

## INDICATIONS AND LIMITATIONS OF HYPOTENSIVE DRUGS IN THE TREATMENT OF HYPERTENSION OF PREGNANCY \*

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This survey was undertaken to determine the value of the hypotensive drugs in toxæmia of pregnancy. Because of lack of regular ante- and post-natal attendances we were unable to establish definitely whether our patients were suffering from toxæmia or whether the hypertension was due to other causes. The problem is further complicated because toxæmia may be superimposed on pre-existing hypertension or on chronic nephritis. From the therapeutic point of view it is important to differentiate because hypotensives appear to react differently in the different types of case.

*Classification.* Hypertension in association with pregnancy and labour occurs in about 5% of all pregnancies which progress beyond the 28th week. Hypertension in pregnancy may be classified as follows: (1) Pure pregnancy toxæmia (pre-eclamptic toxæmia), (2) essential hypertension, (3) essential hypertension with supervening pregnancy toxæmia, and (4) chronic nephritis. The significance of the classification is twofold; it enables one to decide whether hypotensive drugs are required and it assists one in prognosticating the foetal chances of survival.

For the purpose of this study any blood pressure above 140/100 mm. Hg was treated with hypotensive drugs; complications usually occurred above this critical level, though it is accepted from clinical experience that in uncomplicated essential hypertension hypotensive therapy is usually unnecessary if the blood pressure does not rise above 160/95.

### THE REGULATION OF BLOOD PRESSURE

#### *Physiopathology*

The following 4 factors are important in regulating the blood pressure: (1) Cardiac output and cardiac force, (2) blood volume, (3) viscosity of the blood, and (4) peripheral resistance. These factors are intimately integrated and controlled by a complex system of humoral and neurogenic reflexes. It will be easier to understand the manner in which hypotensive drugs operate if these four factors in blood-pressure regulation are borne in mind.

In both hypertension and toxæmia there is generalized vasoconstriction of the arteriolar system. This vasoconstriction is in turn responsible for an increase in peripheral resistance; studies on the kidney and on the brain have shown a greatly increased vascular resistance. Burt (1950) in his symposium on haemodynamics in pregnancy, states that peripheral areas such as the skin and the muscles of the extremities are exempt from this vasoconstriction. The increased vascular resistance in the kidney causes a reduction in renal blood flow and in the glomerular filtration rate. Both neurogenic vasoconstrictor impulses and humoral

factors are responsible in varying proportions for the arteriolar constriction. In toxæmia it is the humoral factors that predominate in the elevation of vascular resistance. The vasoconstriction has a damaging effect because it results in anoxæmia, retention of waste products, oedema, and necrosis. Autopsy shows ischaemia in most organs and varying degrees of infarcts in the placenta. The principal causes of death are cerebral haemorrhage, cardiac failure, and the accidental haemorrhage and anuria syndrome. Deaths from hyperemesis gravidarum and acute yellow atrophy are very rare. An acute cardiovascular accident overshadows the toxæmia problem. Stated in another way, hypertension is the most resistant feature in toxæmia while the other aspects of the varying toxæmia syndrome have proved much more amenable to control. Corkill (1957) analysed 435 cases of eclampsia occurring in New Zealand between 1950 and 1955: the principal causes of death were massive cerebral haemorrhage (5), sudden cardiac failure from toxic myocarditis (5) and the accidental haemorrhage and anuria syndrome (4).

