Management options

Modern management of eclampsia

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Summary

Eclampsia, the occurrence of a seizure in association with pre-eclampsia, remains an important cause of maternal mortality and morbidity. Despite being recognised since antiquity, consistent management practices are still lacking. Given that the aim of good care is to prevent seizures, it is disappointing that in the majority of cases the first eclamptic convulsion occurs after admission to hospital. This indicates that either the women who are likely to have a convulsion were not identified accurately, or the treatment given was ineffective. The answer to poor management of eclampsia lies in better education and training of all obstetricians, anaesthetists, midwives, and general practitioners in the diagnosis and treatment of severe pre-eclampsia and eclampsia. Protocols for the management of fluid balance, antihypertensive and anticonvulsant therapies should be available and reviewed regularly. The universal adoption of such guidelines in all obstetric units would substantially reduce elements of substandard care which have repeatedly been identified in the triennial reports of the confidential enquiries into maternal deaths in the UK.

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Eclampsia is defined as the occurrence of one or more convulsions in association with the syndrome of pre-eclampsia. Pre-eclampsia is a multisystem disorder that is usually associated with raised blood pressure and proteinuria in pregnancy. In Europe and other developed countries eclampsia complicates approximately 1 in 2000 deliveries,[1] while in developing countries estimates vary between 1 in 100 to 1 in 1700.[2-4] Forty-four per cent of seizures occur postnatally, the remainder being antepartum (38%) or intrapartum (18%).[1]

Over half a million women die each year of pregnancy-related causes, and 99% of these deaths occur in the developing world.[5][6] Although rare, eclampsia probably accounts for 50 000 maternal deaths a year world-wide.[7] In areas where maternal mortality is highest, infection and haemorrhage are the main causes of death,[8] but as deaths from these causes become less common, those associated with hypertension and eclampsia assume greater importance. In the UK, eclampsia is a factor in 10% of direct maternal deaths.[9][10] Successful prevention of all cases of eclampsia is likely to be difficult,[1] therefore it is important to assess the relative merits of alternative treatments for eclampsia.

The pathophysiology of eclampsia is thought to involve cerebral vasospasm leading to ischaemia, disruption of the blood–brain barrier and cerebral oedema. Neurological complications may include coma, focal motor deficits and cortical blindness. Cerebrovascular haemorrhage is a complicating factor in 1–2%.[1] The principal post-mortem lesions described in the brains of women who died of eclampsia are hyperaemia, focal anaemia, thrombosis, and haemorrhage. Severe and persistent headache, blurred vision, photophobia, irritability, transient mental changes, epigastric or right upper-quadrant pain, nausea, and vomiting are important warning signals.[11] At the onset of convulsions, 23% of patients had minimal or absent hypertension, 19% did not have proteinuria, and in 32% oedema was absent.[11] Miles *et al*[12] studied patients with eclampsia who experienced post-partum seizures. Early (<48 hours) post-partum eclampsia was experienced by 72% of patients and 28% had late (>48 hours) post-partum eclampsia. Only 83% were considered to have had pre-eclampsia before seizures, and haemolysis, elevated liver enzymes and low platelets (HELLP) syndrome was present in 30% of cases.

Place of care

Due to the incidence of eclampsia, the average doctor, even the average consultant, working in a hospital of 3500 deliveries a year may not see an eclamptic patient while on duty within a 5-year period. Most obstetricians will therefore be inexperienced in the management of this condition. This is reflected by the findings of the last two Confidential Enquires into Maternal Deaths, which have identified elements of substandard care in nearly 50% of cases of maternal deaths due to eclampsia, and highlighted delays in senior clinical decision making as well as the failure of junior staff to recognise the severity of symptoms and signs.[9][10]

The Confidential Enquires into Maternal Deaths have recommended that treatment of all women with eclampsia and severe pre-eclampsia should be in a regional centre. However, the transfer of an undelivered woman with eclampsia is both difficult and dangerous. The ambulance journey may precipitate more convulsions which may be extremely harmful to the woman and her baby. It may be equally difficult to get experts from a regional centre to physically assess an eclamptic woman in a district hospital bearing in mind the unpredictable and untimely nature of eclampsia. The notion of experts giving advice over the phone about a patient they have not seen is also of doubtful benefit. Thus the answer to substandard care and poor management of eclampsia lies in better education and training of all obstetricians, anaesthetists, midwives, and general practitioners in the diagnosis and treatment of severe pre-eclampsia and eclampsia. To reduce the maternal mortality and morbidity from eclampsia, standard protocols that are known and understood by all labour ward personnel should be available and reviewed regularly.

