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# Feto-Maternal Haemorrhage at Delivery – Can the Dose of Anti-D be Reduced?

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**Summary**

2-5% of Indian population is Rh negative. Currently 300 micrograms of Anti-D is administered to unsensitised Rh negative women delivering an Rh-positive child. The extent of fetomaternal leak is not determined in majority of centers in India. In England and Australia the standard dose of Anti-D has been reduced to 100-125 micrograms following fetomaternal haemorrhage studies showing that in general the fetal cell leak is well covered by this reduced dose. As recommended by WHO, a Kleihaur Betke test or other test for fetal cell leak is done in all women receiving Anti-D to identify the rare patient who requires a higher dose. Considering the financial implications a need was felt to study the extent of fetomaternal leak during delivery in our population. 204 patients were studied. 37% had no FCL, 92% had <6ml fetal blood leak, 95% had less than 10ml blood leak, 98.5% had upto 15ml fetal blood leak. A dose of 150 micrograms would adequately cover 95-98% of our population. A Kleihauer Betke test is done in all cases. It is a simple test, costing Rs 50/- which can be performed in majority of laboratories without requiring extra or new equipments.

## Aim

1. Determine the incidence and quantity of fetomaternal leak at delivery or caesarean section.
2. Determine the optimal dose of Anti-D for our population.
3. Study cases of massive fetomaternal haemorrhage
4. Study the effect of common obstetric practices on the extent of fetomaternal haemorrhage.

## Methods

Study was conducted between Aug 1999-July2000 in SJMCH. Inclusion criteria-Rh positive or negative normal women delivering a live baby after 37 weeks of gestation, per vagina or by caesarean section (singleton pregnancy). Exclusion criteria patients with pregnancy induced hypertension, cardiac disease, hemolysis, hemoglobinopathies, DIC.

## Method

2ml of maternal blood was collected in an EDTA bottle for acid elution (Kleihaur Betke) test and hematocrit between half to one hour of placental delivery. In the lab a smear was prepared for KB test. The slide was fixed in methanol. A Coplin jar was placed in a waterbath at 37 degrees C. 37.7ml of 0.1 M citric acid was mixed with 12.3 ml of 0.2M Na2HPO4. pH checked and adjusted to 3.3. The solution was poured into the Coplin jar. When the solution reached 37 degrees, the fixed slide was placed in the solution and incubated for 5 minutes. Then remove; rinse with tap water and dry. Stain with Hemotoxylin for one minute. Rinse with tap water. Stain with Eosin for one minute. Rinse with tap water and dry. Fetal RBC were counted in 64 oil emersion fields. Each field contains 125 cells on an average. Thus 8000 cells were seen and percentage of fetal cells among them determined.

$$\text{Fetal RBC in ml} = \frac{\text{Maternal bl volume} * \text{maternal hct} * \text{percentage FRBC}}{\text{Fetal Hematocrit}}$$

Maternal blood volume is taken as 5000ml (only normotensive singleton pregnancies taken for the study) and fetal hematocrit as 50%.

Fetal blood leak=Fetal RBC (ml)*2
Following patient details were recorded:
Gestation, labour spontaneous or induced; method, quantity and duration of induction method; labour accelerated or not, method and duration of acceleration; duration of all stages of labour; III stage complications, mode of delivery and blood loss; placental weight; drugs (with dose) used in III stage, baby wt, apgar and sex.

**Results**

204 samples were analyzed. Table I shows the volume of fetal blood leak. (Throughout this study, fetal blood and not fetal cell volume is reported.)

Effect of Labour induction and acceleration is shown in table II.

There was no significant difference in the above groups mean fetal blood leak. Two cases of massive fetomaternal leak of 25ml and 31ml were affecting the variance and std. Deviation; hence, they were excluded from the analysis.

The number of Cerviprimes used or the dose or duration of oxytocin use did not show any correlation with the amount of fetomaternal leak (r value were 0.07, 0.02, -0.02 repectively).

The duration of I stage, II stage and III stage of labour also did not show any correlation with FMH (r value 0.11, 0.13 and 0.09 respectively).

Effect of Atonic PPH is shown in Table III.

