

# Hemodynamic changes during exchange transfusion in early neonatal period

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## Abstract

**Background:** Exchange transfusion(ET) has remained the gold standard for rapid lowering of higher bilirubin levels, it is not risk free and mortality rate vary from 0.5 to 3.3%. The present study was carried out to study hemodynamic parameters changes during ET in neonates. **Materials and Methods:** 22 neonates who suffered from hyperbilirubinemia and required double volume ET were enrolled in this prospective study. ET was carried out according to standard practice guidelines. Clinical hemodynamic parameters including heart rate, respiratory rate, blood pressure, temperature and ECG, % saturation of oxygen (SpO<sub>2</sub>) and CVP were monitored continuously before 15 min (pre exchange) during 60-120 min(mid exchange) and after 30 min(post exchange). All data was analysed statistically. **Results:** There was significant increase in mean heart rate 152.78(19.88),155.12(20.50), mean respiratory rate 46.02(8.87),50.92(6.98) and drop in mean Spo<sub>2</sub> 91.19(4.17),90.67(4.28) in mid-exchange and post-exchange values respectively as compared to pre exchange values 138.72(17.74),36.79(7.58),93.51(3.28) for mean heart rate, respiratory rate and mean SpO<sub>2</sub> respectively. There was significant increase in mean diastolic blood pressure values in post-exchange 45.43(13.88) as compared to pre exchange values 41.83(9.80). Mid-exchange value 8.66(2.12) of mean central venous pressure was significantly lower from pre-exchange 10.10(1.92) and post-exchange 9.56(1.98) values. ECG changes did not show any significant changes during ET. **Conclusion:** There were significant adverse effects on all hemodynamic clinical parameters. Monitoring of neonate is essential during ET which will prevent complications of ET. Current recommendations for performing ET are based on balance between the risk of encephalopathy and the adverse events related to the procedure holds true.

**Keywords:** Exchange Transfusion, Hemodynamic changes, Hyperbilirubinemia, Neonate

## Introduction

Jaundice is most common and one of the most vexing problems for a pediatrician that can occur in neonate. All newborn infants are born with hyperbilirubinemia which is defined as total serum bilirubin (TSB) of 2mg/dl or more [1]. Newborns however, may not appear jaundiced until TSB concentration exceeds 5-7 mg/dl [2]. About 60% of term and 80% of preterm infants have clinical jaundice in the first week after birth but only 0.02 to 0.16 of them develop severe hyperbilirubinemia (TSB >25mg/dl), which is an emergency because it may cause neonatal bilirubin encephalopathy which can result in death or irreversible

brain damage in survivor. The terms bilirubin encephalopathy and kernicterus represents clinical and pathological abnormalities resulting from bilirubin toxicity in central nervous system [3-5].

The most common cause of jaundice in neonates are usually due to hemolysis from ABO incompatibility and Rh incompatibility. Other causes are G6PD deficiency, polycythemia, cephalhematoma, sepsis, hypothyroidism, metabolic disorders, prematurity and breastmilk jaundice [6]. Exchange transfusion (ET) and intensive phototherapy play important roles in the treatment of severe hyperbilirubinemia of newborns [7]. If phototherapy fails to control rising bilirubin levels, ET is necessary to lower serum bilirubin concentration. Although ET has remained the gold standard for rapid

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lowering of higher TSB levels, it is not risk free and mortality rate vary from 0.5 to 3.3% [8]. Despite improvement in Neonatal Intensive Care in past two decades, ET remains a high risk procedure. Most of these complications are asymptomatic and transient such as apnea, bradycardia, cyanosis, vasospasm, hypothermia, hypoglycemia, hypocalcemia, hyponatremia and hypokalemia but death can occur because of cardiac arrhythmias, cardiac arrest and respiratory arrest during ET [9-13]. There were no studies which showed cardiorespiratory status of newborn during ET. The present study was carried out to study hemodynamic clinical parameters change during ET in early neonatal life