Prevention of eclampsia

Sometimes a woman will have an eclamptic fit with no prior warning. More usually, eclampsia occurs in women who have established pre-eclampsia. Anticonvulsants are used for women with pre-eclampsia in the belief that they will prevent the onset of eclampsia and so improve the outcome for both mother and baby.[13] [14] Although eclampsia is certainly associated with a poorer outcome than pre-eclampsia, it does not necessarily follow that anticonvulsants will halt the progression to eclampsia.[15] Even if they do prevent the onset of convulsions, it does not necessarily mean that other serious complications, such as renal failure, liver failure and disseminated intravascular coagulation, will be avoided.

Most women with pre-eclampsia will do well and go on to be delivered of a healthy baby. For those with severe disease the outcome may be poorer, and it is these women who are at highest risk of eclampsia. Nevertheless, only a tiny proportion of women with severe pre-eclampsia will develop eclampsia and occasionally someone with only very mild disease will convulse.[16] Predicting whether an individual woman will have an eclamptic fit is, therefore, difficult. Hence, the routine use of anticonvulsant prophylaxis in all women with pre-eclampsia has been questioned.[15] This controversy is not surprising, since the incidence of eclampsia in women with pre-eclampsia is extremely low and varies greatly among different groups of women.[17] For example, in two large, observational studies in the US, the average rate of eclampsia among 13 924 women with pre-eclampsia who received prophylaxis with magnesium sulphate was 0.26%,[18] which does not differ substantially from the rate of 0.18% among 3885 women with pre-eclampsia who did not receive prophylaxis in a Scottish study.[19] It is therefore important to redirect the aim of management of patients with severe hypertension away from prevention of the convulsions and towards the lowering of blood pressure and control of fluid balance which are the two main causes of maternal mortality.[16]

Principles of treatment of eclampsia

ANTICONVULSANT THERAPY

The aim of anticonvulsant therapy is to stop any convulsion that is present and to try and prevent any recurrence of convulsions. If the patient is convulsing, intravenous (iv) diazepam 5 mg boluses, repeated as required, up to a maximum of 20 mg can be used to stop the convulsion. The airway should be secured and the patient should be placed in the recovery position and given facial oxygen.

The Collaborative Eclampsia Trial showed a significant reduction in the incidence of recurrent convulsions in women treated with magnesium sulphate compared with women treated with diazepam or phenytoin.[20] Eclamptic women given magnesium sulphate in the trial also showed a reduction in maternal mortality, need for ventilatory support, and admission to intensive care units. The rational for the use of magnesium sulphate stems from its combined actions as a vasodilator[21] [22] and a membrane stabiliser.[23] This not only reduces cerebral ischaemia but also blocks some of the subsequent neurological damage that may be associated with it.[22] [24] Magnesium sulphate may also exert its effects by blocking the *N*-methyl-D-aspartate receptor in the hippocampus, thus acting as a central anticonvulsant.[25]

When given by intramuscular injection, magnesium sulphate treatment was associated with abscess formation in 0.5% of cases, as well as being a painful process.[20] The iv route is therefore preferred. A loading dose of 4 g should be given slowly over 5–10 minutes followed by a maintenance infusion of 1 g/hour continued for at least 24 hours after the last seizure. Recurrent seizures should be treated with a further bolus of 2 g.[26]

In most cases therapy can be monitored safely by hourly measurement of patellar reflex and respiratory rate. If there are any signs of magnesium toxicity further doses must be withheld until these disappear. Significant respiratory depression should be treated with 1 g calcium gluconate given intravenously over 10 minutes. As magnesium is excreted by the kidneys regular monitoring of serum levels should be considered in women with renal disease or in women with oliguria (urine output of <100 ml in 4 hours). The therapeutic range is believed to be between 2 and 4 mmol/l.[26]

If repeated seizures occur despite magnesium sulphate therapy, options include diazepam (10 mg iv) or thiopentone (50 mg iv). Intubation may become necessary in such women in order to protect the airway and ensure adequate oxygenation. Further seizures should be managed by intermittent positive pressure ventilation and muscle relaxation.

