THE MANAGEMENT OF ECLAMPSIA*

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Eclampsia is a serious obstetric emergency which could complicate a patient with pre-eclampsia and is characterized by epileptiform convulsions.

The word "eclampsia" is derived from the Greek term used by Hippocrates to designate a fever of sudden onset. "Eclampsia" means flashes of light and vividly indicates the fulminating character of the disease.

The important component for both pre-eclampsia and eclampsia is hypertension. Hypertension occurs in 6-8 % of women making it the most common high risk complication of pregnancy. Hypertensive disease contributes significantly to intra-uterine growth retardation and iatrogenic prematurity leading to fetal, neonatal and infant deaths. It is also acknowledged that pre-eclampsia and eclampsia are also major contributors to maternal deaths both in developing and developed countries.

Antepartum eclampsia carries with it the highest mortality, as shown by Krishna Menon (1961) in his study dealing with 1, 151 cases (Table.1).

However, it is the impression amongst Obstetricians to day that ante-partum eclampsia is becoming less common, and this is attributed to good antenatal screening, early and appropriate treatment of hypertension and good management of severe pre-eclampsia and impending (imminent) eclampsia.

The aetiology of eclampsia is the same as that of pre-eclampsia, since it is universally agreed that the onset of fits/convulsions merely indicate a very severe stage of the same disease.

Theories, which account for the fits include:

- cerebral anoxia – due to intracranial vascular spasm
- hypertensive encephalopathy
- cerebral oedema
- excessive retention of sodium ions and
- cerebral dysrhythmia

Macintosh (1952) explained the

* Review Lecture

convulsions as due to an epileptic tendency.

It should be emphasised that convulsions (fits) are not essential for a diagnosis of eclampsia, as occasional patients have been found post-mortem to have pathological changes in the liver characteristic of eclampsia, and to such cases a diagnosis of "eclampsia without convulsions" is given.

It is no exaggeration to think of eclampsis in general as carrying a 10% maternal risk, although several series of over 100 cases of eclampsia without a death has been recorded.

Maternal mortality and morbidity due to eclampsia can be brought to a MINIMUM by:

- predicting and preventing or reducing the incidence of pre-eclampsia
- aggressively managing all the cases of severe pre-eclampsia and impending eclampsia
- appropriate management of eclampsia and the ensuing complications

Prevention of Eclampsia

Eclampsia may be averted by prophylactic treatment of susceptible groups based on known risk factors, either from the history, present obstetric condition or by screening the low risk population through various tests to identify those who are likely to develop hypertension and by treating them (Table.2).

Control of Severe Pre-Eclampsia / Impending Eclampsia

This can abort an attack of eclampsia and involves the appropriate and adequate use of anti-convulsant and anti-hypertensive therapy.

Symptoms and Signs of Impending Ecalampsia

Identifying symptoms and signs of impending eclampsia will be present in about 80% of those at risk (Table.3).

The management of eclampsia can be considered under the following headings:

- General Management /Emergency Measures
- Immediate control and prevention of further fits/convulsions
- Anti-hypertensive therapy
- Specific Obstetric management

General Management / Emergency Measures

Although, ideally, all rooms in the labour ward should be suitably equipped to manage a patient with eclampsia, this may not be possible when funds are limited and so at least one room should have such facilities.

The room should not have bright lights that might dazzle the eyes of the patient but should be adequately lit so that cyanosis, which may be the first sign of cardiac failure in these patients, is not missed. Undue sound should be avoided.

The patient should be nursed in a bed with facilities to tilt the head down. Suction apparatus should be there by the bed side to suck out secretions which otherwise might lead to aspiration and its consequences. An eclamptic patient might develop respiratory arrest (with anticonvulsant therapy) breathing problems (due to laryngeal oedema/heavy sedation) or status eclampticus (repeated convulsions despite maximal anticonvulsive therapy).

In these situations the only lifesaving measure is endotracheal intubation and ventilation and therefore facilities should, ideally be available to carry out this procedure or at least to initiate it and then to transfer the case to an I.C.U.

Emergency measures and nursing regime for a 'fitting' patient should include:

- Keeping the foot of the bed raised or the head of the patient lowered
- Placing her flat on her side and loosening tight clothing
- Ensuring a free airway, by opening the jaws with a gag or spoon, pulling the tongue forward (with a tongue forceps) inserting an air-way (if available) and aspirating any secretions or vomitus
- Administering oxygen if the patient is cyanosed
- Commencement of external cardiac massage if there is cardiac arrest

In regard to nursing care the following should be emphasised:

- skilled and gentle nursing is of the greatest importance; an attendant should be by the patient throughout
- all manipulations, including passing a catheter must be expertly done so as to not stimulate her more than is absolutely necessary

Success of treatment depends on unremitting care and attention to detail.