#### *Rationale for Employing Hypotensive Drugs*

In general, the severity of pre-eclampsia is proportional to the degree of hypertension. In the previous paragraph I have quoted several references which show that the vasoconstriction has a damaging effect on tissues. While it seems logical that the vasospasm of toxæmia should be treated, such treatment was frowned upon by many on the grounds that hypertension was a necessary compensation to ensure that blood flows adequately through areas of increased vascular resistance. It was contended that to lower the blood pressure was dangerous because a sufficient pressure was then not available to give the vital organs an adequate supply of blood. Another argument that has been raised is that in reducing the blood pressure one is treating a symptom and not the disease. The fact is that until the 'toxin' responsible for toxæmia of pregnancy has been isolated treatment will have to be symptomatic. Since the chief cause of maternal death is an acute cardiovascular accident, which in turn is the end-result of uncontrolled hypertension, we shall look towards the hypotensive drugs to aid us in controlling this pernicious complication. The mere lowering of blood pressure is not enough; the ideal drug must also improve the circulation of the kidneys, brain and placenta. The alternative to treatment with hypotensive drugs is the time-honoured use of sedatives. Stroganoff, in 1897, advocated the use of morphine, which was and still is used widely. The other sedatives in common use are parenterally administered paraldehyde, barbiturates and magnesium sulphate. McCall *et al.* (1952) studied the effects of heavy sedation on the brain and was disturbed to discover that these agents (especially the intravenously administered barbiturates) depress oxygen metabolism of the brain almost to the same

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degree as eclampsia itself. Others have demonstrated a depressing effect on kidney function and urinary output. Another disadvantage of heavy sedation is the clinical undesirability of prolonged coma and the depressing effect on the foetus. Once the blood pressure is controlled heavy sedation is unnecessary in the vast majority of patients. By controlling the blood pressure it is possible to avoid the eclamptic convulsions and the subjective symptoms of headache, disorientation and blurred vision so commonly present in the hypertensive crises. The avoidance of heavy sedation offers the best chance of survival for the foetus and tends to reduce the incidence of respiratory morbidity in the mother. The comparison between the wide-awake, cooperative patient and the comatose women under heavy sedation who, despite skilled nursing, is liable to develop pulmonary complications, is most striking. As delivery approaches the claims of the foetus may conflict with the requirements of the mother as regards heavy sedation.

The consensus of opinion is that reduction of an elevated blood pressure without reducing the cardiac output and the blood supply to the vital organs is a sound and logical aim. It reduces the cardiac work, and prevents cardio-vascular accidents. As Assali (1954) points out, 'Just as lowering the fever may permit the patient to tolerate the toxic process more successfully, reduction of excessive hypertension may help the patient to tolerate better the ravages of the disease and its noxious effects on the vital organs'.

#### THE OBSTETRICAL AIM IN TREATING HYPERTENSION OF PREGNANCY

From the obstetrical point of view the aim is to obtain a sufficient degree of maturity of the foetus to render probable a fair chance of survival.

##### 1. Pre-Eclamptic Toxaemia

The majority of cases of pre-eclamptic toxaemia respond to bed rest, diet and sedatives. In the minority where this simple treatment is unsuccessful, do the hypotensive drugs help? After the 35th week, when obstetrical viability has been attained, pregnancy can be terminated by surgical induction if conservative medical measures fail to control the hypertension. But if the cervix is 'unripe' the procedure is fraught with grave risks. To 'ripen' the cervix with a Pitocin-drip may take a few days. During this interval can one depend on the hypotensives to control the blood pressure?

Another group of cases which present a great deal of difficulty are those in which the toxaemic manifestations commence before the 35th week. If the toxaemia commences early, the development of the baby is often severely affected owing to deficient nutrition resulting from the associated placental damage. If there is a heavy daily loss of albumen in the urine, intra-uterine death of the foetus is common. The problem in this group is two-fold. In the interests of both mother and foetus Caesarean section is indicated. But because of prematurity one aims at continuing the pregnancy up to the 35th week. The continuance of such pregnancies with a view to gaining further maturity is liable to result only in intra-uterine death, and the prompt decision to terminate them once the 35th week has been reached will often result in saving a baby who otherwise would have been

lost. Has the use of hypotensives altered the picture in this group? Can it reduce the Caesarean-section rate and prematurity rate for this group?

