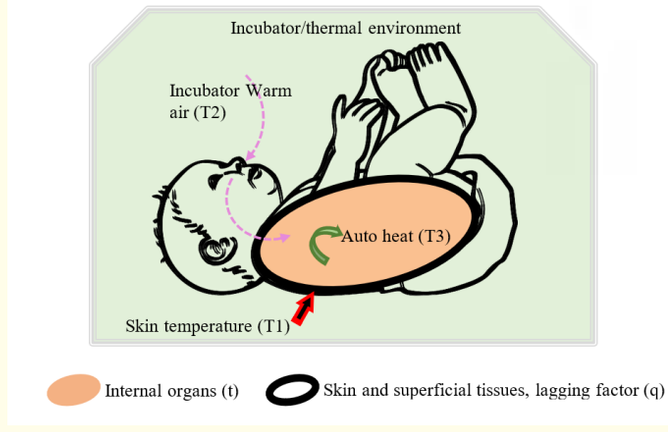

Figure 1: *Model of neonatal thermal interplay during normal incubator care. Air supply for infant breathing is exclusively provided by the warm microenvironment of the incubator.*

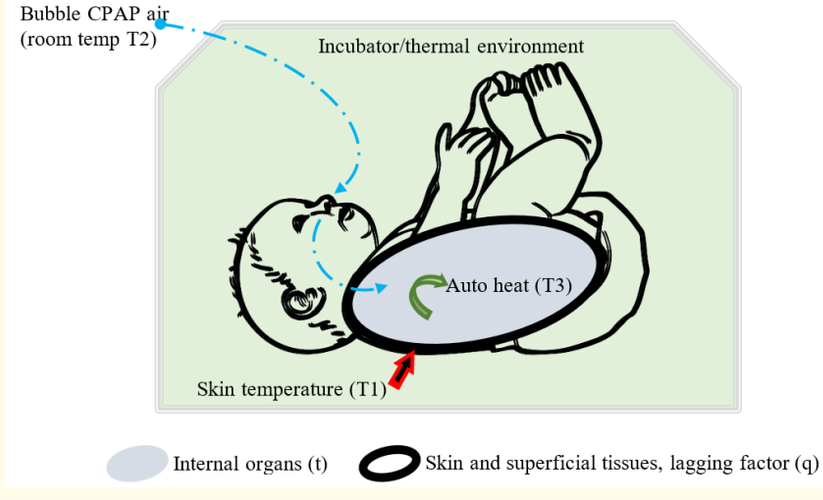

Figure 2: *Model of neonatal thermal interplay during bubble CPAP intervention at room temperature. Air supply for infant breathing is exclusively provided by IbCPAP operating at room temperature. Final internal organ temperature is the interactive output between: qT1, zT2 and T3, where q and z are heat transfer factors for T1 and T2, respectively.*

The interplaying thermal effects in the models could be described as follows:

1. Body surface temperature (T1) (Figure 1 and Figure 2) which represents neonate's skin temperature, normally measured via the axilla in Nigeria. Nigerian neonatal attendants would regulate their incubators or radiant warmers to stabilise T1 at approximately 36.9°C using the initial set-point algorithm (ISA) and the handy approach (HA) techniques [5,10]. This could also be seen as the temperature at the interface of the body and the immediate environment housing the neonate. The resultant value of T1 reaching the deeper organs depends on the dermatological insulation responses of the more superficial tissues and total body surface area for heat transfer. This represents the heat-transfer factor (q) of which value could always be expected to be less than 1. This means that 'qT1' is expected to be less than T1.
2. The incubator or CPAP-gas temperature (T2). This temperature is delivered directly to the internal organs via the nostrils without any transfer hindrances. For non-RDS infants undergoing incubator care, T2 is the temperature of incubator warm air - normally close to physiological temperatures for normal incubator care [5]. This warming via respiration is vital for maintenance of thermoneutrality as it supplements warming coming through the exposed skin surface (Figure 1). For RDS infant temperature T2 remains same as prevailing room temperature during CPAP intervention using a non-warming CPAP device. Literature revealed that room-temperatures in Nigeria can often be lower than 31°C during the day and could rapidly drop below 26°C during the night [4]. The internal respiratory warming is hence replaced with cooling (Figure 2). The intensity of internal temperature drop owing to bubble CPAP gas is also a function (z) of the gas flowrate and respiration rate.
3. Autonomous heat (T3): This represents the thermal contributions of all other brain-controlled body mechanisms that try to generate or conserve physiological body heat. T3 tends to zero in value with decreasing gestational age of neonates, and can be absolute zero for extremely low-birthweight neonates (<1000 g) [5].
4. Internal organ temperature (t) is the output of the interplay between T1, T2 and T3. This could assume the simple mathematical model: $t = {}^{(qT1 + zT2)}/_{2} + T3$

