Original Article

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Paediatrics Section

Comparing the Effect of Room Air versus Commercially Available Oxygen for the Resuscitation of Asphyxiated Neonates in Kabul City: A Randomised Clinical Trial

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ABSTRACT

Introduction: Perinatal asphyxia is one of the leading causes of neonatal death in Afghanistan. Recent recommendation has accepted room air as preferred therapy in the resuscitation of asphyxiated term neonates. Since the quality of air is poor in Kabul city so a study was needed to assess its efficacy in the resuscitation of neonates.

Aim: To evaluate the effectiveness of room air versus commercially available oxygen for the resuscitation of asphyxiated term and preterm neonates.

Materials and Methods: This study was a randomised clinical trial conducted at Neonatology ward of Malalai Hospital in Kabul city, Afghanistan. Total 300 neonates of 30-41 weeks gestation diagnosed as severe perinatal asphyxia were randomly resuscitated with either room air or commercially available oxygen. The clinical parameters were the Apgar score, oxygen saturation and neonatal mortality percentage. Statically analysis was performed by SPSS 20.

Results: One hundred and fifty neonates in the room air group and 150 neonates in commercially available oxygen group were investigated. The term neonate percentage was 76% and 75.3% in the room air and oxygen group respectively. Term neonates resuscitated with room air had obtained higher mean oxygen saturation (83.4±14.9, p=0.001) than oxygen (77.1±13.1, p=0.001) at 5 minute of birth. Median Apgar score was the same in both groups (5, p=0.001). The difference of mortality during hospital stay in both groups was not statistically significant (5.26% vs 7%, p=0.59). Mean oxygen saturation in preterm newborn babies were 80.58±15.62 and 78.41±11.91 with p=0.22, respectively in both groups. Median Apgar score in room air was 6 and in oxygen group was 5 with p=0.33. Preterm infant also showed non-significant difference of mortality during hospital stay in both groups (11.1% vs 18.9%, p=0.5).

Conclusion: Despite poor air quality in Kabul city, room air was significantly more effective than commercially available oxygen to increase oxygen saturation and as effective as commercially available oxygen to elevate Apgar scores in the resuscitation of asphyxiated term neonates. The difference in the mortality was not statistically significant in both the groups. The efficacy of room air did not appear statistically significant for the resuscitation of preterm neonates.

Keywords: Air pollution, Bag-mask ventilation, High concentration oxygen, Perinatal asphyxia

INTRODUCTION

The estimated number of neonatal deaths in 2017 was 2.4-2.8 million and 99% of these deaths occurred in low-income and middle income countries [1,2]. The neonatal mortality rate in Afghanistan is one of the highest in the world and it is reported by UNICEF in 2018; 39 death per 1000 live births [3,4]. The main causes of neonatal mortality in Afghanistan are preterm birth (35%), perinatal asphyxia (26%), pneumonia (15%) and sepsis/meningitis/tetanus (16%) [5]. World Health Organisation (WHO) define perinatal asphyxia as ''Failure to initiate or sustain breathing at birth" [6]. National Neonatal Perinatal Database accepted perinatal asphyxia as Apgar score of less than 7 at one minute of age [7,8]. Perinatal asphyxia is one of the major causes of early neonatal mortality in Afghanistan [5]. Annually, about 5 million asphyxiated babies are born worldwide and approximately one million of these babies die. Apart from high mortality in perinatal asphyxia about one million of these infants develop neurodevelopmental sequels such as hypoxic-ischemic encephalopathy, cerebral palsy, mental retardation and epilepsy [8-10].

All asphyxiated newborns need resuscitation soon after birth and oxygen therapy is an important part of this procedure

[8]. The current resuscitation guidelines recommend to start resuscitation with room air in all term infants and titrated up to 100%. Although, for preterm infants, no definitive recommendation has been made [11,12]. According to the meta-analysis published in the Lancet, Resuscitation with room air in term infants is equally effective and may reduce the risk of hyperoxia, which is associated with decreased cerebral blood flow and generation of oxygen free radicals [13].

In the neonatal wards of Kabul city hospitals, severe asphyxiated newborn infants are ventilated with bag and mask using room air or commercially available oxygen. The air of Kabul is severely affected by various pollutant sources, the impacts of which often cause acute health problems. In recent years, the ambient air quality in the city has deteriorated so much that it can be ranked among the dirtiest cities in the world [14,15]. According to WHO estimation the prevalence of prematurity and low birth weight in Afghan neonate are higher, all of which affect the utilisation of oxygen [4,5]. With such population and geographic difference there is no research done to determine the effectiveness of room air versus commercially available oxygen for resuscitation of neonates in the Kabul city of Afghanistan.