It is important to remember that many patients who go on and have further seizures in the presence of anticonvulsant therapy do so because their blood

pressure is inadequately controlled. Therefore, it is paramount that antihypertensive therapy is used in conjunction with anticonvulsants if the blood pressure is raised.

BLOOD PRESSURE CONTROL

The aim of lowering the blood pressure is to minimise the risks to the mother from events such as cerebral haemorrhage, cardiac failure, myocardial infarction, and placental abruption.[27] Treatment must induce a smooth sustained fall in the blood pressure, rather than an acute drop, which is dangerous both to the mother and to the foetus.[19] The threshold for treatment is usually a sustained diastolic blood pressure of 110 mmHg or higher[28–31] or a mean arterial pressure greater than 125 mmHg.[27] The aim of therapy is to gradually lower the blood pressure by 10 mmHg systolic and diastolic from pre-treatment levels and maintain the mean arterial pressure below 125 mmHg (but not less than 105 mmHg) and the diastolic pressure below 105 mmHg (but not less than 90 mmHg).[27 32] The most common drugs used are labetalol (20 mg iv escalating to 80 mg every 10 minutes up to a maximum cumulative dose of 300 mg)[33–35] or hydralazine (5 mg iv repeated every 20 minutes up to a maximum cumulative dose of 20 mg.[32–37] Both, however, may precipitate foetal distress and therefore continuous foetal heart rate monitoring is necessary.[26] Alternatively, nifedipine can be used,[31 38 39] although if administered to patients receiving concomitant magnesium sulphate, it may exaggerate the hypotensive response.[40]

Currently there is insufficient evidence to recommend one antihypertensive agent in preference to another; the choice of which to use is likely to depend on availability and personal preference. Research is required to determine which one is most effective, not only by measurement of systemic arterial pressure but also by assessment of cerebral arterial blood flow as measured by Doppler blood velocity wave forms.

FLUID MANAGEMENT

One of the main causes of maternal death is cardiorespiratory failure. Eclamptic women, although possibly hypovolaemic, are grossly fluid overloaded if total body fluid is taken into account. This is due to oedema which is common in these patients and any fluid management policy should take this into consideration. In order to reduce the chances of iatrogenic complications, especially pulmonary oedema, left ventricular failure and adult respiratory distress syndrome, both fluid input and output should be closely monitored. In an effort to increase the plasma osmotic pressure, colloid solutions are often used. However, there is no evidence to suggest that this improves the outcome and crystalloids therefore provide the mainstay of fluid therapy.[41] Intravenous fluid should be given at a rate of 80 ml/hour (1 ml/kg/hour) or the previous hour's urine output plus 30 ml.[26] Urine output is best monitored by siting an indwelling urethral catheter and maintaining an hourly fluid balance chart.

There is uncertainty about the treatment of oliguria which often occurs in eclampsia. The temptation is to insert a central venous pressure (CVP) catheter to monitor fluid balance. However, CVP may be difficult to interpret since interstitial oedema may be present and the CVP may be normal or low. If a CVP line is used, it is important that trends are monitored, levels are kept generally below 5 cmH$_2$O and no attempt is made to replace fluid up to any particular level. Fluid challenges to try and improve fluid output should never be used, as this will tend to aggravate an already dangerous situation.