The autonomous heat 'T3' is the body's automatic compensation for countering external inputs so as to maintain the required functional values of organ temperature 't'. The temperature (t) of an internal organ of the neonate must be kept optimally within the allowable physiological range for this to function and keep the neonate alive. A full-term neonate is expected to have well-functional 'T3' responses unlike preterm neonates. The lower the gestation age or birthweight, the lower the efficiency of the 'T3' function for any neonate. Hence, as gestational age decreases, 't' value would be expected to depend absolutely on T1 and T2. Neonates of birthweights greater that 1000 g may benefit from a minimally functional T3 to assist to achieve acceptable 't'; however, an extremely-low birthweight (up to 1000 g) neonate is completely incapable of such autonomous functions as to guarantee an effective T3. The model for an ELBW neonate hence reduces to: $t = (qT1 + zT2)/2$

Substituting average values: For a typical case of an ELBW neonate maintained at axilla temperature of 36.9°C in an incubator whilst undergoing bubble CPAP intervention during the night at room temperature of 26°C, and a volume flow such that z-value tends to 1; then 't' equation could lead to internal organ temperatures such that:

$t = {}^{(36.9q + 26)}/_{2}$

$= 18.5q + 13$

At the very likely values of $q < 1$, internal organ temperature would be: $t < 18.5+13$ or $t < 31.5$°C.

This suggests the possibility of recording a neonatal axilla temperature of 36.9°C from the clinical thermometer when the actual internal organ or lungs temperature is lower than 31.5°C. This hidden information of hypothermic situation is sufficient to cause neonatal death if prolonged [9]. We therefore hypothesise a likely event of 'dodgy iatrogenic hypothermia' that could be responsible for the high mortality of ELBW neonates that received IbCPAP intervention in Nigeria [11]. This could also explain the mortalities recorded for neonates of lower-birthweight for other bubble CPAP devices such as the system reported from Malawi [3].

Validation of model

The model was clinically validated based on a prior ethical clearance obtained from the Heath Ethics Committee of the Niger State Ministry of Health, Minna, Nigeria (reference STA.495/Vol/132). The protocol followed a documented 'informed consent' from neonates' mothers, and after verbally explaining that the data collected from the patient would be used in a study but without the disclosure of the identity of the neonate. It was needful to test hypothesis on neonates of the highest risk category so as to allow a clearer manifestation of the condition being investigated. Hence, the recruitment of study candidates was limited to neonates that weighed 1000 g or less at birth and that had also been diagnosed with RDS or associated diseases but without infection complications such as sepsis. This class and condition of neonate would require assiduous incubator care coupled with respiratory support, perhaps using Nigeria's readily available intervention technique of IbCPAP. The neonate's treatment followed the normal intervention standards at the special care baby unit (SCBU) - without any alterations - except that the temperature of the gas being delivered to the neonate was also recorded each time vital sign of neonate's temperature was taken via the axilla.

Neonate's vital signs were recorded every two hours in line with normal practice standards at the SCBU until death or successful weaning from CPAP intervention. 'Control' patients were treated using the Politeheart® bubble CPAP (politeCPAP device, Neonatal Concerns Limited, Owerri, Nigeria). The politeCPAP system is equipped with a controllable warming delivery channel that could keep the delivered gas at operator's choice of temperature [11]. The system was set to run at 35.5°C or as appropriately prescribed by the clinician, but the instantaneous operational temperature display of the unit was recorded during vital signs data collection.

