ROLE OF 5-HYDROXYTRYPTAMINE IN TOXAEMIA AND ABORTION

By
S.C. Sen and S.K. Ganeriwal
Department of Physiology, Medical College, Nagpur

The clinical and pathological features of toxaemia have been produced by injecting 5-Hydroxytryptamine (5-HT). Spies and Stone (15) found increase of blood pressure by injecting 5-HT in normotensive, hypotensive and hypertensive subjects. Studies of Ro and Benditt (12) show that 5-HT is responsible for edema formation in rats. Intravenous infusion of 5-HT causes renal cortical necrosis in rats (9). The work of the latter authors also suggests a possible relationship between toxaemia of pregnancy and 5-HT. Krupp (7) found an apparently increased plasma 5-HT level in toxaemia of pregnancy as compared to that in non-pregnant and normal pregnant females. Urinary excretion of 5-HT does not change significantly in toxaemia of pregnancy unless complicated by chronic hypertension (13). Urinary level of 5-Hydroxyindoleacetic Acid (5-HIAA), a chief metabolite product of 5-HT, has been estimated by Berry and Hughes (2) and Parikh and Bellare (10) in cases of toxemia of pregnancy. The former group of authors did not find any change whereas the latter authors found a significantly reduced level of urinary 5-HIAA in toxemia of pregnancy.

There are some experimental evidences which suggest the role of 5-HT in abortion. It brings about contraction of mammalian uterus (1). It also elicits powerful rhythmic contractions of amniotic membrane of 10 to 12 days incubated chick (4). Erspamer (3) utilised the mammalian uterus for bioassay of 5-HT. 5-HT can interrupt pregnancy at various stages in mice (8). Schmidt and Pokorny (13) have reported a raised urinary excretion of 5-HT in cases of inevitable abortions.

Though there is some evidence to show the role of 5-HT in toxemia of pregnancy and abortion, very few attempts have been done to uncover its role in the above conditions and results are equivocal. Therefore it was found of interest to estimate the level of 5-HT in serum during toxemia of pregnancy and abortion, as well as it might also help introduce some useful drugs in the treatment of above conditions.

MATERIALS AND METHODS

In the present work, level of serum 5-HT was determined in 11 cases of toxemia of pregnancy and 16 cases of inevitable abortion. All cases of toxemia belonged to third trimester of pregnancy (beyond 24 weeks of gestation) having a group of common objective symptoms; hypertension (B.P. 130 mm/85 mm of Hg...
EMIA AND ABORTION

College, Nagpur

have been produced by injecting an increase of blood pressure by intense subjects. Studies of Rowley into the formation of rats. Intravenous

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2) and Parikh and Bellare (10) in authors did not find any change, level of urinary 5-HIAA in toxaemia suggested the role of 5-HT in abortion. It also elicits powerful rhythmical

HT in toxaemia of pregnancy and edema and proteinuria. Cases of inevitable abortion belonged to second trimester of pregnancy (from 12 to 24 weeks of gestation).

About 2 ml. of blood was obtained from each patient and was kept in sterile non-oxalated bottles and allowed to clot completely after which it was placed overnight in refrigerator and serum separated next morning.

Biological assay of serum 5-HT was done on isolated rat stomach strip preparation (16), using Tyrode’s solution as the bathing fluid, the temperature of which was kept constant at 37°C. Oxygen was continuously passed in the bath. Atropine in 10⁻⁷ concentration was always added as a routine to the bathing fluid so that low concentrations of 5-HT could be assayed without being interfered with acetylcholine and histamine in small doses (16). Starting with the known concentrations of 5-HT, contractions with 0.1 ml. of serum were recorded. Doses of known 5-HT concentrations and 0.1 ml. of serum were alternately added till the response obtained by 0.1 ml. of serum directly matched with the response obtained by known concentrations of 5-HT solutions. The effect of 5-HT was identified as 5-HT by seeing the blocking effect of Cyproheptadine in doses of one microgram per ml. of the bath.

Level of 5-HT in non-pregnant females in childbearing age and normal pregnant females in second and third trimesters of pregnancy, estimated by us in our previous work (5) was used as a control for the present study. Comparison of serum 5-HT level in cases of inevitable abortion was done with that of non-pregnant and normal pregnant cases in second trimester of pregnancy. Comparison of serum 5-HT level in cases of toxaemia was done with that of non-pregnant and normal pregnant cases in third trimester of pregnancy.

RESULTS

The results of estimation of serum 5-HT level in 11 cases of toxaemia of pregnancy are shown in detail in Table I. A representative graph of the biological estimation is given in Fig. 1.

Individual variations were present in this group. Average serum 5-HT level in these cases was found to be 29.28±18.59 nanograms (ngs.) per ml. This when compared to the level of serum 5-HT in non-pregnant females (19.89±10.63 ngs. per ml. (5) and the level in normal pregnant females during 3rd trimester of pregnancy (25.8±12.83 ngs. per ml. (5) shows an apparent rise. This rise is insignificant at P=0.05.

The results of estimation of serum 5-HT level in 10 cases of inevitable abortion are shown in detail in Table II. A representative graph of the biological estimation is shown in Fig. 2.