Immediate Control of Fits and Prevention of Further Fits

Concurrent with the first aid/emergency measures instituted, specific anticonvulsive and antihypertensive therapy should be commenced to control convulsions to prevent recurrence and to avoid complications of the severe hypertensive process.

A variety of anticonvulsive regimes have been used (Table. 4).

Those in current use are

- Clonazepam or Diazepam
- Magnesium sulphate and
- Chlormethiazole disylate (HEMINEVRIN)

Magnesium sulphate was once used almost universally in the U.S.A, while Diazepam and Chlormethiazole were usually used in the U.K. but to day Magnesium sulphate is being widely employed even in the U.K.

Though as to what might be the ideal treatment is disputed the most important factors are the skill and experience of the Obstetrician and the standard of care given to the patient.

The "LYTIC COCKTAIL" – Chlorpromazine – promethazine or diethazine – pethidine was introduced by Laborit in 1950.

This mixture induced a state of artificial hibernation characterised by:

- HYPOTHERMIA
- HYPOTENSION
- BRADYCARDIA
- REDUCED RESPIRATION
- AMNESIA
- MUSCULAR RELAXATION

The depressant effect of the mixture upon the CNS has found it useful in the control of fits in eclampsia.

Krishna Menon (1960 – 1961) had the greatest experience with this treatment.

- Used it in 402 cases with a maternal mortality of only 2.2%
- Thiopentone – 0.5 g I.V. given as first aid treatment in severe cases
- On admission

(i) Chloropromazine 25mg, Pethidine 100mg } I.V. in 20ml 5% dextrose

(ii) 50mg of diethazine (Diparcol) or Promezathine (Phenergan) and

- an I.V. drip of 20% glucose containing 200mg Pethidine in one litre

  The drip rate adjusted to last for 24 hrs or longer

- in addition he gave alternate I.M. injection every 4 hours of Chlorpromazine ('Largactil') or Promethazine (Phenergan) 50mg for 48 hours.

If after 8-10 hours fits were not controlled, he performed Caesarian section if patient was not in labour, if head was not engaged or cervix was unfavorable: in others he ruptured the membranes.

The modified lytic – cocktail regime

I have used my own "modified" Lytic Cocktail regime for the management of eclampsia with good results, both at the University Unit Kandy Hospital and Jaffna.

The regime is shown in Table. 5

Though some consider the Lytic-Cocktail had become historical following the introduction of the benzodiazipines in 1960, I still think it is a very effective and suitable regime for the management of eclampsia

An ideal sedative for use in eclampsia should:

- calm and sedate the patient
- possess anticonvulsive activity
- possess, ideally, also antihypertensive action
- not aggravate any existing pathology in the liver and/or kidneys
- be easy to prepare and administer and also be cheap and
- not unduly harm the fetus and or the mother

Our regime seems to fulfil most of these criteria.

Magnesium Sulphate

May be administered according to the schedule prepared by Pritchard (1975) or that described by Zuspan (1966) (Table. 6).

Magnesium Sulphate is an effective cerebral depressant and also blocks the neuromuscular junction.

The effects associated with various serum magnesium level is indicated in Table. 7.

It is important to test the patellar reflex before each injection. Also the drug should not be given if the respiratory rate is less than 16 per minute or the urine output less than 25-30ml / hour.

Though magnesium crosses the placenta freely there is no evidence of

toxicity to the baby, so long as maternal safe limits are observed.

Diazepam (Valium) Regime

The immediate therapy is 10mg diazepam over 1 – 2 minutes and repeated every 5 minutes, if necessary. The total dose that could be given, with confidence, without fear of respiratory depressions is 40mgs. for any one episode.

The Maintenance Therapy

Although chlordiazepoxide (Librium) 100mg in 500ml saline would be ideal, the non-availability of Librium, makes maintenance with diazepam the alternative acceptable regime. A total dose of 40mg diazepam in 500ml saline can be titrated to keep the patient well sedated and drowsy but arousable. To prevent recurrent 'fits' the maintenance regime is continued for 24 hours after the last fit or after delivery whichever was the last event.

Benzodiazepins have stood the test of time as useful agents in the management of imminent eclampsia and eclampsia.

A combined Diazepam/Phenytoin regime has been recently tried. Following bolus doses of 5mg Diazepam, until convulsions stop, therapy is then maintained using phenytoin, starting with loading dose of 1 mg/kg followed by 5 mg/kg two hours later. Oral phenytoin is then given 12 hours later in a dose of 200 mg and continued 12 hourly for a period of 48 hours after delivery to prevent recurrence of convulsions.