The IbCPAP setup [2,11] was produced as 'test' and used to intervene for any presenting ELBW neonate whenever there was no available politeCPAP system to apply. The gas delivery temperature of the IbCPAP was quantified as follows: An inspiratory channel tube was modified for checking gas temperature by creating a hole for the probe of a digital thermometer as illustrated in figure 3. The applied thermometer was the same model as the politeCPAP temperature process controller assembly (STC-1000 professional, unbranded, China). The measuring tip of the digital thermometer was inserted into the tube, across the streaming gas. The passing gas temperature was hence recorded directly as displayed on the thermometer readout. The IbCPAP gas bubbled off for delivery at room temperatures. Assiduous care was taken to ensure that neonate maintained the physiologically allowable temperature range of 36.5°C - 37.4°C [5].

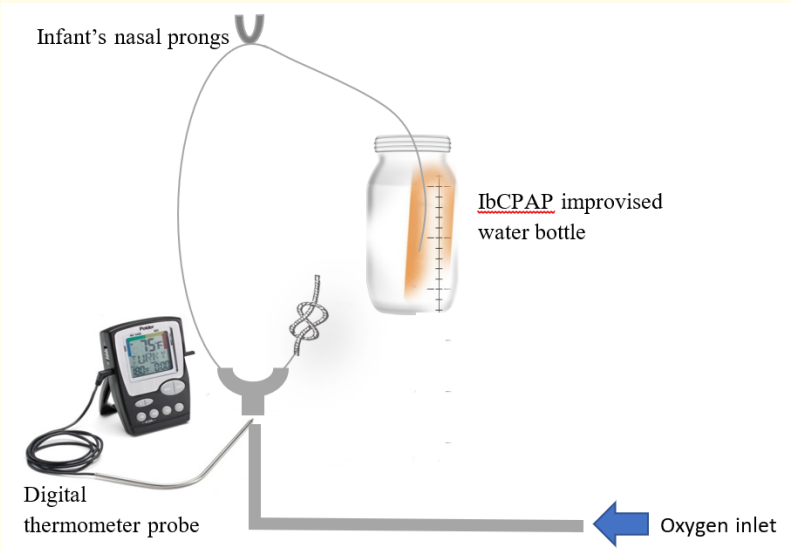

Figure 3: *Modified Nigerian improvised bubble CPAP (IbCPAP) set-up. Commercial breathing circuit nasal prong - modified, extended and inserted into a graduated water bottle. Pure oxygen delivered from oxygen cylinder or oxygen concentrator goes through a humidifier bottle (not shown) before being channeled into the breathing circuit as indicated above at the 'oxygen inlet'. Inspiratory gas tube was further modified to allow temperature probe for monitoring inspiratory gas temperature.*

A panoramic temperature plot covering the entire timeline of treatment period for each patient was produced. This provided 'at-a-glance' perception of lifetime reality of temperature differences between the standard axilla measurements and the streaming gas temperatures that emptied in the neonate's lungs.

Results

Thirteen infants received inspiratory CPAP gas via either of the techniques. Four patients were successfully weaned off CPAP intervention being treated with the politeCPAP device, while 100% (9 of 9) treated with the disposable IbCPAP devices died before successful discharge (Table 1). All patients' data showed that adequate care was given by SCBU standards to maintain acceptable neonatal physiological temperatures, measured via the axilla (Figure 4). There were remarkable differences in the measured gas temperatures from the two categories. All patients treated with the temperature-controlled politeCPAP device received inspiratory gas at temperature values > 35°C at all times; however, gas temperatures delivered to patients that were treated with IbCPAP devices were predominantly below 32°C, especially during the night times when this often fell much lower than this (Figure 4).

