THE ROLE OF THE RAUWOLFIA ALKALOIDS IN THE TREATMENT OF HYPERTENSION IN PREGNANCY

BY

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The Rauwolfia Serpentina plant extracts have been in use for a very long time in ancient Indian ayurvedic medicine known as "sarpagandha", the chief use being for insomnia, insanity, nervous disorders, insect and snake-bites and various other ailments. It was only recently that modern scientific scrutiny rediscovered its properties. Since the isolation of its different alkaloids, the scientific medical world is closely observing with great interest the action of the drug in various ailments, particularly hypertension, insanity and insomnia, the three inevitable accompaniments of civilisation, cold war and increased struggle for existence. The present paper is a preliminary study, dealing with its effect on cases of hypertension associated with pregnancy. The pregnant state presents several special features when hypertension is associated. Preeclamptic toxaemia plays a special role in the production of hypertension. A detailed study of the effect of the drug on 50 cases of hypertension of different etiology along with the study of 50 control cases is presented in this paper.

Rauwolfia Legend

At the outset, it may be interesting to give a brief historical background of the evolution of the drug. The plant known as "sarpagandha" in Sanskrit and Bengali had been in use in ancient Ayurvedic medicine for various ailments, chiefly, insomnia and insanity, though its specific use for hypertension was not so much realised.

Interest in the drug was renewed about 25 years ago, when an eminent Kaviraja of Calcutta, Mahamohopadhya Bijoyratan Sen heard about its efficacy when he visited Patna (in Bihar State) on professional work. An eminent Muslim gentleman, father of the late Sir Ali Imam and Sir Hasan Imam, told him of the plant's efficacy in hypertension and insanity, which was divulged to him by an old sanyasi.

The plant was shown to Kaviraj B. R. Sen, who carried some of it to Calcutta and showed it and spoke about it to his friend Kaviraj Gana Nath Sen.

As Kaviraj B. R. Sen died soon after, the plant was given a fair trial

by Kaviraj G. N. Sen and his friend Dr. K. C.. Bose. Extracts were prepared at the laboratory of Dr. K. C. Bose.

In the same year Siddiqui and Siddiqui working in a research laboratory at Delhi, founded by Hakim Ajmal Khan, extracted five crystalline alkaloids: Ajmaline, Ajmalinine, Ajmalicine, Serpentine and Serpentinine. They conducted laboratory study of the drugs on frogs but the results were disappointing.

Studies were made by Bose and Sen with some extracts which were found to be very effective in hypertension, insomnia and insanity. It was however more through the researches at the School of Tropical Medicine, Calcutta, by Sir R. N. Chopra and others, that interest was created in the scientific medical circle all over India.

R. J. Vakil of Bombay sent questionnaires to fifty physicians all over India and 46 of them voted that Rauwolfia extract was the best drug for the control of hypertension. He himself carried out experiments on patients and his results were published in British Heart Journal. This created first interest in the drug outside the shores of India.

Experiments at the Calcutta School of Tropical Medicine (Gupta et al) found that the potency of the different alkaloids varied considerably and that the crude drug was more powerful than any of the known alkaloids of the Rauwolfia plant. This they attributed to a resin factor of the root. Unfortunately further analysis of this fraction was not possible at that time due to want of more modern laboratory equipment.

It was through the enthusiasm of Dr. E. Schlittler, working at the Ciba Laboratories in Basle and the encouragement and interest of Sir Robert Robinson of Oxford, that further chemical analysis of the resin fraction ultimately resulted in the isolation of a chemical now named Reserpine.

In America, first trial started after the publication of Vakil's article in British Heart Journal. Dr. R. Wilkins, working at Boston, carried out experiments on his patients, which first produced no results as the dose was insufficient and the time interval was short. Continued administration, however, produced slow gradual and sustained fall in blood pressure which maintained even after withdrawal of the drug.

The author's first knowledge of the drug came in 1940, during the treatment of a case of acute mania, which precipitated as a result of repeated haemorrhage after a gynaecological operation. The sedation of the case was a baffling problem and Rauwolfia root powder, prescribed by a Kaviraj, produced good result. The administration of a large quantity of this powder to a maniac was a very difficult problem and had to be given up ultimately.