In order to find out which of the 3 anticonvulsant drugs (Magnesium Sulphate, Diazepam or Phenytoin) was most effective in the management of eclampsia a large multicentric randomised trial of 1680 cases was conducted by the Eclampsia Trial Collaborative Group (1955) which concluded that "there is now compelling evidence in favor of Magnesium Sulphate rather than Diazepam or Phenytoin in the treatment of eclampsia".

Maternal Mortality and Eclampsia

Maternal mortality is essentially due to cerebro-vascular accident and other cerebral lesions [*Table. 8(a)*].

Antihypertensive Therapy

Due to the great risk of cerebro-vascular accidents, antihypertensive therapy is the mainstay in reducing maternal mortality.

Immediate reduction of BP is essential if the systolic BP is over 170 mm Hg and the diastolic BP over 110 mm Hg. Hydralazine can be given as

2 mg. I.V. bolus (or 5 mg. I.M injections) and repeated every 15-30 mts. For maintenance therapy 100 mg Hydralizine in 500 ml saline can be titrated to get the desired effect-usually the drip rate is increased by 10 drops every 5 mts. till the diastolic BP is less than 110 mg Hg and the systolic BP is less than 170 mm Hg.

As an alternative 'Labetalol' has also be tried in recent times. A dose of 200 mg. Labetalol can reduce the BP by 10-20 mg Hg in 60 minutes.

Obstetric Management

In severe pre-eclampsia prompt termination of pregnancy may avert the onset of fits, but once eclampsia has occurred the pregnancy must be terminated but the question is when and how 'For many years most Obstetricians practiced conservatism in established eclampsia, controlling the fits first and delivering the patient 24-48 hours after the fits have ceased, by inducing labour or performing caesarian section. Krishna Menon (1961) found that the longer the interval between the first fit and the time of delivery, the higher the mortality, rising from 70% when the interval was 0-2 hours, to 22% when it was 8-12 hours and to 42% when it was over 24 hours [Table 8(b)]. Therefore there is no doubt that earlier the delivery is undertaken, the better it is for the mother and the fetus. The delivery will result in the resolution of the Pre-eclampsia process and hence is of great advantage to the mother. However it may not be optimal for the baby, depending on its maturity and whether it had already been compromised by the process of Pre-eclampsia. If the fetus is over 34 weeks and is mature and alive, C.S. gives it the best chance, if the patient is not in labour, and if the anticipated induction delivery interval is going to be long. If the fetus is immature and / or dead the feasibility of induction and vaginal delivery should be sought However if induction fails early resort to C.S will help to arrest the Pre-eclampsia process.

The associated complication of Eclampsia (and severe Pre-Eclampsia) include :

- Fatal cerebral hemorrhage
- Left ventricular failure
- Status eclampticus
- Respiratory failure
- Aspiration with fits
- Rupture of the Liver
- Abruptio placentae
- Renal impairment / failure
- DIVC / HELLP syndrome
- Hyperpyrexia

Recent advances in management of eclampsia include:

- Use of Nifedipine sublingually for hypertensive crisis, and
- Use of diazepam rectal tube ('STESOLID') for prevention of fits

These are increasingly used in clinical practice, especially when there is difficulty in establishing an I.V line immediately.

- Total paralysis and intermittent ventilation

This can be life-saving under these circumstances:

- when the patient gets repeated fits despite full anti-convulsive therapy
  i.e. status eclampticus
- where despite maximal doses of sedation the patient continues to be restless
- where it is not possible to increase the sedative dose because of respiratory depression, as shown by cyanosis
- when breathing becomes difficult (with sedation) due to laryngeal oedema pre-operatively or after intubation and surgery

Paralysis can be obtained by d-tubocurarine and the patient incubated and ventilated. This is best carried out by the anesthetist preferably in the I.C.U.

Prognostic Factors – Signs of Poor Prognosis

- Fits exceeding 10 in number
- Patient in deep coma between fits
- B.P remains high between fits and exceeds 200 mm.Hg
- Maternal pulse rises and exceeds 120
- Hyperpyrexia
- Moist lungs and cyanosis
- Anuria/oliguria particularly if preceded by a small quantity of blood stained urine
- A falling platelet count (indicating DIC)

The "key" to successful management of eclampsia lies in :

- using a familiar drug regime
- early and aggressive treatment of hypertension, to avoid cerebro-vascular accidents, with peripheral vaso-dilator drugs, and thus avoid mortality.
- Terminating the pregnancy to resolve the crisis and to reduce the mortality
- Managing the patient with an anaesthetist, if it is felt that paralysing and ventilating the patient for 24-48 hours might save her life

Acknowledgement

I thank Mrs.S.Gnanabasharan of my department for secretarial assistance.