The current study was carried out to test the hypothesis that room air is more effective than commercially available oxygen for resuscitation of asphyxiated term and preterm newborns at birth in neonatal wards of Kabul hospitals. This information will help in cost-benefit analysis. Room air is available everywhere without any charges and its usage prevent the extra payment of commercial oxygen used for the resuscitation of neonates in governmental and private hospitals.

This RCT was performed to compare the effectiveness of room air versus commercially available oxygen for the resuscitation of asphyxiated neonates with a gestational age of ≥30 week and birth weight of ≥1500 g in the Kabul city, Afghanistan.

MATERIALS AND METHODS

Study design: To be able to fulfill the objective of the proposed study, Randomised Controlled Trail design was employed. Blinding was not possible because of clinical reason.

Study population and setting: The study population comprised of neonates (Infant up to 28day old) delivered at Malalai hospital in Kabul city during December 2018 until May 2019.

Ethical consideration: This RCT was approved by the Department of Neonatology, KUMS and the Research Committee of Ministry of Higher Education of Afghanistan. The consents of newborn mothers were received. The Research Committee of Ministry of Higher Education checked and approved the RCT on the basis of Helsinki Declaration. The proposal of this RCT was also approved by the same Department (Letter number 102 on date 4/9/2019, registered protocol number 5 on date 27/7/2017) and Research Committee (Letter number 146/329 on date 28/5/2018). The facilities were prepared by Higher Education Development Program and the World Bank.

Inclusion criteria: Neonates fulfilling all of the following criteria were enrolled in the study:

- Gestational age of 30 weeks or more; or birth weight 1500g or more.
- Diagnosed as severe perinatal asphyxia.
- Need for oxygen therapy during resuscitation.

Exclusion criteria: Neonates who had visible or physically detected malformation of CNS, chest and heart were excluded from the study.

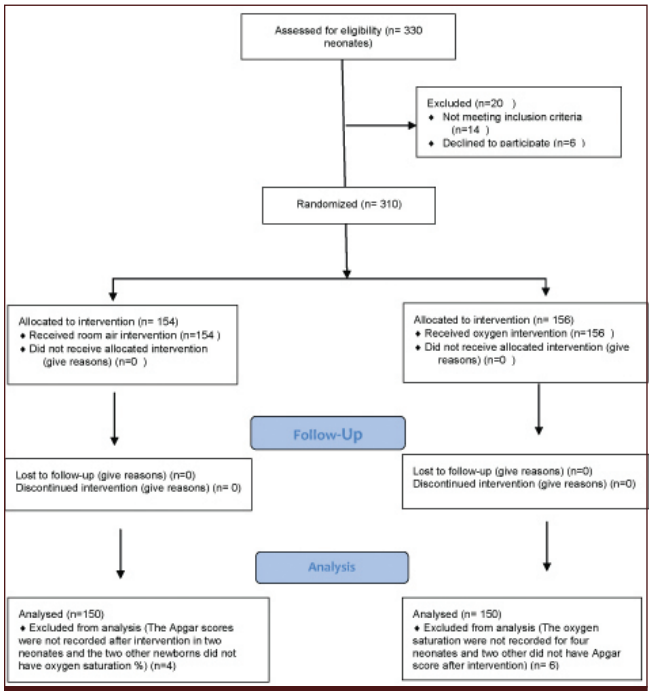
Sampling strategy: For this clinical trial randomised sampling was done to recruit the study participants. In the first step we randomly selected even days for one group and odd days for second group. In the second step, asphyxiated newborn babies were randomly assigned on the basis of their birth order for each group. Asphyxiated neonates born on even days were resuscitated with room air and the asphyxiated neonates born on odd days were resuscitated with commercially available oxygen.

Sample size: Stata 14 was used for sample size calculation. To detect a difference of 5 with a standard deviation of 15 in the oxygen saturation at 5 minutes with a 5% error probability and power of 80%, it was estimated that both group would require 286 patients. It was decided to recruit a total of 300 subjects. Total of 150 neonates were resuscitated with room air and the resuscitation of another 150 neonate was done by commercially available oxygen.

Material: For the resuscitation of asphyxiated neonates; resuscitation kits, room air and commercially available oxygen in balloons were used. Effectiveness of room air and commercially oxygen were assessed by oxygen saturation percentage and Apgar scores determined with pulse oxymeter and Apgar score table respectively.

Procedure: Three hundred and thirty newborns, diagnosed with severe birth asphyxia (Apgar score of 0-3), were studied for the comparative effects of room air versus commercially available oxygen during the resuscitation. Fourteen neonates did not meet the inclusion criteria and six mothers refused to participate. From 310 patients 154 neonates were resuscitated with room air and the other 156 neonates were resuscitated with commercially oxygen. In the room air group, the Apgar scores of two neonates were not recorded after intervention

and the two other newborns did not have oxygen saturation percentage. In the oxygen group, the oxygen saturation percentage was not recorded for four neonates and two other did not have Apgar score after intervention. Finally, 150 neonates were assessed for the effect of room air and the other 150 neonates for the effects of commercially available oxygen during the resuscitation [Table/Fig-1].



