

# STUDY OF METABOLIC EFFECTS OF AGENTS USED FOR TERMINATION OF MID-TRIMESTER PREGNANCY

by

KUSUM C. GUPTA,\* M.D., D.G.O.

U. K. SHETH,\* BSc., M.D., F.A.M.S., F.C.P.S.

USHA KRISHNA,\*\* M.D., D.G.O., F.G.C.S.

and

V. N. PURANDARE,\*\* M.D., F.R.C.S.

Several agents like hypertonic saline and urea are in use for termination of mid-trimester pregnancy. Some of these agents alter metabolic functions and lead to unwanted effects like coagulopathies. Hence, a comparative study was undertaken using intra-amniotic and vaginal prostaglandins, intra and extra-amniotic saline and ethacridine lactate and various metabolic parameters were estimated to find out whether these agents produced any changes.

## Material and Methods

Women admitted to K.E.M. Hospital for 2nd trimester termination of pregnancy were included in the study and divided into 2 groups. In Group I, coagulation studies were carried out and in Group II, renal function tests and electrolytes were estimated. Haemogram was done in both the groups. The number of patients in each group varied between 5-8.

The following tests were carried out for studying coagulation and platelet functions.

1. Prothrombin time (Quick 1935).
2. Partial thromboplastin time (Biggs 1972).
3. Thrombin time (Biggs 1972).
4. Platelet aggregation (Born 1962).
5. Platelet adhesiveness (Mackenzie *et al* 1974).
6. Plasma fibrinogen (Goodwin 1961).
7. Platelet count (Brecher and Cronkite 1950).
8. Euglobulin clot lysis time (Buckell 1958).

Renal function tests included:

1. Blood urea nitrogen.
2. Blood urea.
3. Plasma creatinine.

Serum sodium, potassium and chloride were also estimated.

The methods for renal function tests and serum electrolytes were those given in standard Text-Book of Clinical Biochemistry.

These tests were carried out before use of abortifacients (basal), post-abortal and 6 weeks after the abortion when the patients came for follow-up.

\*Department of Pharmacology and Clinical Pharmacology Unit, Seth G.S. Medical College and K.E.M. Hospital.

\*\*Department of Obstetrics and Gynaecology, K.E.M. Hospital, Parel, Bombay-400 012.

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## Results

The changes in coagulation tests and platelet functions, with the use of various abortifacients are given in Table I.

TABLE I

*Changes in Coagulation Tests and Platelet Functions (Mean  $\pm$  S.E.)*

|                            | Intra-amniotic PG (n = 10) |                     |                   | Intravaginal PG (n = 13) |                     |           | Pre-abortal         |
|----------------------------|----------------------------|---------------------|-------------------|--------------------------|---------------------|-----------|---------------------|
|                            | Pre-abortal                | Post-abortal        | Follow up         | Pre-abortal              | Post-abortal        | Follow up |                     |
| P.T.<br>(secs)             | 20.7<br>$\pm$ 2.2          | 20.4<br>$\pm$ 1.0   | 2.0 $\pm$<br>22.0 | 19.80 $\pm$<br>0.7       | 20.2 $\pm$<br>1.3   | 19        | 20.7 $\pm$<br>0.5   |
| P.T.T.<br>(secs)           | 87.5<br>$\pm$ 3.20         | 85.40<br>$\pm$ 1.36 | 85.50             | 84.0 $\pm$<br>1.4        | 82.2 $\pm$<br>3.1   | 84        | 86.0 $\pm$<br>1.4   |
| T.T.<br>(secs)             | 6.7<br>$\pm$ 1.1           | 7.0<br>$\pm$ 0.9    | 7.50              | 7.00 $\pm$<br>0.6        | 7.0 $\pm$<br>0.6    | 7         | 6.3 $\pm$<br>0.5    |
| Plasma<br>Fib.<br>(mg%)    | 297.5<br>$\pm$ 16.0        | 299.0<br>$\pm$ 15   | 300.0             | 321.8 $\pm$<br>32.6      | 313.0 $\pm$<br>20.3 | 315       | 318.3 $\pm$<br>33.2 |
| ECLT<br>(mins)             | 108.75<br>$\pm$ 4.7        | 107.0<br>$\pm$ 5.1  | 105.0             | 107.0 $\pm$<br>6.0       | 106.0 $\pm$<br>3.7  | 100       | 105.0 $\pm$<br>4.1  |
| Pl. aggr.<br>ADP           | 33.7                       | 40.4                | 32.5              | 44.4                     | 42.8                | 55        | 42.3                |
| EPI                        | 37.5                       | 38.7                | 35.0              | 44.4                     | 41.0                | 55        | 47.5                |
| COLL                       | 38.3                       | 33.4                | 35.0              | 47.0                     | 51.0                | 55        | 44.0                |
| Pl.<br>Adhesiv-<br>ness %  | 35.7<br>$\pm$ 0.5          | 32.2<br>$\pm$ 11.4  | 28.5              | 40.6 $\pm$<br>1.4        | 41.6 $\pm$<br>6.1   | 51        | 38.5 $\pm$<br>6.7   |
| Platelet<br>count<br>(cmm) | 187400                     | 184600              | 204500            | 206400                   | 210400              | 217000    | 20,000              |

