ERGOMETRINE MALEATE AS A CAUSATIVE FACTOR IN POSTPARTUM ECLAMPSIA

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The vasopressor effects of ergometrine administered at the end of the second or third stages of labour have been reported by several investigators.[1,4,5,9-13,16-19,22,23,26,27] The incidence of postpartum elevation of systolic or diastolic blood pressure of more than 20 mm.Hg in previously normotensive patients after administration of ergometrine has been quoted as between 20%[16] and 31·6%,[27] while patients with pre-eclamptic toxaemia and hypertension have demonstrated the much higher incidence of 50%[1] and 60%.[27] An intensive search of the literature, however, has produced only 1 documented case of eclampsia in which ergometrine was considered to be the causal agent.[17] It is the purpose of this paper to report a second case and to discuss its probable pathogenesis.

Case Report

M.W., a 17-year-old married primigravida who had her last menstrual period on 1 October 1962 was first seen in the antenatal clinic at the 16th week of gestation on 21 January 1963. Previous medical history was negative. There was nothing contributory in her family history and no history of hypertension or epilepsy was obtained on subsequent interrogation.

Examination. General examination, including that of the cardiovascular and respiratory systems, was normal. Radiological chest examination and routine serological tests were negative. The antenatal period was uneventful, the highest blood pressure recorded in her 11 visits being 130/80 mm.Hg.

Labour. On 9 July 1963, she was admitted in labour with a blood pressure of 120/80 mm.Hg. and slight oedema of the ankles. Abdominal examination showed uterine enlargement consistent with a normal-term pregnancy. Weight gain and urinalysis was normal as before. Labour progressed satisfactorily. Tricloryl was given in early labour followed by pethidine on 2 occasions. The blood pressure throughout labour did not exceed 124/80 mm.Hg and urinalysis remained negative. A spontaneous normal delivery of a healthy baby weighing 6lb. 11oz. occurred after a labour of 13 hours 35 min. An intramuscular injection of 0·5 mg. ergometrine maleate was administered to the patient as the head crowned. The third stage was normal, total blood loss being 120 ml. The placenta appeared perfectly healthy. Local anaesthetic had not been used during delivery.

The blood pressure at the end of the third stage, i.e. 12 minutes after the ergometrine injection, rose sharply to 170/115 mm.Hg. 20 mg. of Omnopon was injected and the blood pressure recorded as 130/105 mm.Hg after 30 minutes. Approximately 25 minutes later the patient developed a severe frontal headache, the blood pressure rose to 170/110 mm.Hg and typical generalized eclamptic convulsions ensued. The usual eclamptic regimen including sedation with morphine and paraldehyde controlled the fits. The blood pressure 5 hours after delivery and until she was discharged remained below 130/80 mm.Hg.

Investigations after the convulsions were as follows: haemoglobin 94%, white blood count 12,800, blood urea 26 mg./100 ml., uric acid 4·1 mg./100 ml., serum electrolytes normal, serum cholesterol 334 mg./100 ml., fibrinogen 214 mg./100 ml., serum proteins normal. Urinalysis showed no abnormal constituents and microscopy was negative. Neurological opinion and investigation failed to show any cause for the generalized convulsion apart from eclampsia. Screening test for phaechromocytoma was negative. Follow-up examination 6 months later showed no abnormality.

DISCUSSION

Although it was not to be expected from its initial pharmacological research,[20] there is little doubt today that ergometrine and methylergometrine may cause the blood pressure to rise to eclamptogenic heights on rare occasions.[6,17,24] The pressor response of this oxytocic usually resolves within an hour if given intravenously,[19] and reaches its maximum effect in 30 - 120 minutes, returning to normal within 8 hours if given intramuscularly.[15]

Bulfin and Lawler[4] reported 12 cases of twin pregnancy with toxaemia who were given intravenous ergometrine and developed acute postpartum hypertension, creating all the appearances of impending eclampsia. In a review of 19 cases of postpartum eclampsia, Samuels[25] was convinced that ergometrine may have caused eclampsia in some of the cases. Subsequent reports have appeared in the literature as further evidence for incriminating ergometrine.