**Materials and Methods**

This prospective study was carried out in the Division of Neonatology, Department of Pediatrics, Dr D.Y.Patil Medical College and Hospital after obtaining clearance from Ethical Committee of the Institution. Neonates suffering from hyperbilirubinemia, who required ET were enrolled after informed consent from parents. Indications for ET in idiopathic hyperbilirubinemia in term neonates were TSB >20 mg/dl in less than 48 hrs of age, TSB > 25mg/dl in >48hrs of age with failure of intensive phototherapy and in preterm neonates TSB 15-18mg/dl in 1.5-2kg, TSB 18-20mg/dl in 2-2.5kg [2,14 ]. In haemolytic disease indications were TSB>10mg/dl in <24 hrs of age, TSB rise >5 mg/dl/day or 0.5mg/hr in >48hrs of age and PCV>40 at any time [15 ]. Babies having birth weight <1500 gm, gestational age <33 weeks, chronological age >7 days, previous partial exchange transfusion or multiple exchanges, gross congenital anomalies, perinatal asphyxia, clinically suspected chromosomal anomalies, hydrops fetalis and anemia at birth were excluded from this study. ET procedures were performed by the medical team of the unit under all aseptic precaution. The double volume exchange method (170ml/kg) was

carried out by repeatedly removing and replacing a small amount of blood (5ml/kg)[Pull-Push Technique] according to standard practice guidelines through umbilical vein with fresh whole blood (<72 hours), cross matched with appropriate blood group.

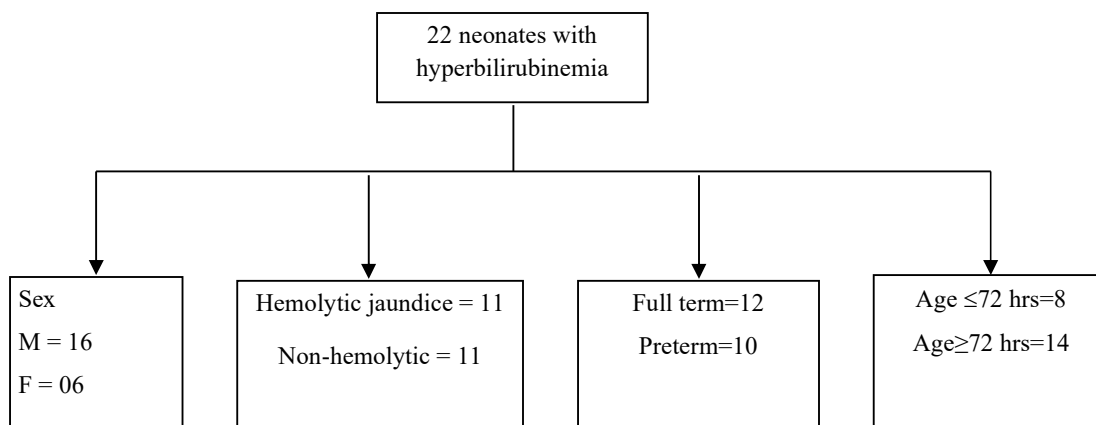
Hemodynamic clinical parameters like heart rate, SpO2 and blood pressure were monitored by multipara monitor RMS Phoebus p512 manufactured by Recorder and Medicare systems Ltd. Skin temperature was measured with the help of skin temperature sensor of warmer. ECG monitoring was done in lead-II and duration of P wave, PR interval, QRS complex, and QT interval were measured. Respiratory rate was detected by ECG electrodes by impedance of chest movements. The CVP was measured by holding calibrated umbilical catheter at 90° to the infant’s body. All the parameters were monitored continuously before 15 minutes (pre exchange) during 60-120 minutes (mid exchange) and after 30 minutes (post exchange) and mean of all the parameters were calculated.

Baby was kept nil by mouth for 2 hrs before and after ET. The baby was kept under CFL blue light phototherapy unit before and after ET. Laboratory investigations like serum bilirubin, hemoglobin, packed cell volume and other relevant investigations like direct Coomb’s test and glucose-6-phosphate dehydrogenase (G-6-PD) as and when required were done prior to ET. At 6 hours post ET serum bilirubin, hemoglobin and packed cell volume were done and clinical monitoring was done in the form of heart rate, respiratory rate, blood pressure, capillary filling time and liver size. Total time taken for exchange blood transfusion after cannulation was recorded for each baby. Statistical analysis was done by repeated measure ANOVA design, for one group factor and one within factor and pair-wise comparison was done using Tukey test at 5% level for all parameters.