When the drug was presented recently in smaller bulk by different extractions, through different manufacturers, the author found some of them having remarkable beneficial effects in cases of hypertension in pregnancy. A detailed trial was then conducted with the purified crystalline product Reserpine (Serpasil — CIBA) on 50 cases of hypertension

in pregnancy along with 50 control cases.

Selection of Cases

The cases of hypertension in pregnancy were selected irrespective of their etiological variations. The cases selected for trial with Reserpine had a blood pressure above the range 140/90 mm. of Hg. in systolic and diastolic. The maximum systolic blood pressure was 214 and maximum diastolic pressure was 130 mm. of mercury.

At first, every alternate case was being studied as a control, but when the author was convinced of the beneficial effect of the drug it was morally difficult to conscientiously withhold the drug from any case having a very high B.P. or showing other signs and symptoms of impending fits. The result was that most severe cases received the drug and less severe cases had to be tried as a control. This will be evident from the average B.P. of the trial cases and the control cases at the starting of the treatment.

The details of the cases selected for trial and control are given in a tabulated form in Tables I and II. The perusal of the tables will show that each of the groups is almost an average cross section of the other, with the exception that the trial cases had a higher range of average blood preasure, for reasons stated above.

The trial with Reserpine was conducted on cases as shown in Table I. As there is, in most cases, some fall in blood pressure following rest and standard treatment, trial with Reserpine was undertaken mostly from the second or the third day after admission. Only when the blood pressure was very high or when dangerous symptoms were present, the trial with Reserpine was started on the day of admission. Besides Reserpine, all the cases had restricted salt in diet, saline laxatives, occasionally diuretics and injections of glucose 50% 50 c.c. and calcium

TABLE I

Details of the Cases Studied

Trial with Reserpine (50 cases)

Blood pressure on admission	Urine condition on admission	Duration of Reserpine therapy	Nature of cases
Average=S/D= 176.5/118.8	Trace of albumen, 14 cases	6.5 days per case on average	Pre-eclamptic toxaemia, 31 cases
Maximum B. P.= S/D=214/130	Fair amount of albumin, 30 cases. Plenty of albumen, 6 cases.	Maximum time, 34 days	Essential hypertension, 13 cases. Eclampsia, 5 cases
Minimum B.P.=S/D= 140/92	R.B.C. present, 4 cases. Granular cast, 1 case.	Minimum time, 3 days	Chronic nephritis, 1 case

TABLE II

Control with Conservative Treatment (50 cases)

Blood pressure on admission	Urine condition on admission	Nature of cases
Average=S/D= 167/115.1	No albumen, 1 case Trace of albumen, 11 cases	Pre-eclamptic toxaemia, 29 cases Essential hypertension, 19 cases
Maximum B. P.=S/D= 210/126	Fair amount of albumen, 34 cases Plenty of albumen, 4 cases	Eclampsia, 2 cases
Minimum B. P.=S/D= 138/90	R.B.C. present, 4 cases Casts, nil	Chronic nephritis, nil

gluconate 10% 10 c.c. daily by the intravenous route. Bromides and chloral were used on 3 cases but as the effect of Reserpine produced sedation, this was not necessary in other cases.

The dose of Reserpine had usually been .25 mg. tablet orally 2 or 3 times a day. In three cases the dose was increased to .5 mg. 3 times a day.

In one case the double dosage had to be curtailed after 5 days due to feeling of drowsiness and depression. Nine out of the fifty cases, or 18%, presented side reactions such as drowsiness, depression, slight headache and giddiness, but treatment could be continued in all the cases except the one stated above.

One of the cases failed to respond satisfactorily and ultimately Apresoline (1-hydrazino-phthalazine-hydrochloride), in 20 mg. doses twice a day was added. This brought about a fall of 50/30=S/D of blood pressure in 3 days' time, when the drug was withheld. One case had history of 3 successive premature stillbirths and no living issue. She had a blood pressure of 210/130=S/D on admission at the 32nd week. With Reserpine treatment for 34 days, her blood pressure was maintained at a level between 160 to 180 systolic and 100 to 110 diastolic. She was then confined of a living female child weighing 4 lbs. 15 ounces which survived with usual care.