		ELBW, *n* = 13			
	politeCPAP 4		IbCPAP 9		
Oct 2017 - March 2018		Alive	Dead	Alive	Dead
		4	None	None	9
	BW, mean (range)	0.9 (0.8 - 1.0)		0.86 (0.6 - 1.0)	
	Treatment duration, days, mean (range)	3 (2-5)	NA	NA	Lifetime

Table 1: *Quantitative data for politeCPAP and IbCPAP neonates.*

NA: Not Available; Lifetime: From CPAP commencement until death.

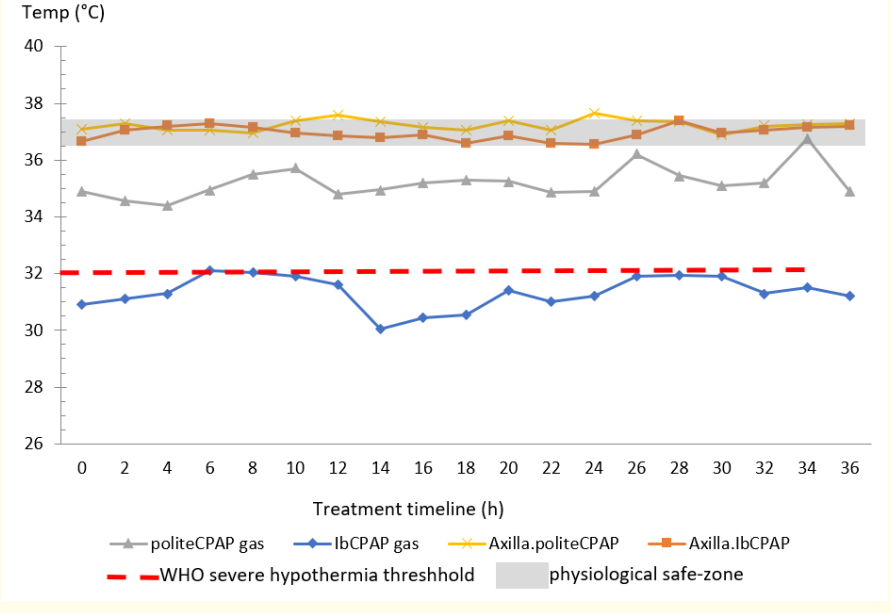

Figure 4: *Thirty-six hours median-temperature profiles for politeCPAP and IbCPAP group infants. The 2-hourly median axillary temperature record across all infants in each category plotted against their corresponding inspiratory gas temperatures, as shown against the WHO threshold for severe hypothermia.*

Discussion

The standard of practice in Nigeria accepts checking of neonatal temperature through axillary measurements and using this to control neonate's thermal environment. Practitioners do not have any need for fear of risks of catastrophic thermal inadequacies provided neonates maintained axillary temperatures between 36.5°C - 37.4°C. It is also of no essence to have doubts about inadequacy of internal organ temperatures at these values since literature declares that the peripheral or shell temperature - the temperature of the skin and subcutaneous tissues - would be less than the core temperature unless the environment is very hot or the body well insulated [6]. Hence, Nigeria practice would always assume that core organ temperatures would remain slightly higher than axilla temperature or in the worst case scenario, remain similar. It is evident from our preliminary hypothesis that this might not be as assumed for neonates undergoing bubble CPAP treatment via devices that deliver CPAP gas at 'room temperatures'. Nigeria room temperatures can drop as low as 20°C at night times, especially during the hamarttan season. This poses the possibility of depositing continuous streaming gas at < 25°C in the neonate's lungs whilst the superficial temperatures are controlled at 37°C with an incubator or radiant warmer. The internal organ, hence, could keep chilling down unnoticed and soon fails due to this dodgy severe hypothermia. Our present findings indicate an urgent need to review the Nigerian standards, especially the use of such CPAP devices that are incapable of helping very tiny neonates.