Casady *et al.*[6] cite 9 cases of postpartum hypertension with rupture of a cerebral vessel after administration of a vasoconstrictor drug or an oxytocic or both, and add a case of subarachnoid haemorrhage occurring in their series in which the blood pressure had risen to 180/120 mm.Hg within 35 minutes of an intramuscular injection of 0·2 mg. of ergometrine maleate. Ringrose[24] gave fresh emphasis to this risk when he reported a postpartum death in a 17-year-old primigravida. The patient had an uneventful pregnancy with no evidence of pre-eclamptic toxaemia on any occasion. The blood pressure during labour never exceeded 140/80 mm.Hg. She was given 0·2 mg. of ergometrine maleate intravenously at the crowning of the head. The blood pressure rose sharply to 190/120 mm.Hg within minutes. Neurological complications ensued and the patient died 7 days later from intracranial haemorrhage. Ringrose[24] questions the need of ergot derivatives and especially their routine prophylactic use.

Of particular interest is the case of postpartum eclampsia reported by Hamilton.[17] He performed an elective caesarean section under spinal anaesthesia on a patient who had been normotensive with normal urinary and blood chemistry. Intravenous Ergotrate was given on opening the uterus. Within 45 seconds the blood pressure rose from 112/72 mm.Hg to 210/118 mm.Hg and she complained of severe headache and blurring of vision. She was immediately given ¼ gr. of morphine intravenously. Being unaware of this potential effect of Ergotrate the routine administration of oral Ergotrate was continued. Eleven hours after the birth an eclamptic convulsion occurred. The ergotrate was discontinued and the patient had no further fits. Hamilton strongly believes that intravenous Ergotrate has been the cause of several cases of postpartum eclampsia.

That postpartum hypertension occurs in the absence of oxytocics has been reported in 2 series of cases. McGinty[19] injected normal saline instead of ergometrine and demonstrated an elevation of 20 mm.Hg systolic or diastolic pressure in 15% of previously normotensive patients. Friedman[13] omitted to give any oxytocic to a control group of 177 cases and demonstrated an elevation in the blood pressure in 15%, while his ergometrine group showed an equivalent vasopressor effect in 30% of cases.

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PATHOGENESIS

Among the possible physiological causes of postpartum hypertension is the overloading of the cardiovascular system resulting from (a) the hypervolaemia normally present during pregnancy, and (b) the sudden shift of blood from the uterine vascular space after delivery, as postulated by Casady *et al.*[6] In addition, contraction of the uterus which is effected by an oxytocic drug and the vasoconstrictor effect of the oxytocic drug on blood vessels may cause a sudden postpartum hypertension. Since postpartum hypertension is known to occur in some patients who have received no oxytocic drug, it appears likely that other intrinsic factors are involved in the causation of this phenomenon. The above also fails to explain the higher incidence of postpartum hypertension in cases of pre-eclamptic toxaemia and essential hypertension. It has been shown by Dieckmann and Michel,[8] De Valera and Kellar,[7] and Mukherjee[21] that the vascular system is hypersensitive in pre-eclamptic toxaemia. Furthermore Gemzell[14] has demonstrated that the blood concentration of 17-hydroxycorticosteroids in the last 3 months of normal pregnancy was 4 times the pre-pregnancy level, but 7 times the normal value immediately after delivery. One would, therefore, expect excess pressor and salt- and water-retaining substances to be present in the circulation in the last 3 months of pregnancy. Browne[2] believes that these substances are inactivated by an oxygen-sensitive oxidase, furnished by the healthy placenta, but that if from any cause the placenta is made ischaemic and its oxygen tension lowered, the protective enzyme is made ineffective and hypertension results. It has been shown by Browne and Veall[3] that the maternal blood-flow through the intervillous space is reduced by more than 50% in essential hypertension and pre-eclamptic toxaemia, and the placenta is thus rendered ischaemic.

Postpartum hypertension is probably caused by an interplay of all these factors, the most important being (1) the sudden shift of blood from the uterine vascular space after delivery into the circulation, (2) the hypersensitivity of the vascular mechanism, and (3) the removal of the 'protective placental' enzyme[2] after the third stage of labour, resulting in increased concentration of 17-hydroxycorticosteroids and therefore pressor substances in the circulation. The injection of a vasopressor substance such as ergometrine, superimposed on this clinical situation, may cause dangerous eclamptogenic elevations of the blood pressure.

SUMMARY

A case of postpartum eclampsia occurring in a previously normotensive patient 65 minutes after an injection of ergometrine is reported, and the probable pathogenesis discussed.

It is suggested that the use of ergometrine in pre-eclamptic and hypertensive states be selective rather than routine.

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