INVESTIGATIONS

The eclamptic seizures are usually a manifestation of a multisystem disorder. Associated features include HELLP syndrome (3%), disseminated intravascular coagulation (3%), renal failure (4%) and adult respiratory syndrome (3%).[1] Frequent monitoring of haemoglobin, platelet count, coagulation factors, liver function tests, urea and creatinine together with oxygen saturation is therefore necessary. Cerebral imaging (magnetic resonance imaging or computed tomography) is not indicated in uncomplicated cases of eclampsia, although it is mandatory to exclude haemorrhage and other cerebral abnormalities in women with focal neurological deficits or prolonged coma.[42]

DELIVERY

The definitive treatment of eclampsia is delivery. If the patient is already in labour or if labour can be easily induced, then vaginal delivery may be contemplated provided there are no other obstetric complications. Nevertheless, it is inappropriate to deliver an unstable mother, even in the presence of foetal distress.[26] Once seizures are controlled, blood pressure is stabilised and hypoxia corrected, delivery can be expedited. Caesarean section, rather than induction of

labour, is much safer in a patient remote from term with an unfavourable cervix.[26] Whatever the mode of delivery, anaesthesia is a problem. Although no controlled trials have been reported, epidural analgesia has been recommended in the management of pre-eclamptic women in labour.[43 44] Maternal cardiac output is unaffected,[45] placental intervillous blood flow appears to be enhanced,[46] and control of maternal blood pressure is improved.[45 47] Vasodilatation and pooling of the blood in the veins of the lower extremities may cause hypovolaemia. Pre-loading the circulation with 400–500 ml of colloids prior to regional anaesthesia will reduce the risk of hypotension and foetal distress.[26] Hence, when epidural analgesia is performed with sufficient care and anticipation, it seems to be safe for the baby[44 47] and its benefits seem to outweigh its disadvantages. Similarly, a spinal block may cause hypotension in the face of hypovolaemia but has the added advantage of being quicker.

Regional analgesia is contraindicated if there is evidence of actual or incipient disseminated intravascular coagulation. A knowledge of at least the platelet count is essential and, if less than 100×10^9/l, the procedure should be avoided.

Occasionally, a Caesarean section has to be done too quickly to consider using epidural anaesthesia. Although general anaesthesia allows more precise control of the speed and timing of surgery, it carries its own complications. Intubation may be difficult,[48] or impossible[49] because of laryngeal oedema which may also cause post-operative respiratory obstruction and cardiac arrest. Laryngoscopy is a well-known cause of extreme transient reflex hypertension in all individuals. The problem is aggravated in eclamptic women[50 51] and may be so extreme as to cause acute pulmonary oedema.[52]

Anticipating these problems is the key to their management. Therefore, an experienced and well-briefed anaesthetist should be involved in the management of all eclamptic patients.

Ergometrine should not be given either before or after delivery but an infusion of oxytocin (40 IU/h in dextrose) should be given to prevent post-partum haemorrhage.[53]

POST-PARTUM MANAGEMENT

After delivery, high-dependency care should be continued for a minimum of 24 hours.[26] If blood pressure is under control, intravenous antihypertensive therapy can be gradually withdrawn and replaced with oral treatment. If magnesium sulphate has been commenced, it should be continued after delivery for at least 24 hours and a strict fluid balance should be maintained until natural diuresis ensues.

The underlying cause of the hypertension in pregnancy may not be apparent until the pregnancy is over. Hence, it is important to follow the patients up until normal blood pressure has returned. If normotension is not achieved by 6 weeks post-partum, further investigations should performed to detect any underlying cause(s). Furthermore, the couple should be seen for post-pregnancy counselling regarding any future pregnancies. There appears to be a risk of around 10% of recurrence of severe disease in any subsequent pregnancy while a further 10–15% women may experience a milder form of the disease.[54]

Conclusion

Eclampsia remains a rare but serious complication of pregnancy. Medical staff should be aware of its pathophysiology and acute management in order to reduce the maternal morbidity and mortality which are still associated with this condition. Protocols for the management of fluid balance, antihypertensive and anticonvulsant therapies, should be available and reviewed regularly.[55] The universal adoption of such guidelines in all obstetric units should substantially reduce elements of substandard care which have repeatedly been identified in the triennial reports of the confidential enquiries into maternal deaths in the UK. The Collaborative Eclampsia Trial has shown that magnesium sulphate is the drug of choice for routine anticonvulsant management of women with eclampsia; a similar study is warranted to establish the antihypertensive drug of choice.

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