\* Not significant. ADP — Adenosine diphosphate. EPI — Epinephrine. COLL —

\*\* Significant  $P < 0.05$ .

| Intra-amniotic<br>Post-<br>abortal | Saline (n=5)<br>Follow<br>up | Extra-amniotic Saline (n=10) |                            |                | Ethacridine Lactate (n = 10) |                 |                 |
|------------------------------------|------------------------------|------------------------------|----------------------------|----------------|------------------------------|-----------------|-----------------|
|                                    |                              | Pre-<br>abortal              | Post-<br>abortal           | Follow<br>up   | Pre-<br>abortal              | Post<br>abortal | Follow<br>up    |
| 21.5                               | —                            | 20.0 ±<br>1.4                | 22.8 ±<br>0.4              | 21.0           | 19.5 ±<br>3.8                | 20.2 ±<br>2.9   | 21.0 ±<br>2.7   |
| 87.0                               | —                            | 72.4 ±<br>25.9               | *89.0 ±<br>5.3             | 90.5 ±<br>5.5  | 89.4 ±<br>22.3               | 97.5 ±<br>27.8  | 90.12 ±<br>27.6 |
| 7.0                                | —                            | 7.2 ±<br>0.7                 | *7.6 ±<br>1.02             | 6.5 ±<br>0.5   | 8.3 ±<br>1.71                | 7.8 ±<br>1.9    | 9.4 ±<br>2.7    |
| *292.5 ±<br>7.5                    | —                            | 309.9 ±<br>18.3              | *284.0 ±<br>11.6           | 292.5 ±<br>2.5 | 423.5 ±<br>102.8             | 458.4 ±<br>85.1 | 350.4 ±<br>61.5 |
| 102.5 ±<br>7.5                     | —                            | 101.2 ±<br>4.1               | 98.0 ±<br>8.1              | 105.0 ±<br>5.0 | 118.4 ±<br>11.8              | 121.0 ±<br>15.8 | 121.8 ±<br>17.4 |
| *30.0                              | —                            | 33.5<br>43.5<br>31.0         | 32.25<br>**22.33<br>**12.0 | 27<br>27<br>27 | 43<br>—<br>—                 | *38.1<br>—<br>— | 41.8<br>—<br>—  |
| *10.5 ± 0.5                        | —                            | 25.4 ±<br>11.5               | **14.2 ±<br>10.6           | 35.0 ±<br>10.0 | 43.3 ±<br>4.3                | 45.7 ±<br>4.56  | 49.6 ±<br>9.5   |
| 20,000                             | —                            | 202750                       | 207600                     | 232500         | 242840                       | 245600          | 299000          |
| Collagen.                          |                              |                              |                            |                |                              |                 |                 |

