Therapeutic Management of Pre-Eclampsia and Eclampsia in Nigeria

by

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A paper presented to the faculty of The University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Public Health in the Department of Maternal and Child Health.

Chapel Hill, N.C.

April 15, 2011

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Abstract: Pre-eclampsia/eclampsia is the fourth most common cause of maternal mortality worldwide, affecting a disproportionate number of women in developing countries. Nigeria has a maternal mortality ratio (MMR) of 840/100,000 live births and an estimated 10,000 women die from pre-eclampsia/eclampsia annually. Magnesium Sulfate (MgSO4) is proven to reduce the likelihood that pre-eclampsia will progress to eclampsia by 58%, halt ecliptic seizures, and it is likely to reduce risk for maternal mortality related to this disease. A review of the research of pre-eclampsia/eclampsia conducted in Nigeria reflects the gross underuse of MgSO4 as a life-saving therapeutic. Changes in current health policy are needed to improve antenatal care (ANC) services, provider education, and provision of essential medicines to improve maternal-fetal outcomes in Nigeria.
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Problem statement and its relevance to Maternal and Child Health (MCH)

It is well documented that ninety-nine percent of the approximately 350,000 maternal deaths occurring annually worldwide are in low-resourced, developing countries (World Health Organization, WHO, 2011). Over half of the maternal mortality worldwide occurs in six countries: India, Nigeria, Pakistan, Afghanistan, Ethiopia, and Democratic Republic of the Congo (Hogan, et al., 2010). The most common direct causes are post-partum hemorrhage (25%), sepsis (13%), unsafe abortions (13%), pre-eclampsia and eclampsia (12%), and obstructed labor (8%). Between 75 and 50 thousand women are thought to die annually from complications resulting from pre-eclampsia and eclampsia (Ridge, Bero & Hill, 2010; Tukur, 2009; WHO, 2011). Conversely, 3.3 million babies are stillborn annually and approximately 4 million die within the first 28 days of life (Hogberg, 2005). 814,000 neonatal deaths and 1.02 million of these stillbirths are a result of intrapartum complications such as chronic oxygen deprivation (intrauterine hypoxia) and intrauterine growth restriction (IUGR) or other consequent sequelae, such as placenta abruption and poor fetal circulation. These pathological conditions directly result from pre-eclampsia and eclampsia (Turner, 2010; Wall et al., 2010). Pre-eclampsia/eclampsia and uterine rupture are the two conditions which will most often result in the death of mother and baby, often called the double tragedy (Onwuahfua, 2002). Improving health care services related to pre-eclampsia and eclampsia is in direct response to the United Nations Millennium Development Goals (MDG) four and five, which aim to reduce rates of mortality for children (2/3 reduction) and mothers (3/4 reduction) by 2015 (UN Summit, 2000).
Pre-eclampsia and Eclampsia

Pre-eclampsia and eclampsia are vascular, hypertensive disorders specific to pregnancy ranging in severity from mild to fatal. There appears to be no preventive measures for this disease and etiology is variable and determined by gestational age at time of onset (Turner, 2010; Wall et al., 2010). Time of onset is delineated as antepartum (after 20 weeks gestation), intrapartum (during the labor and delivery period) and postpartum (after the delivery of the baby). The disease affects the placenta and maternal multiple-organ systems throughout its course. It is also somewhat unpredictable in that pre-eclampsia is not necessarily a precursor to eclampsia, since about 25% of women will become eclamptic without first having pre-eclampsia symptoms (Duley, Henderson-Smart, Walker, & Chou, 2010). It is likely though that a pregnant woman with a pre-eclampsia diagnosis will progress to eclampsia if left untreated.

Pre-eclampsia is described as tissue edema and high blood pressure, categorized as a systolic blood pressure of >140 mmHg and diastolic blood pressure >90 mmHg, proteinuria (2+ or ≥300mg/24hr), and occurring after 20 weeks gestation, which are all likely to ultimately resolve for the mother at six weeks postpartum given the symptoms remain mild (Turner, 2010). A recent review article published in the International Journal of Women’s Health states disease severity can be determined by “blood pressure, liver dysfunction, and deteriorating neurological status” (Turner, 2010, p. 328).