The burden of high neonatal mortality rate in Nigeria is exacerbated by high rate of early neonatal deaths, especially among neonates below 1500g birthweight. Literature quantified that nearly 4-in-5 deceased neonates in Nigeria would die in the first seven days of life [12]; and up to 83% of those that died within 48 hours were categorized below 2000g birthweight [9]. Nigeria's greatest burden, and hence priority need for assistive technology, must be applications that can save the very tiny neonates. Therefore, a bubble CPAP device that is incapable of supporting < 1500g neonates in Nigeria is basically substandard for the reduction of high neonatal mortality rate in the country. All the 13 neonates studied in this research had many survival determinants in equal proportions: They were all treated by the same clinicians and nurses during the same time period. They were all of comparable extremely-low birthweights and gestational ages. All 13 were satisfactorily maintained within the allowable physiological thermal range. Nonetheless what separated these was that all four that were treated with appropriately pre-warmed respiratory gases survived while all nine that were treated with gases at 'room temperature' died. We hypothesise that a dodgy organ hypothermic complication exists, and perhaps responsible for non-successful treatment of ELBW neonates undergoing bubble CPAP intervention in Nigeria.

Conclusion

In conclusion, the use of assistive devices for neonatal respiratory support is essential for the reduction of ever high neonatal mortality rate of neonates in Nigeria and must especially be effective for infants of >1500 g birthweight or >32 weeks gestational age. Therefore, such devices must possess the capability of pre-warming of blended air-oxygen gases before delivery to the neonate to avoid the catastrophic consequences of iatrogenic severe hypothermia of the internal organs.

Acknowledgements

This study was funded by Neonatal Concerns for Africa. The medical missions of Professor H Amadi to Nigeria were, in part, supported by the Hornchurch Baptist Church, Essex England, United Kingdom.

Bibliography

1. Olusanya BA., *et al*. "Incidence of retinopathy of prematurity at the University College Hospital, Ibadan". In: Proceedings of the 10th scientific meeting of Nigerian Society of Neonatal Medicine, Ibadan Nigeria (2017): 33.

2. Audu LI., *et al*. "Improvised bubble continuous positive airway pressure (BCPAP) device at the National Hospital Abuja gives immediate improvement in respiratory rate and oxygenation in neonates with respiratory distress". *Nigerian Journal of Paediatrics* 42.1 (2015): 12-16.

3. Carns J., *et al*. "Impact of hypothermia on implementation of CPAP for neonatal respiratory distress syndrome in a low-resource setting". *PLoS ONE* 13.3 (2018): e0194144.

4. Amadi HO., *et al*. "Synthesis and validation of a weatherproof nursery design that eliminates tropical Evening-Fever-Syndrome in neonates". *International Journal of Paediatrics* (2014): 986760.

5. Amadi HO., *et al*. "Validation of a Novel Technique that Minimises Early Neonatal Deaths - a Comparative Study". *Journal of Pediatrics and Neonatal Care* 6.1 (2017): 00232.

6. Dougherthy L and Lister S. "Royal Marsden Hospital Manual of Clinical Nursing Procedures". Oxford: Blackwell Publishing (2008).

7. Subhashchandra Daga., *et al*. "Home-Made Continuous Positive Airways Pressure Device may Reduce Mortality in Neonates with Respiratory Distress in Low-Resource Setting". *Journal of Tropical Pediatrics* 60.5 (2014): 343-347.

8. World Health Organization. "Thermal Protection of the Newborn: a Practical Guide". Geneva: WHO (1997).

9. HO Amadi., *et al*. "Neonatal hyperthermia and thermal stress in low- and middle-income countries: a hidden cause of death in extremely low-birthweight neonates". *Paediatrics and International Child Health* 35.3 (2015): 273-281.

10. Amadi HO and Kawuwa MB. "Reducing early neonatal mortality in Nigeria - the solution". In book: Selected topics in neonatal care. Barria R Mauricio editor: Intech open access publishers Croatia (2018): 221-237.

11. Amadi HO., *et al*. "A new low-cost commercial bubble CPAP (bCPAP) machine compared with a traditional bCPAP device in Nigeria". *Paediatrics and International Child Health* 8 (2019): 1-9.

12. MCA, World Health Organisation. "Maternal and Perinatal Health Profile of Nigeria, Africa Region". Maternal and Perinatal Country Profile (2014).

Volume 8 Issue 6 June 2019