[Table/Fig-1]: Flow diagram for the patient distribution.

The neonates were ventilated by a neonatologist and two neonatal nurses with an infant resuscitation bag with a ventilator frequency of 40-60 breaths per minute. The resuscitation bag with a ventilator frequency of 40-60 breaths per minute. The resuscitation bag had a facility to attach an oxygen reservoir to deliver 4 liters/minutes commercially available oxygen or room air.

Primary outcome measure was Apgar score and oxygen saturation at 5 minute of age. Secondary outcome measures were neonatal death during hospital stay.

Variables

- Apgar score at 1 and 5 minute of age.
- Gestational age by weeks at birth which is determined by Last Menstrual Period (LMP) or antenatal maternal ultrasound or gestational age assessment by neonatal heel-toe distance.
- Percentage of oxygen saturation at 5 minutes of age by the use of Pulse oxymeter.
- Percentage of neonatal death during hospital stay (secondary outcome).

STATISTICAL ANALYSIS

Initially raw data were collected in assessment and data collection sheets and then entered in SPSS 20 software for statistical analysis. To detect the significance level, for comparing the mean of normally distributed data independent t-test and for non-normally distributed data Mann-Whitney test were used. Chi-square test was performed for dichotomous data. Since we accepted alpha errors of 0.05 so the p-value <0.05 is significant.

RESULTS

Totally 300 newborn babies were studied for the effectiveness of room air and commercially available oxygen during the resuscitation in Neonatal ward of Malalai Hospital of Kabul city, Afghanistan. One hundred fifty asphyxiated neonates resuscitated by room air and another 150 asphyxiated neonates resuscitated by commercially available oxygen. The baseline characteristics of neonates are shown in [Table/Fig-2].

As shown in [Table/Fig-2] majority of neonates in room air and oxygen groups had normal mean birth weight and gestational age but these finding were not significant. The oxygen saturation percentage and Apgar score before intervention were approximately similar in both groups with statistically significant p-value for first finding and non-significant for second one. Term and boys neonates percentage are high in mentioned groups which were not significant.

We compared the result of oxygen saturation percentage and Apgar scores before and after intervention for the effectiveness of both group, percentage of mortality during hospital stay was also compared. Before intervention oxygen saturation percentage and Apgar scores were assisted and after resuscitation at 5 minute of age they were recorded for second time. The result of oxygen saturation percentage, Apgar scores and percentage of mortality during hospitalisation in both group are shown in [Table/Fig-3].

[Table/Fig-3] describes that oxygen saturation percentage at 5 minute of live was significantly higher in term neonates resuscitated with room air. Room air was as effective as oxygen to improve the Apgar score at 5 minute of birth in term neonates. However, the percentage of mortality was higher in term newborn baby resuscitated with oxygen but not statistically significant.

As shown in [Table/Fig-4], however room air was more effective than oxygen in the resuscitation of preterm neonates to increase oxygen saturation and Apgar score at 5 minute of live and decrease mortality rate during hospital stay but all these finding are not statistically significant.

Characteristics	Room air group (150 neonates)	Commercial O_2 group (150 neonates)	p-value
Birth weight in gram (Mean±SD)	2785.33±730.94	2787.33±670.60	0.98
Term	3031.58±596	3002±553.95	
Preterm	2005.56±551.85	2129±562.66	
Gestational age in week (Mean±SD)	37.23±3	37.43±2.62	0.54
Term	38.7±1.2	38.65±1.25	
Preterm	32.67±2.3	33.76±2.3	
Apgar scores, Median (Range)	2 (0-3)	2 (0-3)	0.22
Term	2 (0-3)	2 (0-3)	
Preterm	2 (1-3)	2 (1-3)	
Oxygen saturation % (Mean±SD)	44.21±8.57	46.72±12.22	0.04
Term	44.1±8.54	46.38±12.22	
Preterm	44.56±8.75	47.76±12.26	
Class of GA, No (%)			
Term	114 (76%)	113 (75.3%)	0.5
Preterm	36 (24%)	37 (24.7%)	
Sex, No. (%)			
Boy	90 (60%)	88 (58.7%)	0.9
Girl	60 (40%)	62 (41.3%)	

[Table/Fig-2]: Baseline characteristics of neonates.
SD: Standard deviation; GA: Gestational age

Findings	Room air group (114 neonates)	Commercial O_2 group (113 neonates)	p-value
Oxygen saturation % at 5 minutes, (Mean±SD)	83.4±14.9	77.1±13.1	0.001
Apgar Scores at 5 minutes, Median (Range)	5 (2-9)	5 (1-9)	0.001
Mortality, No. (%)	6 (5.26%)	8 (7%)	0.59

[Table/Fig-3]: The efficacy of room air and commercially available oxygen in term neonates.