The control cases were treated with rest, laxatives diuretics, sedatives, as chloral hydrate and potassium bromide, barbiturates and injections of morphia. Injections of glucose 50% 50 c.c. and calcium gluconate 10% 10 c.c. intravenously were also given daily. They also had salt restricted or salt-free diet. Details of the cases are given in Table II.

Results of Trial

The results of the trial and control cases are presented below in tabulated form in Tables III and IV.

TABLE III

Reserpine Trial (50 cases)

Nature of cases	Average B. P. on commencement of trial	Appreciable fall in B. P. over-S/D = 25/15	Slight fall in B. P. over-S/D = 15/10	Rise in B. P.	Average B. P. on discharge	Average fall in B. P.	Result on baby	Result on mother		
								Presence of albumen in urine on 5th day after confinement	Onset of fits during treatment	Death
Pre-eclamptic toxaemia (31 cases)	S/D = 173.4/116.7	27 cases (87.1%)	4 cases (12.9%)	Nil	S/D = 125.9/84.5	S/D = 47.5/32.2	No still-birth or neo-natal death	Albumen present in 19.3% of cases	Nil	Nil
Essential hypertension (13 cases)	S/D = 181.7/123	9 cases (69.2%)	4 cases (30.8%)	Nil	S/D = 153.8/103.8	S/D = 25.9/19.2	1 case of still-birth	Albumen present in 15.3% of cases	Nil	Nil
Eclampsia (5 cases)	S/D = 185/121	4 cases (80%)	1 case (20%)	Nil	S/D = 128/87	S/D = 25/34	1 case of still-birth	Albumen present in 40% of cases	Nil	Nil
Chronic nephritis (1 case)	S/D = 170/112	Nil	1 case	Nil	S/D = 160/96	—	No still-birth or neo-natal death	Albumen present	Nil	Nil

TABLE IV

Control with Conservative Treatment (50 cases)

Nature of cases	Average B. P. on commencement of trial	Appreciable fall in B. P. over-S/D = 25/15	Slight fall in B. P. over-S/D = 15/10	Rise in B. P.	Average B. P. on discharge	Average fall in B. P.	Result on baby	Result on mother		
								Presence of albumen in urine on 5th day after confinement	Onset of fits during treatment	Death
Pre-eclamptic toxaemia (29 cases)	S/D = 167.6/117.9	23 cases (79.4%)	5 cases (17.2%)	1 case (3.4%)	S/D = 126/84.9	S/D = 41.6/33	4 cases of still-births (13.9%)	7 cases (24.1%)	4 cases (13.9%)	1 case (3.4%)
Essential hypertension (19 cases)	S/D = 164.8/113	6 cases (31.6%)	9 cases (47.4%)	4 cases (21%)	S/D = 148.6/98.8	S/D = 16.2/14.2	1 case of still-birth (5.2%)	4 cases (21%)	Nil	Nil
Eclampsia (2 cases)	S/D = 201/125	1 case	1 case	Nil	S/D = 154/99	S/D = 47/29	No still-birth or neo-natal death	2 cases	Nil	Nil

On perusal of Table III, it will appear that of the 31 cases of pre-eclamptic toxaemia having an average blood pressure of S/D=173.4/116.4, an appreciable fall in blood pressure was noticed in 87.1% of cases. These had a drop above the range of S/D=25/15 mm. of Hg. Again 12.9% cases showed slight fall in blood pressure (above the range S/D=15/10.) The overall drop in blood pressure, calculated from the date of Reserpine therapy and the date of discharge shows an average drop of 47.5/32.2=S/D. There had been no rise in blood pressure in any of the cases. None of the cases had a still-birth or neonatal death. As regards results on the mother, there was no death or onset of fits, and 19.3% had albumen in urine on the fifth day after confinement.