Prostaglandins (intra-amniotic and vaginal) showed no effect on any of the coagulation factors. Extra-amniotic saline produced a significant fall in post-abortal platelet aggregation due to ADP. The fall in plasma fibrinogen was not statistically significant. Extra-amniotic saline produced an increase in partial thromboplastin time, significant decrease in platelet aggregation with epinephrine and collagen as well as significant decrease in platelet adhesiveness. Changes in thrombin time and plasma fibrinogen were not significant. Ethacridine lactate produced slight changes in partial thromboplastin time and platelet aggregation. The significant changes produced by extra-amniotic saline returned to normal at 6 weeks. In the group with intra-amniotic saline it was not possible to find out whether the changes returned to normal as these patients did not come for follow up.

Blood urea, blood urea nitrogen and

plasma creatinine showed slight increase with all the abortifacients but these changes were within normal limits. No significant changes were found in serum electrolytes.

No changes in haemogram were found in post-abortal period as compared to basal values. There was a slight increase in haemoglobin levels at 6 weeks follow-up in all the groups studied. Basal ESR was increased and there was a mean rise of 7-10 mms. after abortion in all groups. Increased ESR returned to normal at the time of follow-up.

#### Discussion

Introduction of a new abortifacient requires investigations about its possible systemic and metabolic side-effects to prove its safety. Several abortifacients, though effective, may lead to serious unwanted effects. Major concern has been

TABLE II

Changes in Renal Function Tests and Serum Electrolytes (Mean  $\pm$  S.E.)

|                               | Intra-amniotic PG (n = 6) |                    |              | Intra-amniotic saline (n = 5) |                    |                    | Extra-<br>Pre<br>abortal |
|-------------------------------|---------------------------|--------------------|--------------|-------------------------------|--------------------|--------------------|--------------------------|
|                               | Pre-<br>abortal           | Post<br>abortal    | Follow<br>up | Pre<br>abortal                | Post<br>abortal    | Follow<br>up       |                          |
| Blood urea<br>(mg%)           | 16.9 $\pm$<br>0.3         | 20.1 $\pm$<br>4.5  | —            | 17.1 $\pm$<br>1.5             | 21.6 $\pm$<br>4.6  | 20.7 $\pm$<br>1.7  | 16.2 $\pm$<br>1.2        |
| Bl. urea N <sub>2</sub>       | 7.9 $\pm$<br>0.2          | 9.3 $\pm$<br>2.2   | —            | 8 $\pm$<br>0.7                | 10.1 $\pm$<br>2.2  | 9.9 $\pm$<br>0.8   | 7.6 $\pm$<br>0.5         |
| Plasma<br>creatinine<br>(mg%) | 0.43 $\pm$<br>0.05        | 0.4 $\pm$<br>0.0   | —            | 0.44 $\pm$<br>0.07            | 0.50 $\pm$<br>0.13 | 0.57 $\pm$<br>0.12 | 0.42 $\pm$<br>0.04       |
| Na<br>(meq/L)                 | 133.7 $\pm$<br>5.3        | 138.7 $\pm$<br>1.9 | —            | 142.0 $\pm$<br>5.6            | 136.2 $\pm$<br>7.2 | 141.2 $\pm$<br>2.0 | 138.4 $\pm$<br>7.5       |
| K<br>(meq/L)                  | 4.1 $\pm$<br>0.1          | 3.8 $\pm$<br>0.1   | —            | 4.0 $\pm$<br>0.3              | 4.00 $\pm$<br>0.3  | 4.3 $\pm$<br>0.3   | 3.9 $\pm$<br>0.4         |
| Cl<br>(meq/L)                 | 101.0 $\pm$<br>5.4        | 106.7 $\pm$<br>5.0 | —            | 102.7 $\pm$<br>3.5            | 102.0 $\pm$<br>4.1 | 99.2 $\pm$<br>4.0  | 101.0 $\pm$<br>2.0       |

about the changes induced by intra-amniotic saline (Spivak *et al*, 1972; Cohen and Ballard, 1974) and intra-amniotic urea (Mackenzie *et al*, 1975, Burkman *et al*, 1977). Efforts have been made to combine some of these agents in the hope of increasing their efficacy and reducing their side-effects (Mackenzie *et al*, 1975).