Individual variations were very marked. Mean level of serum 5-HT in these cases was found to be 30.0±14.31 ngs. per ml. When compared to the level of serum 5-HT in non-
TABLE I

*Level of serum 5-HT in females during pregnancy complicated with Toxaemia*

<table>
<thead>
<tr>
<th>No.</th>
<th>Blood pressure in mm Hg.</th>
<th>Level of serum 5-HT in ng/ml.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>140/100</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>130/92</td>
<td>13</td>
</tr>
<tr>
<td>3</td>
<td>130/90</td>
<td>35</td>
</tr>
<tr>
<td>4</td>
<td>140/100</td>
<td>42</td>
</tr>
<tr>
<td>5</td>
<td>145/100</td>
<td>2.5</td>
</tr>
<tr>
<td>6</td>
<td>140/104</td>
<td>12</td>
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<tr>
<td>7</td>
<td>230/130</td>
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<tr>
<td>9</td>
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<td>180/110</td>
<td>33</td>
</tr>
<tr>
<td>11</td>
<td>130/90</td>
<td>58</td>
</tr>
</tbody>
</table>

TABLE II

*Level of serum 5-HT in females during pregnancy complicated with inevitable abortion*

<table>
<thead>
<tr>
<th>No.</th>
<th>Blood pressure in mm Hg.</th>
<th>Level of serum 5-HT in ng/ml.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100/70</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>114/68</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>120/74</td>
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<td>4</td>
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<td>7</td>
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<td>8</td>
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<tr>
<td>9</td>
<td>118/78</td>
<td>20</td>
</tr>
<tr>
<td>10</td>
<td>102/62</td>
<td>35</td>
</tr>
</tbody>
</table>
Complicated with Toxaemia

Level of serum 5-HT in ng/mL.

| Level | 45 | 13 | 35 | 42 | 2.5 | 12 | 37 | 6 | 45 | 33 | 58 |

Complicated with inevitable abortion

Level of serum 5-HT in ng/mL.

| Level | 12 | 40 | 38 | 33 | 33 | 12 | 42 | 15 | 20 | 35 |

Fig. 1
Assay of the serum of the patient No. 3, Table No. I, on contractile response of rat stomach. HT stands for 5-HT and 'S' stands for serum. Activity of 0.1 ml. of serum is equivalent to the activity of 3.5 ng. of 5-HT (Time interval—3 seconds).

Fig. 2
Assay of the serum of the patient No. 2, Table II, on contractile response of rat stomach. 'HT' stands for 5-HT and 'S' stands for serum. Activity of 0.1 ml. of serum is equivalent to the activity of 4 ng of 5-HT (Time interval—30 seconds).

DISCUSSION

From our results it is obvious that there is an apparent increase in 5-HT content in serum during toxaemia of pregnancy and abortion compared to that in non-pregnant and normal pregnant females. When the results are scrutinised with the help of statistical methods, it was found that this increase of 5-HT in serum in the above conditions is statistically insignificant.

Our results of the serum 5-HT levels in toxaemia of pregnancy are in agreement with those of Berry and Hughes (2), and Schmidt and Pokorny (13). Increase in plasma 5-HT levels shown by Krupp and Krupp (7) might be apparent rather than significant. Decrease in 5-HIAA, excretion in urine with normal serum 5-HT level as shown by Parikh and Bellare (10) can be explained on the basis of decreased production or change in distribution of 5-HT. There is more possibility of a change in distribution as suggested by the work of Senior et al. (14), who found an increase in 5-HT level in placenta in cases of toxaemia of pregnancy without significant change in blood 5-HT level. Whether this change in distribution plays a role in causation of toxaemia is difficult to say but there is some indication of its role as suggested by
the beneficial effect of Methyldopa, an antagonist of 5-HT in cases of toxaemia of pregnancy (6).

Few data are available on estimation of serum 5-HT in inevitable abortion. Increase of 5-HT excretion in urine in inevitable abortion as shown by Schmidt and Pokorny (7) and no change in serum 5-HT level, as shown by us, can be explained on increased production of 5-HT in this condition. This gives some indication for the role of 5-HT in inevitable abortion which is supported by other evidences like interruption of pregnancy in mice by 5-HT (8) and good therapeutic response of 5-HT antagonist in animals (11). A therapeutic trial with less toxic and more effective 5-HT antagonists is suggested in cases of inevitable abortion.

SUMMARY AND CONCLUSIONS

Serum 5-hydroxytryptamine (5-HT) has been biologically estimated on the rat isolated stomach strip preparation in toxaemia of pregnancy and inevitable abortion. Level of serum 5-HT in these conditions when compared to that in nonpregnant and normal pregnant males shows an apparent rise which is insignificant statistically at P=0.05.

Our results are discussed with those of others and it is inferred that 5-HT might be playing some role in toxaemia of pregnancy as well as in inevitable abortion.

A therapeutic trial with potent and less toxic 5-HT antagonists in inevitable abortion is suggested.

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REFERENCES

In cases of toxaemia of pregnancy, increase of 5-HT in inevitable abortion. Increase estimated on the rat isolated uterine preparation. Level of serum 5-HT in normal pregnant females at P=0.05. It is inferred that 5-HT might be implicated in inevitable abortion.

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5-HT in Toxaemia and Abortion