Reference

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Table.1 : Type of Eclampsia in 1,151 cases (Krishna Menon, 1961)

	No.of cases	Percent	No.of deaths	Percent
Antepartum	826	71.5	145	17.5
Intra-partum	61	5.5	4	6.5
Post-partum	264	23.0	25	0.3
Total	1151	100.0	174	15.1

Table. 2 : Risk factors in Eclampsia and their identification

Risk Factors	**Tests available**	**Drugs**
History of hypertension Renal disease SLE	Roll over test Angiotensin sensitivity studies	Low dose aspirin as little as 75 mg per day
Past history of pregnancy induced hypertension	Uterine arcuate arterial Blood flow velocity waveform by 20-24 weeks	Magnesium and calcium supplementation reported to be effective
Strong family history of hypertension, diabetes	Angiotension II receptors in platelets in early pregnancy	
Multiple pregnancy In current - pregnancy	Absence of the fall of B.P in the 2nd trimester of pregnancy	

Table. 3

Symptoms	Patients in whom present(%)
Headache	83
Hyperreflexia	80
Proteinuria	80
Oedema	60
Clonus	46
Visual signs	45
Epigastric pain	20

Table. 4 : Anticonvulsant regimes employed in the management of Eclampsia

1	Morphine and chloral	Stroganoff (1930)
2	Tribromethanol ("Avertin")	Dewar and Morris (1947)
3	Sodium Thiopentone (Pentothal)	O' Donel Browne (1950)
4	Veratrum group of drugs	Byrant and Fleming (1940)
5	The "Lytic – Cocktail " Modified "Lytic Cocktail"	Laborit (1950) Krishna Menon (1955 – 1958) Sivasuriya (1974)
6	Magnesium Sulphate	Stringanoff (1930) Pritchard and Stone (1967)
7	Diazepam ("Valium") "Chlordiazepoxide" (Librium)	Lean and Ratnam et. al. (1968)

Table. 5 : The modified lytic cocktail regime – Sivasuriya (1974)

On admission 'with fits' or 'following a fit' concurrent with the first aid measures:

- An I.M injection of a combination of 50 mg pethidine and 50 mg chlorpromazine ('Largactil') is given and repeated every 6 hours.
- The following solutions/drugs were also administered at the same time
  - 50 – 100 ml of 50% dextrose I.V
  - 10 ml of 10% cal.gluconate V slowly
  - ½ Mega unit penicillin I.M and repeated twice a day (12 hourly)
  - 40 – 80 mg Frusemide ('Lasix') I.V. followed with 40 mg every other day or daily depending on the extent of oedema/response
- Either after 3 hours after the initial dose Pethidine-Largactil or earlier (if fits recurred) 3 grains (200 mg) if Sodium phenobarbitone were given I.M and repeated, six hourly, or whenever necessary depending on the level of sedation and the response to treatment.

Table. 6 : Magnesium sulphate regime

- **PRITCHARD (1975)**
  - Immediate dose of 4g I.V as 20 ml 200% solution given over 3-5 minutes
  - Followed by 10g as 10 ml of 50% solution given deep I.M into each buttock
  - The follow up dose is 5g as 5 ml of 50% solution every 4 hr. alternately in each buttock
- **ZUSPAN'S REGIME (1966)**
  - **Primary dose**

    4g – 20 ml 20% solution I.V given over 3-5 minutes
  - Followed by an infusion of 1g every hour

Table. 7 : Effects associated with various serum magnesium levels

Effect	Serum Level m/Eq/Litre
Anti-convulsant prophylaxis	4 - 6
ECG changes	5 - 10
Loss of deep tendon reflexes	10
Respiratory paralysis	15
General anaesthesia	15
Cardiac arrest	> 25

Table. 8(a) : Maternal mortality in the U.K. (1985 – 1987)

	n	%
Pulmonary embolism	29	20.9
Hypertensive disorders	27	19.4
Ectopic pregnancy	16	11.5
APH/PPH	10	7.2
Amniotic fluid embolism	09	6.5
Causes of maternal deaths from hypertensive disease – U.K. (1985 – 1987)		
	n	%
Cerebral hemorrhage	11	41
Other CNS pathology	11	41

Table. 8(b): Convulsion – delivery interval and maternal mortality in eclampsia

First Convulsion and Delivery (HR).	Maternal Mortality (%)
0 - 2	07
2 - 4	13
4 – 8	19
8 - 12	22
12 - 18	25
18 - 24	32
> 24	42
887 cases	17

Convulsion – delivery interval & perinatal mortality in eclampsia

First Convulsion to Delivery (HR)	Perinatal Mortality (%)
6	14
6 – 12	19
12 – 24	62
24	53
88 cases	33