Intra-amniotic instillation of saline has been associated with consumptive coagulopathy and while only a few patients develop the full picture of coagulopathy many patients exhibit changes in blood coagulation factors. Brown *et al* (1972) reported a significant decrease in platelet count, factor VIII, profibrinolysin and fibrinolytic inhibitors 3-24 hours after intra-amniotic saline. In the present study, there was a significant decrease in platelet aggregation and increase in partial thromboplastin time. Some change was observed in thrombin time and plasma fibrinogen also. Changes reported by Brown *et al* (1972) were at 3 and 24

hours and Spivak *et al* (1972) observed that peak changes occur 2-12 hours after injection. Beller *et al* (1972) suggested that most severe changes occur with abortion. In the present study, coagulation tests were done in the immediate post-abortion period. Significant changes were also observed with extra-amniotic saline, and hence caution is necessary even when hypertonic saline is used by extra-amniotic route.

Prostaglandin F<sub>2</sub>-alpha and ethacridine lactate did not reveal significant changes in coagulation and platelet function tests. Phillips *et al* (1974) reported an increase in platelets, fibrinogen, factors V and VIII as well as profibrinolysin and fibrinolytic inhibitors probably as a response to a mild inflammatory process produced by the prostaglandin.

In the present study, haematological data revealed no changes due to various agents. The increase in haemoglobin level during follow-up period may be due

| amniotic saline (n = 6) |             | Intra-vaginal PG (n = 5) |              |           | Ethacridine lactate (n = 10) |              |             |
|-------------------------|-------------|--------------------------|--------------|-----------|------------------------------|--------------|-------------|
| Post abortal            | Follow up   | Pre abortal              | Post abortal | Follow up | Pre abortal                  | Post abortal | Follow up   |
| 18.8 ± 3.8              | 20.3 ± 0.5  | 17.6 ± 2.8               | 20.9 ± 4.6   | —         | 20.4 ± 3.5                   | 24.2 ± 5.9   | 22.4 ± 5.8  |
| 8.8 ± 1.8               | 10.5 ± 1.2  | 8.3 ± 1.3                | 9.5 ± 2.2    | —         | 9.3 ± 2.0                    | 11.6 ± 2.4   | 10.5 ± 2.7  |
| 0.49 ± 0.16             | 0.50 ± 0.00 | 0.45 ± 0.05              | 0.48 ± 0.04  | —         | 0.75 ± 0.27                  | 0.86 ± 0.27  | 0.99 ± 0.23 |
| 141.4 ± 2.0             | 140.0 ± 0.0 | 144.2 ± 3.8              | 142.2 ± 3.0  | 145.0     | 143.0 ± 6.7                  | 142.2 ± 6.6  | 138.4 ± 9.4 |
| 3.8 ± 0.4               | 4.2 ± 0.3   | 4.1 ± 0.3                | 4.2 ± 0.1    | 4.3       | 4.0 ± 0.4                    | 3.9 ± 0.3    | 3.8 ± 0.4   |
| 98.7 ± 0.9              | 85.0 ± 35.8 | 99.0 ± 3.0               | 105          | —         | 108.1 ± 13.5                 | 103.3 ± 4.1  | 105.5 ± 4.4 |

to administration of haematinics to these patients. Rise in ESR occurs during pregnancy and a further small rise in post-abort value was observed in all groups.

Renal function tests as evaluated by blood urea, blood urea nitrogen and plasma creatinine showed slight rise with the use of all the abortifacients, but all the values were within normal limits indicating no damage to kidneys with the use of the abortifacients studied.

Serum electrolytes showed no changes, indicating that no electrolyte imbalance was caused by any of these abortifacients.

Though some coagulation and platelet function tests showed significant changes with the use of hypertonic saline by intra as well as extra-amniotic routes, clinically no consumptive coagulopathy was observed. This may be because incidence of severe defibrination is approximately 1:1500 abortions induced by hypertonic saline (Brown *et al*, 1972).

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