However, the WHO Safe Motherhood Guidelines set forth in 2008 identify proteinuria coupled with high blood pressure as diagnostic for pre-eclampsia after 20 weeks gestation (WHO, 2008). For the fetus pre-eclampsia problems are evident with placental dysfunction and poor fetal circulation. The placenta functions as the conduit for oxygen
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and nutrients to the growing fetus. Disturbance of adequate blood flow to the fetus through the placenta often leads to intrauterine growth restriction (IUGR) and a low birth weight baby.

Severe pre-eclampsia is observed as systolic blood pressure $\geq 160$mmHg and diastolic blood pressure $\geq 110$ mmHg, nephrotic-range proteinuria (>3.5g/24hr), headache, visual disturbances, upper abdominal pain, oliguria (low urine output), hyperreflexia, pulmonary edema, and central nervous system and liver dysfunction (Turner, 2010; WHO, 2008). Also, it can cause placental abruption, when the placenta detaches from the uterine wall, and HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets). Placenta abruption requires careful monitoring and likely cesarean delivery if the mother and baby do not stabilize. The characteristics of HELLP syndrome are enlarged liver, liver bleeding and elevated blood pressure. This condition is sometimes fatal and occurs in 10-20% of women who have severe pre-eclampsia or eclampsia (Sabai, 2007).

Eclampsia is marked by the symptoms for severe pre-eclampsia with the addition of convulsive seizures, hemorrhage, and coma often leading to fatal maternal and neonatal outcomes. As stated in the 2005 WHO midwifery education module “Managing eclampsia” the second and third stages of eclampsia are referred to as the tonic and clonic stages. The tonic stage characteristics include violent muscle spasms, rigid limbs, decreased breathing, bulging eyes, an arched back and clenched teeth. The clonic state refers to severe contraction and relaxation of muscles, foaming at the mouth, labored breathing and a swollen purplish face (WHO, 2008). Likely, with the onset of eclampsia there is systemic capillary and vascular damage caused by high blood pressure. Cerebral
edema results from an influx of red blood cells and blood plasma in the perivascular space in the brain tissue. This leads to ischemia (vascular blockage) and infarction in the brain, leading then to the neurological trauma and seizures (Okafur & Efetie, 2008). Delivery of the baby and the placenta is the only known effective treatment for life threatening severe pre-eclampsia and eclampsia (Churchill & Duley, 2002; Druzin, Charles, & Johnson, 2008). Onset and progression of the disorder are highly variable thus consistent monitoring and therapeutic care of a patient suspected of having pre-eclampsia or eclampsia are necessary to avoid poor outcomes.

Significance of pre-eclampsia and eclampsia in Nigeria

It is estimated that pre-eclampsia and eclampsia causes 10-15% of maternal morbidity in the developing world, and accounts for as much as 40% of maternal deaths in some countries (Turner, 2010; WHO, 2005). Okafor and Efetie (2008) report eclampsia as the most common cause of maternal mortality in northern regions of Nigeria, which is known to be rural and isolated; and eclampsia contributes significantly to maternal demise in the southern region. Nigeria has the highest population of African countries, with 158 million people (CIA World Factbook). Nigerian women also suffer from the highest maternal mortality ratios (MMR), reported by the WHO in 2008 as 840 maternal deaths per 100,000 live births, which is put into perspective when compared to the U.S. MMR of 24/100,000 live births. In 2008 the neonatal mortality ratio (NMR) in Nigeria was 49/1000 live births (World Health Statistics, WHO 2010). In the U.S. the NMR was approximately 4.5/1000 live births according to Center for Disease Control and Prevention and the U.S. Department of Health and Human Services.
Management of pre-eclampsia and eclampsia

The World Health Organization (WHO) has published guidelines and education modules for nurses and midwives for the immediate management of pre-eclampsia and eclampsia in under-resourced settings (WHO, 2005). However, without adequate antenatal care (ANC) and early presentation at the onset of symptoms poor outcomes are likely. Often the opportunity to provide anti-hypertension therapy is missed because of the lack of antenatal care or what is commonly referred to as the unbooked patient (Tukur, 2009). The unbooked patient has no formal medical home and is often seen by contemporary health care providers for the first time in cases of emergency. ANC that incorporates health education and proper blood pressure screening will ensure that onset and progression of disease are either diverted or properly managed. Management at the onset of uncontrolled hypertension using anti-hypertensive medications such as nifedipine, hydralazine, and methyldopa will regulate blood pressure to safe levels, with the intent of preventing disease progression to severe pre-eclampsia or eclampsia.