##### 2. Essential Hypertension and Pregnancy

If the pressure remains within moderate limits and there is no albuminuria, these cases usually terminate normally. The real danger associated with chronic hypertension is the supervention of pregnancy toxaemia, which forthwith changes the prognosis to one of grave danger to the foetus and appreciable risk to the mother. The main aim of the obstetrician is to carry the pregnancy till the 35th week so as to attain foetal maturity before resorting to termination of the pregnancy. If strict bed rest and sedation fails to control the hypertension the judicious administration of a hypotensive may be helpful. In the cases where the basis is essential hypertension the ganglion-blocking agents may be more successful. Once albuminuria occurs there is a very high risk of intra-uterine death of the foetus. A liberal view should be taken of termination by Caesarean section. The fulminating cases in which the blood-pressure readings are excessive (systolic pressure over 200 mm. Hg) may become evident at an early stage, often about the 6th or 7th month. In such cases the mother is exposed to grave danger and the outlook for the foetus is hopeless. In many cases the problem resolves itself by the intra-uterine death of the foetus, which is speedily accompanied by a lessening of the maternal symptoms.

##### Advantages of Hypotensives over Sedatives

*Cerebral Physiology.* Recent experimental studies of McCall and Taylor<sup>3</sup> on cerebral blood flow and oxygen metabolism in toxaemia show that barbiturates (especially those administered intravenously) depress cerebral blood flow and are likely to prolong the coma of eclampsia. The basis of the Rotunda treatment with intravenous Pentothal drip is to keep the patient unconscious for the 24 hours after the last fit. In their series of cases (Finnerty and Fuchs) no veratrum-treated patient was unconscious for longer than 2 hours. The persistence of coma in eclamptics is a very grave sign; Dieckmann (1952) quotes a maternal death rate of 34-73% of patients. Heavy sedation, besides adding to the complexity of the management of seriously ill patients greatly increases the incidence of respiratory complications.

The hypotensive drug allows the patient to cooperate (a) with adequate oral fluid intake and (b) by informing the doctor of anything untoward in her symptoms.

*Foetus.* The heavy sedation is harmful to the foetus, especially as most foetuses are premature, since toxaemia is commonest at 7-8 months.

*Pulse.* A constant finding in toxaemia, especially in eclampsia, is tachycardia. Dieckmann<sup>5</sup> states that an increase in pulse rate over 120 is associated with a mortality of 39%. In one of our cases we specifically employed Veriloid, in preference to Nepresol, for its bradycardic effect. The patient was an eclamptic with the pulse racing at 170 per minute. She was initially given the Rotunda treatment; after Veriloid therapy the pulse settled at 140 per minute.

##### Properties of an Ideal Hypotensive Drug

An ideal drug should be (1) rapid in action, (2) prolonged in effect, and (3) harmless to mother and foetus, (4) should have no unpleasant side-effects, (5) should not interfere with

labour, and (6) should have a wide safety margin between toxic and therapeutic dose.

Browne and Veall (1953) using radio-active sodium, showed that the maternal placental blood flow was reduced to one-third in pre-eclampsia and hypertension. It would seem that the ideal drug would be one which would lower the maternal arterial pressure and increase the blood flow through the placenta. A mere fall in the blood pressure without a concomitant dilatation of the spiral arterioles of the placenta might lead to further anoxia of the foetus. A reduced blood supply to the placenta must at a certain stage interfere with its normal functions; an indication which is relatively easy to measure is the transport of oxygen to the

foetus (Walker 1954). In a proportion of pre-eclamptics there is a reduced saturation of oxygen in the umbilical vein.

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#### REFERENCES

- Assali, N. S. (1954): *Obstet. Gynec. Surv.*, **9**, 779.  
Browne, J. C. M. and Veall, N. (1953): *J. Obstet. Gynaec. Brit. Emp.*, **60**, 141.  
Burt, C. C. (1950): *Edinb. Med. J.*, **57**, 18-20.  
Corkill, T. F. (1957): *J. Obstet. Gynaec. Brit. Emp.*, **64**, 67.  
Dieckmann, W. J. (1952): *The toxæmias of pregnancy*, 2nd ed. St. Louis: Mosby.  
Finnerty and Fuchs (1953): *Amer. J. Obstet. Gynec.*, **66**, 830.  
McCall, M. L. and Taylor, H. W. (1952): *J. Amer. Med. Assoc.*, **149**, 51.  
Stroganoff, V. V. (1899): *Terap. Vestnik. S. Petersb.*, **2**, 449.  
Walker, J. (1954): *J. Obstet. Gynaec. Brit. Emp.* **61**, 162.