**Results**

**Table-I: Causes of jaundice in neonates**

Cause of Jaundice	No. of cases
ABO incompatibility	08
Rh incompatibility	03
Cephalhematoma	01
Prematurity	08
G-6-PD	00
Idiopathic	02
<b>Total</b>	<b>22</b>



**Figure-I: Base line characteristics in neonates**

This study was carried out on 22 neonates who underwent ET for hyperbilirubinemia. The baseline characteristics were shown in Figure I. The cause of jaundice was haemolytic in 11 cases, most often being ABO incompatibility seen in 8 cases [Table I] Maximum ET were carried out on day 4<sup>th</sup> of life. The average duration of ET was 60 -120 minutes.

**Table-II: Changes in vital signs during exchange transfusion in neonates**

	Pre-exchange blood transfusion	Mid-exchange blood transfusion	Post-exchange blood transfusion	p-value (repeated measure ANOVA)
HR (bpm)	138.72±17.74*#	152.78±19.88*	155.12±20.50#	<0.001
RR (/min)	36.79±7.58*#	46.02±8.87* <sup>ψ</sup>	50.92±6.98 <sup>#ψ</sup>	<0.001
SpO <sub>2</sub> (%)	93.51±3.28*#	91.19±4.17*	90.67±4.28 <sup>#</sup>	<0.001
Temperature (°C)	36.54±0.39*	36.42±0.37	36.35±0.42*	0.029
SBP (mmHg)	69.86±11.74	69.80±15.86	74.64±20.95	0.066
DBP (mmHg)	41.83±9.80	40.60±11.40*	45.43±13.88*	0.017
MAP (mmHg)	53.64±10.31	53.34±14.08	57.33±17.44	0.116
CVP (cm H <sub>2</sub> O)	10.10±1.92*	8.66±2.12*#	9.56±1.98 <sup>#</sup>	<0.001

\*p<0.05; #p<0.05, <sup>ψ</sup>p<0.05 (intragroup comparison by Tukey test)

**Table-III: ECG changes during exchange transfusion in neonates**

	Pre-exchange blood transfusion	Mid-exchange blood transfusion	Post-exchange blood transfusion	p-value (repeated measure ANOVA)
P wave (msec)	0.059±0.012	0.059±0.013	0.057±0.011	0.483
PR interval (msec)	0.086±0.008*	0.083±0.014	0.080±0.014*	0.011
QRS complex (msec)	0.046±0.056	0.045±0.080	0.044±0.054	0.073
QT interval (msec)	0.255±0.031	0.25±0.034	0.25±0.036	0.071

\*p<0.05 (intragroup comparison by Tukey test)

There was significant increase in mean heart rate 152.78(19.88),155.12(20.50), mean respiratory rate 46.02(8.87),50.92(6.98) and drop in mean SpO<sub>2</sub> 91.19(4.17),90.67(4.28) in mid-exchange and post-exchange values respectively as compared to pre exchange values 138.72(17.74),36.79(7.58),93.51(3.28) for mean heart rate, respiratory rate and mean SpO<sub>2</sub> respectively. There was Significant increase in mean diastolic blood pressure values in post-exchange 45.43(13.88) as compared to pre exchange values 41.83(9.80). Mid-exchange value 8.66(2.12) of mean central venous pressure was significantly lower from pre-exchange 10.10(1.92) and post-exchange 9.56(1.98) values.