Therapy for preventing or halting convulsive seizures using magnesium sulfate (MgSO4) is standard of care in the U.S. and is recognized by the WHO as the preferred method of treatment. Other common therapies in under-resourced settings are diazepam (valium), phenytoin (anticonvulsant), and lytic cocktail (mixture of chlorpromazine, promethazine and pethidine), yet resolution of the disease lies in delivery of the fetus and placenta regardless of gestational age.

Diazepam is currently most often used to treat eclampsia in all regions of Nigeria. It began use as an anti-convulsant treatment for eclampsia in the 1960s (Lean 1968). A team of researchers led by Lelia Duley has done extensive research over the past twenty
years on MgSO4 compared to other therapeutics for eclampsia. They have proven it to be the most effective and safest therapy for treating eclampsia. In regards to the historical and continued popularity and use of diazepam they explain, “Diazepam is a core medicine in the World Health Organization’s ’Essential Drugs List’, which is a list of minimum medical needs for a basic healthcare system, and has been one of the most frequently prescribed medications in the world for the past 40 years. This wide availability probably contributed to its initial acceptance as a treatment for women with eclampsia. Treatment with diazepam usually includes a loading dose of 40mg by intravenous injection, followed by an infusion of 20mg diluted in 500 ml. This infusion is titrated against the level of sedation, with the aim of keeping the woman drowsy but rousable.” (Duley, Henderson-Smart, Walker, & Chous, 2010 p. 4).

They also explain the two common dosing regimens of MgSO4, named after Drs. Pritchard and Zuspan. The Pritchard regimen is characterized as an initial loading dose of 14 grams: intravenous loading dose of 4 grams and 10 grams by intramuscular injection. This is followed for 24 hours by 5 grams intramuscular injection every 4 hours (Pritchard, 1955). The Zuspan regimen is an initial intravenous loading dose of 4 grams, and followed by maintenance intravenous infusions of 1 gram per hour for 24 hours (Zuspan, 1978). There is some concern with toxicity of MgSO4 and so monitoring is needed when administering this therapy. Signs of toxicity include: patellar reflex loss, respiratory paralysis, renal failure and thus monitoring for tendon reflexivity and respiration is sufficient as indications to reduce dosing (Duley, Henderson-Smart, Walker, & Chous, 2010). MgSO4 is found to be safe, effective, and inexpensive as reported from within the Nigerian research community at $.35/dose (Ladipo, 2009).
Ideally, delivery is delayed through expectant care, i.e. treating the symptoms of the disease to allow fetal lung maturity and viability when possible. However in low-resource settings a host of factors often prohibit emergency cesarean delivery, provision of effective therapeutics and conservative expectant management, and adequate monitoring complemented by intensive nursing care (Hunyinbo, Fawole, Sotiloye & Otolorin, 2008; Lombaard, Pattinson, Backer, & Macdonald, 2005).

The relevance of MgSO4 to maternal morbidity and mortality will be discussed throughout this paper, with attention given to the current poor status of women’s health in Nigeria due to this disease. The trends in therapeutic management of pre-eclampsia and eclampsia in Nigeria are discussed using a review of the available research data specific to management practices in this West African country.

Search strategy including criteria for selection of articles

Articles were chosen that: (1) reported therapeutics related to pre-eclampsia and eclampsia; (2) were published in peer-reviewed journals in English between 2000 and 2011, although the research may have been conducted prior to 2000; (3) the research was conducted in African institutions, (4) and reported on the general African population and specifically Nigerian populations. Nigeria was selected because the initial search revealed more published articles for this country in the last ten years than other sub-Saharan African countries. Also, the current status of disease management in Nigeria is significant because it has one of the highest rates of maternal mortality due to pre-eclampsia and eclampsia worldwide, approximately 30% (Tukur, 2009; Ikechebelu & Okoli, 2002).
Literature Search and Retrieval Process

PubMed, Web of Science, African Index Medicus and the WHO database were resources used. MeSH search terms included: pre-eclampsia, eclampsia, therapy, therapeutics, magnesium sulfate, diazepam, phenytoin, lytic cocktail, randomized control trial, Africa, and Nigeria. These terms were joined as needed to produce desired results. Then a hand search was done of the reference lists of research articles and reviews to cross check the articles collected. The article review spanned 2000 to 2011. The articles where then categorized by geographic location within sub-Saharan Africa and therapy. The inclusion criteria for articles in this review are as follows: a description of a specific management strategy was provided to a Nigerian geographical sub-population, and a review of outcomes based on a management strategy.