The 29 control cases of pre-eclamptic toxaemia shown in Table IV gave an appreciable fall in 79% of cases and slight fall in 17% of cases. There had been rise in blood pressure in one case. The average drop in blood pressure, calculated from the date of admission and date of discharge, gave the figure S/D=41.6/33. There had been 4 still-births. Four of the patients developed eclamptic fits and 7 cases, or 24.1%, had albumen in urine on the fifth day after confinement. One patient (who developed fits died).

More favourable results were obtained in cases of essential hypertension, so far as drop in blood pressure was concerned. Comparison of Tables No. III and IV will show that of the 13 Reserpine trial cases, 69.2% gave an appreciable drop and 30.8% gave slight range of fall as against 31.6% and 47.4% respectively. No case had a rise in blood pressure amongst the Reserpine cases whereas 21% of the control cases had a rise. The overall average drop in blood pressure was S/D=25.9/19.2 in the Reserpine cases and 16.2/14.2 in control cases. Albumen was present on the fifth day post-partum in 15.3% of Reserpine cases and 21% in control cases. There was one still-birth in each group. No maternal death occurred in either the trial cases or the control cases.

The cases of eclampsia and chronic nephritis were few and results shown in the tables are self-explanatory and need no comments.

The results demonstrate clearly better effects with Reserpine therapy, but the average clinical impression was definitely superior to that shown above. For this reason one very relevant point needs clarification and statistical scrutiny.

It is well known that in most cases of hypertension, particularly in pre-eclamptic toxaemia, there is a sharp fall in blood pressure following confinement, whether they are treated or otherwise. As many patients of either group were confined shortly after admission or on the same or the following day, the overall differences of blood pressure drop in the treated and control cases are not remarkably high, particularly in pre-eclamptic toxaemias. As such spontaneous drop in blood pressure following confinement is not so marked in cases of essential hypertension, the comparative overall figures of drop in blood pressure in this group of cases show clear difference in the treated cases.

To clarify this point, the blood pressure readings are further dissected up in Tables V and VI given below. The cases who were not confined within 3 days of admission and who had at least 48 hours of Reserpine therapy before confinement are compared with similar cases who were in the hospital for over 3 days prior to confinement and received the routine conservative treatment.

Perusal of the figures in Tables V and VI will show that trial cases with Reserpine showed significantly higher range of drop in blood pressure in cases of both pre-eclamptic toxaemia and essential hypertension. The latter group showed a much higher range in the drop. The minimum drop was 6/2 and maximum drop 32/28 in pre-eclamptic cases of the trial against 2/0 and

TABLE V

Effect of Reserpine on Blood Pressure, calculated on admission and on the day of confinement where the confinement took place at least 3 days after starting Reserpine Therapy (Minimum 3 days — Maximum 36 days)

Type and number of cases	Average fall in range of B.P. on date of confinement	Average rise on date of confinement	Minimum range of drop of blood pressure	Maximum range of drop of blood pressure
Pre-eclamptic toxaemia (14 cases)	S/D = 16/9	Nil	S/D = 6/2	S/D = 32/28
Essential hypertension (10 cases)	S/D = 34/23.6	Nil	S/D = 10/4	S/D = 64/48
Eclampsia (2 cases)	S/D = 15/8	Nil	S/D = 14/8	S/D = 16/8

TABLE VI

Effect of conservative treatment (control) on Blood Pressure, calculated on admission and on the day of confinement where the confinement took place at least 3 days after admission

Type and number of cases	Average fall of B. P. on date of confinement	Average rise of B. P. on date of confinement	Minimum range of drop of blood pressure	Maximum range of drop of blood pressure
Pre-eclamptic toxaemia (19 cases)	S/D = 7.5/3.5 (9 cases)	S/D = 4.9/2.7 (10 cases)	S/D = 2/0	S/D = 18/4
Essential hypertension (14 cases)	S/D = 11/1.5 (4 cases)	S/D = 6.8/3.6 (10 cases)	S/D = 2/0	S/D = 12/6
Eclampsia (1 case)	S/D = 30/10	—	—	—

18/4=S/D respectively in controls. In cases of essential hypertension minimum drop was 10/4 and maximum 64/48 in the treated cases against 2/0 and 12/6 respectively in controls.