**Table-IV: Bilirubin, hemoglobin and PCV changes during and after ET in neonates**

	Pre-exchange blood transfusion	Post-exchange blood transfusion	Post 6 hrs exchange blood transfusion	p-value (repeated measures ANOVA)
Total serum bilirubin	21.79±6.79*	7.86±3.53*#	18.94±5.68 <sup>#</sup>	<0.001
Hemoglobin	13.95±2.75*#	12.07±2.78*	12.29±2.93 <sup>#</sup>	<0.001
Packed cell volume	41.27±8.11*#	36.01±8.14*	36.46±8.42 <sup>#</sup>	<0.001

\*p<0.05; #p<0.05; (intragroup comparison by Tukey test)

CVP did not show fall less than 3 cm H<sub>2</sub>O in any case. [Table II] ECG changes did not show any significant changes during ET except PR interval, in which there was significant difference between pre-exchange and post-exchange values. But it had no clinical significance.[Table III] The temperature was significantly lowered from pre-exchange to post-exchange periods in all neonates.(p=0.029).

TSB immediate post exchange value 7.86(3.53) was significantly lower from pre-exchange 21.79(6.79) and 6hrs post-exchange 18.94(5.68) values [Table IV].

## Discussion

The critical level of TSB, which may be considered to cause bilirubin encephalopathy is a function of birth weight, gestational age, chronological age, internal milieu and other functions like concealed hematomas, hemolysis etc. Therefore ominous serum bilirubin level is highly individualised for neonates. ET remains the only reliable method for removing bilirubin from the body, at a particular time in anticipation that serum bilirubin may cross blood brain barrier and cause kernicterus. There is decrease in frequency of ET in last two decade because of anti Rh immunoglobulin for mothers and widespread use of phototherapy that was the reason behind small sample size in our study. ET is still required in up to 7% of neonates admitted to nurseries [16].

In the present study heart rate, respiratory rate were increased and spo<sub>2</sub>, temperature were decreased significantly in all neonates during ET from pre exchange value without any major changes in ECG. CVP was more in pre exchange and decreased in mid exchange and again raised in post exchange period.

Increased heart rate and respiratory rate was mostly due to cry, irritability, pain and uncomfortable posture during procedure. Decrease in SpO<sub>2</sub> was mostly due to change of neonatal blood with adult blood as HbA has less affinity for oxygen. Hey EN et al [17] observed hypothermia during ET, similar finding in our study. Cardiac arrhythmias mentioned during ET were mainly due to umbilical cannula in heart, electrolyte abnormalities like hyperkalemia, hypocalcemia [2]. Panagopoulous G et al [13] observed cardiac

arrhythmias, cardiac arrest, respiratory arrest, cyanosis and collapse. Pre exchange CVP rise was due to irritability and vasospasm and in post-exchange, it might be due to volume overload, congestive cardiac failure or vasospasm and wrong position of catheter [18].

Hypotension was transient in our study and improved in most cases by adjustments of aliquots in our study. Aranda et al [19] observed 10 ml blood withdrawal and infusion completed within 3 minutes resulted in reversible changes in aortic pressure, whereas the same procedure completed within 45 to 60 seconds resulted in a progressive fall in the systolic pressure and in narrowing of the pulse pressure and advised an exchange rate of 5 ml/kg per 3 minutes.

There was a significant decrease in immediate post-exchange serum bilirubin by 65.52% and rise in serum bilirubin at 6 hrs up to 83.10% in the present study. Similar to earlier studies which reported an average fall of 55% (38-73%) after ET in the pre-exchange value of serum bilirubin [21,22]. The rebound phenomenon could be explained on the basis of influx of tissue bilirubin to the blood circulation. This was due to the stable fraction of serum bilirubin in the tissues which equilibrates with the vascular compartment after ET [22] or it may be new bilirubin from metabolised hemoglobin derived from damaged erythrocytes.

## Conclusion

There were significant adverse effects on all hemodynamic clinical parameters. Monitoring of baby in the form of heart rate, respiratory rate, blood

pressure, SpO<sub>2</sub>, CVP, temperature, ECG, is essential during ET where complications like apnea, congestive cardiac failure, cardiac arrest, hypothermia, hypotension can be easily detected and treated accordingly during procedure. Current recommendations for performing ET are based on balance between the risk of encephalopathy and the adverse events related to the procedure holds true [23].

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