To rate quality of individual articles, the author independently reviewed each article. The method of review was based upon a 12 point checklist (Appendix A) for critical reading of medical literature. A limitation of this review is that there were not randomized controlled trials (RCTs) available within the timeframe of the review and the geographical region chosen. It has been documented that there is a paucity of clinical research in developing countries that uses the gold standard RCT format and is rigorous and consistent (Daniels, Lewin, & Practice Policy Group, 2008; Lavis, Davies et al., 2005). Identified for this review were one prospective case control study and seven retrospective chart reviews as relevant to specific management criteria. With plans for a meta-analysis the author adapted the approach described by West et al. (2002). That system incorporates: (1) quality of the individual studies as assessed by examination of a
checklist of specific elements of study design and conduct; (2) quantity of relevant studies identified; and (3) consistency of findings.

Subsequently, papers regarding management of pre-eclampsia and eclampsia were reviewed for 1. presence of disease, 2. administration of therapeutic for disease, 3. effect of therapeutic treatment on maternal health, and 4. effect of therapeutic treatment on neonatal health. Again, since no RCTs were found during the search that would compare treatment and therapeutic management options within this population, this literature review is a reflection of the lack of rigorous research and information dissemination underway in Nigeria to date. It does, however, reflect outcomes based on current practice as reported within secondary and tertiary health care facilities in the country.

**Critical review of the selected literature**

Eight articles were chosen for review and discussion. All of the selected studies were conducted in a Nigerian research setting. Seven are retrospective chart reviews and one is a prospective case-control study. All of the articles combined cover a time span from 1994-2007. Appendix B describes the location and type of study, therapeutics and observations, and outcomes. This author will discuss the articles chosen for review in chronological order, from oldest to most recently published.

The first is the only prospective case-control study identified, and the only study focusing on antepartum, second trimester, and timing of onset of disease: *Conservative management of early-onset pre-eclampsia and fetomaternal outcome in Nigerians*, Onah, H.E. and Iloabachie, G.C., 2002. The purpose of the study was to compare maternal-fetal
outcomes of patients with disease onset before 30 weeks gestation to the same outcomes for patients with onset after 30 weeks gestation in the presence of conservative management (monitoring and medication). The authors directly hypothesize that the conservative versus aggressive management (surgery or labor induction) of disease in the second trimester would result in more favorable maternal-fetal outcomes.

Using the criteria set forth by Schulz and Grimes (2006) for assessing scientific rigor in case-control studies it was noted that all consecutive cases presenting at the University of Nigeria Teaching Hospital in Enugu were included. “Hypertension was defined as persistent sitting blood pressure of 140/90mmHg or greater using Korotkoff phase V [sounds]” (p. 357). Pure preeclampsia was defined as hypertension combined with proteinuria in a previously normotensive patient, and super-imposed pre-eclampsia occurred in a patient with prior history of hypertension coupled with proteinuria. Confounding between the two groups was not addressed.

749 pre-eclamptics were included in the study group from 1995-2000. Of those, 23% (175) were enrolled before 30 weeks gestation, becoming the case group while the remaining 77% (574) served as the control group with onset of disease after 30 weeks gestation. Of the cases, 91 had pure pre-eclampsia and 84 had superimposed pre-eclampsia. 21 (12%) cases developed eclampsia of which 7 died, and 98 (17%) controls developed eclampsia of which 7 died. Conservative management for all participants was listed as: bed rest, anti-hypertensive medication (methyldopa or hydralazine) as needed, and diazepam for seizures. The regimen for antepartum hypertensive medication was oral alpha-methyldopa and hydralazine infusion 40mg/L of 5% dextrose in water with onset of pre-eclampsia. Blood pressure goal in the absence of labor was 140/90
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to 150/100 mmHg. In the antepartum case group delivery was delayed for as long as maternal-fetal risk did not warrant intervention. For the control group the gestational age at onset likely fell past the 34th week gestation and delivery was not delayed. The mean gestational age for onset in the case group was 24.2 ± 3.5 (SD) weeks with delivery at average 33.0 ± 5.0 weeks; and the mean gestational age at onset for the control group as 35.9 ± 3.0 weeks and delivery at 36.9 ± 3.0 weeks.