No case of the trial group of either variety showed any rise before confinement whereas 51% of cases of pre-eclamptic toxaemia and 71% of cases of essential hypertension had rise in blood pressure. These figures are significant. Reserpine had therefore been able to keep the blood pressure in check before confinement in both the groups of cases, the range of blood pressure drop being higher in cases of essential hypertension.

The study of cases of eclampsia and chronic nephritis were few and no clear result could be shown.

Although in general, Reserpine was found useful in controlling blood pressure where it remained high after confinement, the present study did not follow the cases long enough after confinement to be able to show any significant statistical result. This was for dearth of available beds.

The effect of Reserpine on blood pressure was evident in most cases towards the end of first 24 hours of therapy. The maximum fall was found from the third or the fourth day and then it maintained a fair level till confinement, when it produced a further drop.

On withdrawal of the drug the lowered level of blood pressure was maintained for about 48 hours and then came up gradually, but never to its previous level (of starting of treatment).

The sedative effect was evident in all the cases more or less and supplementation of other sedatives was not necessary. The sleep was more nearly natural than can be produced by any of the known sedatives in use.

The oedema and water retention did not present a problem but it cannot be ascertained if this was due to routine use of glucose and calcium intravenously in all the cases, or due to the general beneficial effect of Reserpine by sedation and lowering of blood pressure.

Toxic Side-reactions

Toxic side-reactions, such as lassitude, weakness, drowsiness and slight headache and giddiness were observed in 9 cases out of the fifty trial cases. These were severe enough to require withholding treatment in one case who received .5 mg. dose 3 times daily. Ambulant cases showed less tolerance than bed cases. Most cases had a fall in rate of pulse but this fall in pulse rate never recorded below 68 per minute, even in cases receiving the drug for 34 days.

Discussion

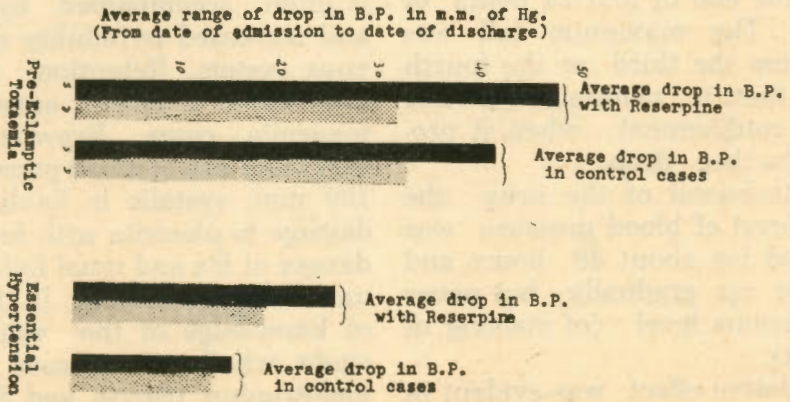
Hypertension in pregnant women is often accompanied by insomnia and increased irritability of the nervous system. Retention of sodium and water is often associated in toxaemia cases. Browne considers that mere rise of blood pressure above 160 mm. systolic is liable to cause damage to placenta with foetal death, danger of fits and renal failure or permanent renal damage. In the absence of knowledge of the exact causal agent, whether increased serum gonadotrophin (Smith and Smith, Go-

van and Mukherjee) or some other unidentified toxins, the accepted principle of treatment has been, sedation, elimination of water and sodium along with the hypothetical toxins, and lastly maintaining the blood pressure below the danger level by some hypotensive drugs. The ultimate object is to prevent the onset of eclamptic fits, ensure a healthy live baby and prevent renal damage of the mother.