Mean leak was 3.6ml with std deviation of 10 and p value 0.32. One of the two cases of massive FMH

**Table 1.**
**Volume of fetal blood leak**

| Vol. Fetal Blood in ml | No of cases | Percentage | Cumulative Percentage |
|---|---|---|---|
| 0.0000 | 76 | 37 | 37 |
| >0-0.1 | 17 | 8.6 | 45.6 |
| >0.1-0.2 | 17 | 8.6 | 53.9 |
| >0.2-0.5 | 14 | 6.9 | 60.8 |
| >0.5-2.0 | 41 | 20 | 80.9 |
| >2.0-6.0 | 24 | 12.7 | 92.6 |
| >6.0-10.0 | 5 | 2.5 | 95.1 |
| >10-15.0 | 7 | 3.4 | 98.5 |
| 16 ml | 1 | 0.5 | 99.0 |
| 25ml, 32ml | 1+1 | 1 | 100.0 |

**Table II.**
**Effect of Labour induction/acceleration**

| | No. of Patients | Mean Fetal Blood leak | Variance | Std. deviation | Maximum value | p |
|---|---|---|---|---|---|---|
| - Spontaneous labour not accelerated | 64 | 1.59 | 9.1 | 3.02 | 14.3 | 0.00011 |
| - Induced Labour, not accelerated | 25 | 2.3 | 21 | 4.6 | 16 | 0.02303 |
| - Induced labour + accelerated | 34 | 1.09 | 4.7 | 2.1 | 11 | 0.0059 |
| - Labour only accelerated | 77 | 1.1 | 4.5 | 2.1 | 12.6 | 0.0001 |

occurred in this group.

**Table III**
**Effect of atonic PPH**

| Fetal blood Leak | No of Patients | Percentage |
|---|---|---|
| 0.00ml | 5 | 55 |
| 0.016ml | 1 | 11.2 |
| 0.7ml | 2 | 22.4 |
| 31 ml | 1 | 11.2 |
| Total | 9 | |

The amount of blood loss in III stage in the absence of PPH did not correlate with FMH, r-value being 0.11.

Placental weight and baby weight also did not correlate with FMH, r-value 0.11 and 0.02 respectively.

Gender had no effect on extent of FMH as shown in table IV.

Effect of Lower segment Caesarean Section on FMH is shown in Table V.

Mean FMH in LSCS was 0.3ml as against 1.7ml in 173 normal vaginal delivery patients. Variance was 0.4 vs 14 and Std deviation 0.6 vs 3.7.

The peculiar finding of lower FMH in caesarean section as against vaginal delivery could perhaps be explained by the difference in routine use of oxytocics. In our hospital, methergine im/iv is routinely given to all patients after vaginal delivery after delivery of the placenta. During caesarean section, the anaesthetists routinely give 10 units of oxytocin IV infusion and avoid the use of Methylergometrine.

**Comparison of extent of FMH with Literature**

Mollison 1979, Gupte and Kulkarni 1994 studies are considered. (Table VI & VII). Mollison found much smaller amounts of fetomaternal haemorrhage while Gupte (1994), Mehta et al (1979) found a smaller overall incidence of fetomaternal transfusion. Biological and immunological differences in placentation could explain the difference from Mollison's study (e.g. PIH more common in Indian women as compared to British women).

**Table VI**
**Comparison of FMH with literature**

| FMH In ml Blood | Mollison | Ours |
|---|---|---|
| <6ml | 99% | 92.6% |
| 6-20 | 0.7% | 7.4% |
| >20 | 0.3% | 1% |

**Table IV**
**Gender and Fetomaternal Haemorrhage**

| | No of Cases | Mean | Variance | Std deviation |
|---|---|---|---|---|
| Entire Study group | 204 | 1.66 | 15.0 | 3.8 |
| Female Babies | 90 | 1.7 | 16.2 | 4.0 |
| Male Babies | 114 | 1.6 | 14.9 | 3.8 |