Findings	Room air group (36 neonates)	Commercial O_2 group (37 neonates)	p-value
Oxygen saturation % at 5 minutes, (Mean±SD)	80.58±15.62	78.41±11.91	0.22
Apgar Scores at 5 minutes, Median (Range)	6 (3-9)	5 (3-9)	0.33
Mortality, No. (%)	4 (11.1%)	7 (18.9%)	0.5

[Table/Fig-4]: The effect of room air and commercially available oxygen in preterm neonates.

DISCUSSION

In this research we compared the effectiveness of room air versus commercially available oxygen for the resuscitation of neonates with gestational age of 30-41 week and birth weight of 1500-4500 g in the Neonatal ward of Malalai hospital of Kabul city. Despite higher air pollution in Kabul city, the result of this research found room air to be more effective than commercially available oxygen to improve oxygen saturation percentage and Apgar score at 5 minute in term neonates. Since the components of Apgar score include respiration, heart rate, activity, skin color and response to the nasal catheter [8,11]; so such findings demonstrates that resuscitation of asphyxiated term neonates with room air highly improve the functions of lungs, heart and brain at 5 minutes of birth. The result are similar to findings of systematic review performed by Ramji S et al and RCTs done by Ramji S et al., Davis PG et al., Saugstad OD et al., and Vento M et al., These studies describe that room air appears as good as 100% oxygen for resuscitation of asphyxic term newborn babies at birth [10,13,16-18].

The current study demonstrated that oxygen saturation percentage was higher with room air than commercially available oxygen. This finding is not consistent to the result of Wang CL study that conducted a RCT in the University of California, San Diego. According to the result of this study room air couldn't achieve the target oxygen saturation at 3rd minute of live [19]. The research included neonates with gestation ages of 23-32 weeks and assessed oxygen saturation at 3 minute of live; which is the key differences with the current RCT (included neonates of 30-41 weeks gestation and assessed oxygen saturation at 5 minutes of live). A systematic review entitled air versus oxygen for resuscitation of infants at birth was performed by Tan A et al., found that fewer babies died when resuscitated with room air than with 100% oxygen but the author concluded that there is not enough evidence to recommend room air over 100% oxygen, or vice versa. In this review a lot of RCTs were excluded because the majority of babies resuscitated with room air also got some oxygen as a supplement, making it difficult to compare the two groups [20]. However, this RCT revealed lower mortality in term newborn baby resuscitated with room air though not statistically significant. This is the same as mentioned in the conclusion of a multicentric quasi randomised trial, carried out at four centers in India at Maulana Azad Medical College. There was also no statistically significant difference in overall mortality in the two treatment groups [12]. The meta-analysis published in the Lancet revealed that mortality of newborns resuscitated with room air is lower compared to neonates those resuscitated with 100% oxygen [13]. The probable explanation for this difference may be related to the sample size of these studies.

The results of the index study demonstrated that room air is not significantly more effective than oxygen in the resuscitation of preterm neonates to increase oxygen saturation and Apgar score at 5 minute of live and to decrease mortality rate during hospital stay. These findings are similar with literature [8,11,12] and also a RCT conducted at the University of California [18]. A systematic review done by Davis P et al., to compare resuscitation with air versus 100% oxygen found that most babies were born at or near term in developing countries. The pooled analysis showed a significant benefit for infants resuscitated with air. They concluded that room air should be used initially for the resuscitation of term and near-term newborn baby. If such a management fails resuscitation with oxygen should be started. The investigators suggested more studies for the assessment of such trials on premature infants and intermediate concentrations of oxygen at resuscitation [13]. Another RCT conducted by Kapadia VS et al., at Parkland hospital Texas concluded that preterm newborns resuscitated with 21% oxygen encounter less oxygen stress and respiratory morbidity; therefore it was more effective than 100% oxygen [21]. The methodology and primary outcome of this trial was different from the index study so the results are not consistent.

LIMITATION

Since the sample size of preterm neonate in present study was small, so we recommend further investigation for the efficacy of using room air in the resuscitation of asphyxiated preterm infants to settle this issue.

CONCLUSION

Although the air quality in Kabul city is poor, the current study demonstrated that room air is significantly superior to commercially available oxygen to increase oxygen saturation and as effective as oxygen for improved Apgar scores in the resuscitation of asphyxiated term neonates. However, the neonatal mortality was higher in oxygen group but this finding was not statistically significant. In the resuscitation of preterm neonates, though room air is more effective than oxygen to elevate oxygen saturation and Apgar score at 5 minute of birth and decrease mortality rate during hospital stay but all these finding were not statistically significant.

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