Sedatives like barbiturates cause little effect on blood pressure and soothing of the nervous irritability is not marked. Morphia, though effective as a hypnotic, does not lower blood pressure in all cases. The toxic side effects prevent its random use. It is still, however, a widely used drug for pre-eclamptic cases. Direct effect on blood pressure by use of hypotensive drugs is being tried by different observers. Tetraethyl ammonium bromide or chloride gives a fall in blood pressure in cases of essential hypertension but not in toxaemic cases (Govan and Mukherjee, Kistner). Veratrone and Verenteral were found effective for toxaemic cases but toxic reactions are not at all negligible to guarantee their wider use (Kistner). The hydrazine compound, Apresoline, is found to be promising particularly in view of its maintenance of efficient renal and coronary circulation (Kistner); its sedative effect however is not so marked. Hexamethonium bromide is found not of much use, toxic reactions are not negligible (Mulcahy).

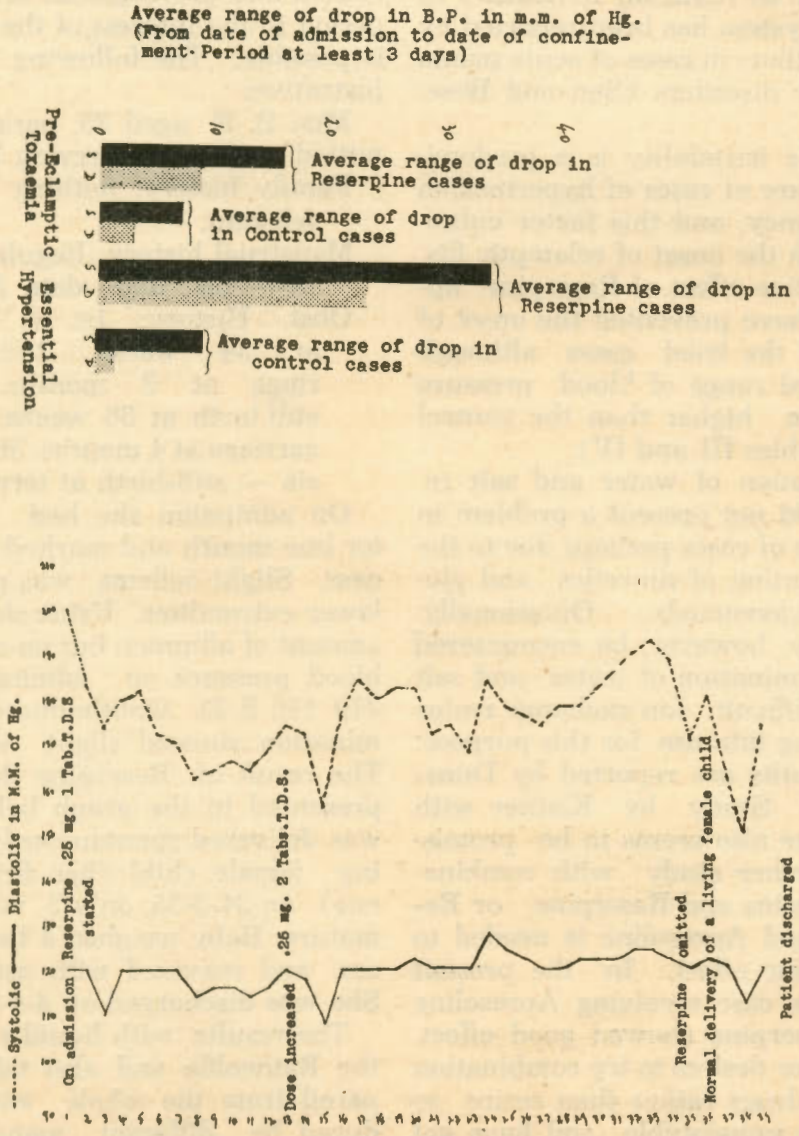
Combination of therapy with T.E. A.B. and Veratrone was found effective by Werko and Brody. Such combination with haxamethonium bromide and ion exchange resins or T.E.A.B. and Apresoline are also being tried.

Sedation by itself causes not very significant fall in blood pressure and the response is not constant. If we have a drug which produces sedative effects as well as a drop in blood pressure, we can achieve two of the three main principles of the treatment. Can Reserpine be effective to achieve these two ends? The results in this trial graphically tabulated below and details given in Tables III, IV, V and VI appear to be promising in respect of the blood pressure drop and the sedative effects produced, which eliminated the use of additional sedatives.