**Table V**
**Effect of Caesarean Section on Fetomaternal Haemorrhage**

| FMH In ml | LSCS Freq. | LSCS Percentage | LSCS Cum. % | Vag. delivery freq. | Vag. Del % | Vag Del Cum. % |
|---|---|---|---|---|---|---|
| 0.00 | 11 | 45.8 | 45.8 | 63 | 36.4 | 36.4 |
| 0.0-0.01 | 3 | 12.5 | 58.3 | 3 | 1.8 | 38.2 |
| 0.01-0.1 | 3 | 12.5 | 70.8 | 8 | 4.8 | 42.8 |
| 0.1-0.2 | 1 | 4.2 | 75 | 15 | 8.7 | 51.4 |
| 0.2-1.0 | 1 | 4.2 | 79.2 | 28 | 16.2 | 67.6 |
| 1-2ml | 5 | 20.8 | 100 | 19 | 11 | 78.6 |
| 2-<6 | 0 | 0 | 0 | 24 | 13.9 | 92.5 |
| 6-<10 | 0 | 0 | 0 | 4 | 2.3 | 94.8 |
| 10-<15 | 0 | 0 | 0 | 7 | 4 | 98.8 |
| 16,31 | 0 | 0 | 0 | 1+1 | 1.2 | 100 |

**Table VII**
**Comparison with literature**

| | Incidence of Fetomaternal haemorrhage after normal delivery |
|---|---|
| Gupte & Kulkarni (1994) | 20% |
| Present study | 63% |

The higher incidence and the higher magnitude of FMH in our population may be due to the routine use of IM or IV Methylergometrine after normal delivery, unless contraindicated. Methylergometrine was withheld in Rh-negative patients but their number was too small to be significant in this study.

Profile of the two cases of massive fetomaternal haemorrhage:

Case 1-G2 P1 L1 at 38-wk. gestation with spontaneous onset of labour, no acceleration or ARM done. Delivered vaginally a 2.8kg male baby, A/S 8, after 9hrs in I stage & 15 min in II stage of labour. III stage lasted for 20 min, Placenta weighed 650 gms and blood loss was 200ml. IV methergine was given. FMH was 25ml.

Case 2-G3 P1 A1L1 at 37 wks gestation Rh negative, isoimmunized, had 3 instillation of cerviprime 8 hrly, I stage was 2 hrs, II stage 18 min, III stage 10 minutes. Delivered normally a 2.6 kg F baby, A/S 8, Placenta 710 gms. Pt had atonic PPH. Received 10 units syntocinon, 1 amp IV Methylergometrine. Blood loss 600ml. FMH=31ml. First case had no high risk factor. Massive FMH occurs in <1% of cases and in many patients this occurrence cannot be predicted.

## Discussion

### Optimal Cost Effective Dose of Anti D

300 ug covers 30ml of fetal blood leak. In U.K. 100ug gives 99% coverage (Robson et al, 1998) and is routinely used currently and a Kleihaur test is recommended for all patients receiving Anti D.

According to Mollison's studies (Mollison, 1973), if it is assumed that 25 ug protects from 1ml fetal RBC or 2ml fetal blood, then only 0.8% of women (with > 8ml fetomaternal blood leak) will benefit from a dose larger than 100 ug. Similarly 200ug will protect from 16ml fetal blood and only 0.4% of his study patients are expected to have this much or more haemorrhage. In Australia 120 ug is routinely used.

In our population ?150ug will be adequate (it will cover 95% with 10-ml fetal blood leak cut off and 98.5% with 15ml cut off).

In all Rh –ve patients requiring AntiD, K-Betke test is done and the dose supplemented if required (Controlled trial 1974; Urbaniak 1998). 300ug covers 99% of the patients (Arias 1993; Mackenzie et al 1991) but does not obviate the need for K-Betke test (Urbaniak 1998). The K-Betke test is comparable to Flow cytometry as a quantitative test, and is more easily available. Flow cytometry has greater objectivity and reproducibility but is more expensive and requires special instrument (Bayliss et al, 1991). According to WHO (1971) the use of a standard dose of 100 ug is likely to have a success rate only slightly inferior to 200-300 ug dose. If screening tests are employed to detect large transplacental haemorrhage and additional Anti-D given as necessary; the success rate could be equally high. When haemorrhage is high, give 25 ug for each ml of fetal cells or 2ml of fetal blood (WHO 1971, Mollison 1973).

## Conclusion

1. Anti-D dose may be reduced to 150 ug with 95 to 98% coverage.
2. Kliehauer-Betke test to be done in all cases receiving Anti D irrespective of dose.
3. Consider KB test in any patient giving birth to a pale baby with no apparent cause.
4. Common obstetric practices like induction of labour or acceleration of labour with prostaglandins or oxytocin do not seem to affect the amount of fetomaternal haemorrhage.

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