For reasons stated previously under results of the trial, more correct results are found where cases did not get confined for three days after admission. Comparison of the trial and control in such antepartum cases are given in details in Tables V and VI and graphically represented below.

Antepartum results of trial and control cases (Minimum antepartum observation 3 days).



Pharmacological study of the drug Reserpine by Bein established that the action of the drug in reducing blood pressure is exerted through its sedative effect on hypothalamic centres reducing neurogenic vasomotor impulses as well as direct action on the vessels.

The profound sedative effect of Rauwolfia in reducing irritability of nervous system has been reported by many authors in cases of acute mania and other disorders (Sen and Bose; Roy).

Nervous irritability is a predominant feature of cases of hypertension in pregnancy, and this factor culminates with the onset of eclamptic fits. The sedative effect of Reserpine appears to have prevented the onset of fits in all the tried cases although their inital range of blood pressure had been higher than the control cases (Tables III and IV).

Elimination of water and salt retention did not present a problem in this series of cases perhaps due to the administration of diuretics and glucose intravenously. Occasionally. cases may, however, be encountered where elimination of water and salt may be difficult. Ion exchange resins are coming into use for this purpose. Good results are reported by Dunster et al. Study by Kistner with Apresoline also seems to be promising. Further study with combination of resins and Reserpine, or Reserpine and Apresoline is needed to verify their effect. In the present study one case receiving Apresoline after Reserpine showed good effect. The author desires to try combination of these drugs rather than resins as these are unpalatable and have got some side-reactions.

The stillbirth rate is definitely favourably influenced by Reserpine and persistence of albuminuria after confinement also seems to have been favourably affected.

It appears that under reserpine therapy dangerous symptoms, calling for termination of pregnancy, are abated and prolongation of gestation period in the interest of the offspring is possible. The following case is illustrative:

Mrs. B. N. aged 25, para 3+2 admitted on 24-2-55 carrying 32 weeks.

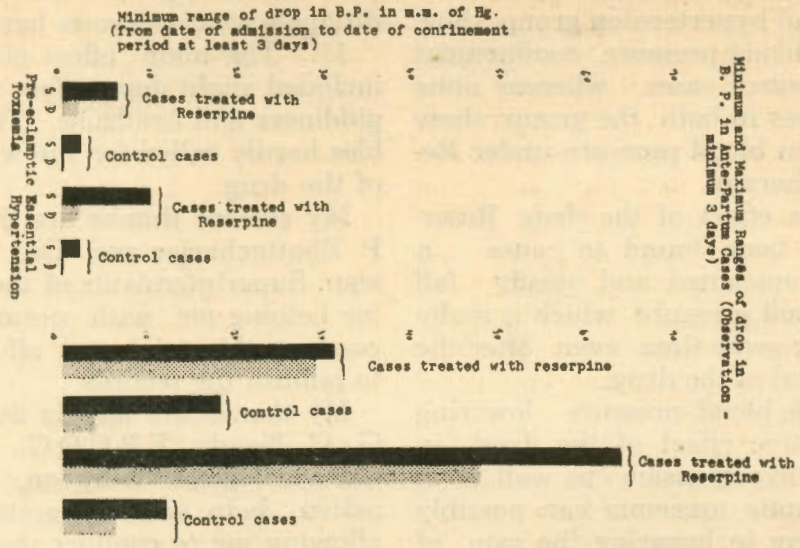
Family history: nothing definitely relevant.

Menstrual history: Regular. L.M.P. 14-7-1954, due date 23-4-55.

Obst. History: 1st = still-birth at 34 weeks. 2nd miscarriage at 3 months. 3rd = still-birth at 36 weeks. 4th miscarriage at 4 months. 5th eclampsia — still-birth at term.

On admission she had headache for one month and marked sleeplessness. Slight oedema was present in lower extremities. Urine showed fair amount of albumen but no casts. Her blood pressure on admission was 210/110 S/D. Ophthalmoscopic examination showed slight exudation. The result of Reserpine therapy is presented in the graph below. She was delivered spontaneously of a living female child (her first living one) on 31-3-55, only 3 weeks premature. Baby weighed 4 lbs. 15 ounces and survived with usual care. She was discharged on 4-4-55.

The results with liquid extracts of the Rauwolfia and also tablets prepared from the whole extract produced by different manufacturers



produced fairly good results, when tried previously but the effect was never constant or predictable. The effect of the purified alkaloid Reserpine had been constant and steady and anticipable.

The toxic effects were few as already described. Vakil describes one case as having ten times the dose by mistake and not having serious toxic effects.

The present study is a preliminary report and facilities for detailed laboratory study had been wanting. The results, however, are promising and deserve detailed study.

Summary and Conclusions

1. Effect of the drug Reserpine shows definite lowering of blood pressure on pregnant women suffering from essential hypertension. Comparison of average fall in B.P. shows a drop of S/D =25.9/19.2 in the trial cases and a drop of S/D=16.2/14.2 in the control cases. This has been calculated from average B. P. on the date of commencement of Reserpine therapy and on the date of discharge.

2. Study of the drug in lowering blood preassure in cases of essential hypertension before confinement shows a higher fall in blood pressure. An average fall of S/D= 34/23.6 is recorded in the trial cases against an average fall of S/D= 11/1.5 in the control cases.

3. The overall effect of Reserpine on cases of pre-eclamptic toxaemia shows an average fall in B.P.=S.D. =47.5/32.2. Whereas the control cases have an average fall in B.P. =S/D—41.6/33. This has been calculated from the average blood pressure on the date of admission and on the date of discharge.

4. In cases of pre-eclamptic toxaemia the effect of lowering of blood pressure in cases before confinement shows an average drop of S/D = 16/9 in the trial cases against S/D =7.5/3.5 in the control cases.

5. 52.6% of cases of pre-eclamp-

tic toxaemia group and 71% of cases of essential hypertension group show a rise in blood pressure confinement in the control cases, whereas none of the cases in both the groups show any rise in blood pressure under Reserpine therapy.

6. The effect of the drug Reserpine has been found to cause a gradual, sustained and steady fall in the blood pressure which is maintained for some time even after the withdrawal of the drug.

7. The blood pressure lowering and sedative effect of the drug in essential hypertension as well as in pre-eclamptic toxaemia can possibly be effective in lowering the rate of still-birth and for preventing the supervention of fits. Placental separation with accidental haemorrhage and permanent renal damage are also prevented, perhaps, by these two effects. There have been much fewer still-births in Reserpine trial cases (2 in 50) 4%, in comparison to the control cases where it was 10% (5 in 50). The persistence of albumen in Reserpine trial cases is evidently less than in the control cases. No case of essential hypertension or pre-eclamptic toxaemia developed fits during Reserpine therapy whereas 8.5% of the control cases (4 cases in 48) developed eclamptic fits, one of which proved fatal.

8. The effect of the drug Reserpine in cases of established eclampsia is inconclusive as yet in the trial and deserves further study.

9. No comment can be made about the effectiveness of the drug in chronic nephritis with pregnancy.

10. The sedative effect of the drug Reserpine has been useful in toxaemia and in hypertension where additional sedatives were hardly used.

11. The toxic effect of the drug included slight depression, weakness, giddiness and headache. These troubles hardly called for the withdrawal of the drug.

My sincere thanks are due to Dr. P. Bhattacharjee and Dr. N. C. Dewan, Superintendants of the Hospital for helping me with permission to conduct this trial and allowing me to publish the records.

My thanks are largely due to Dr. G. C. Nandy, F.R.C.O.G., Visiting Gynaecological Surgeon, for his active help and suggestions and allowing me to conduct the trial on his cases as well.

My thanks are specially due to Dr. S.K. Das, M.B., for compiling the figures and actively assisting in conduction of the trial.

Thanks are also due to Dr. A. Chatterjee and Dr. Miss B. Chowdhury, Medical Officers attached to our Department, for their active help in the aspects of the trial and compilation of the paper.

My thanks are lastly due to CIBA Pharma Limited for adequate supply of Reserpine in the form of Serpasil—CIBA for conduction of the trial.

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