In the cases and controls, other causes of death were renal failure, HELLP syndrome, anesthesia accidents, placental abruption and cerebro-vascular event. MMR for cases and controls combined was 5600/100,000 (42 deaths). The control group saw twice the maternal mortality than the early onset, case group. Nearly half of the women enrolled in each arm of the study delivered via cesarean section most often due to imminent eclampsia and a failure of ripening of the cervix. Neonatal results are as follows: mortality rate for combined study arms was 272/1000. Due to low birth weight and preterm deliveries the case study group diagnosed with pre-eclampsia prior to 30 weeks experienced higher incidence of mortality (48.3% compared to 20.8% of controls).

This article concludes that conservative management at the early onset of preeclampsia is related to better neonatal outcomes, but less favorable maternal outcomes. The incidence in the early onset group was almost twice that of the late onset group. The authors cite an increase in MMR in Nigeria in the past 20 years. They say MMR rose in their health care facility from 270/100,000 to 1406/100,000 between 1976 and 2000. This is attributable, according to this article, to the rise in prevalence of pre-eclampsia and eclampsia coupled with a lack of ANC and the continued inadequate supply of MgSO4 to manage these patients. They also found longer decision-
intervention intervals contributed to the higher mortality rate. Decision time increased an average of 1.5 hours to 6 hours because of hospital policy change and worker dissatisfaction (Onah, 2002).

Second is Review of eclampsia at the Nnamdi Azikiwe University Teaching Hospital, Nnewi (January 1996-December 2000), Ikechebelu, J.I. and Okoli, C.C. 2002. MMR for this hospital during these years was listed as 330/100,000. This five-year retrospective review of 43 cases of eclampsia compared age, parity, booking status, the gestational age and blood pressure at onset of seizures, treatment regimen, and mode of delivery. An eclampsia diagnosis was determined by tonic-clonic convulsions. Briefly, the investigators found at this hospital that 32.6% were young (21-25 year-old), first time mothers (65%), who had received no ANC (83.7%) were more likely to have eclampsia in the antepartum period (55.8%) and delivery via cesarean (85.7%). Diazepam was the anticonvulsant used in all cases. 9.3% (4) of the cases resulted in maternal death. Incidence for eclampsia in this hospital accounted for 0.75% of deliveries. Neonatal mortality was 16.3% of charts reviewed (7 deaths). Two of those babies died at the hospital (low birth weight and asphyxia) and five died before the woman reached the hospital for care. Within the discussion this study further compares eclampsia mortality rates across regions of Nigeria. They compared their institution’s 0.75% (43/5750) eclampsia incidence as similar to Lagos and Ibadan in the southern coastal region of Nigeria; and higher than Enugu (0.29%) and Benin City (0.46%). They also compared age, parity, booking status, and gestational age at onset with other areas of Nigeria. All comparisons were similar except for in Ile-Ife where the majority of eclamptic convulsions occurred intrapartum rather than antepartum.
The authors report their study period as an unstable time for the public health care system in the Nnewi region in which residents were opting for private specialist care resulting in fewer deliveries and referrals and therefore lowering the overall incidence for this study. This study acknowledges that MgSO4 is not available in this hospital and that it is a superior option to diazepam. They noted a lack of prostaglandin pessaries for aid in cervical ripening as a cause of high mortality, morbidity and cesarean outcomes. These authors recommend patient education, provision of management protocols for use and routine review, and infrastructure improvement to increase access to care for women in the region to prevent incidence of morbidity and mortality from eclampsia (Ikechebelu & Okoli, 2002).

Third is, *Pregnancy outcomes of women with eclampsia in Gombe, Nigeria*, Melah, G.S. Massa, A.A., and El-Nafaty, A.U., 2005. Gombe is in the rural northeastern part of Nigeria where eclampsia is the number one cause of maternal death. Modern ANC services are not widely available or accepted in the area. Researchers hypothesize that eclampsia is preventable in women who receive ANC, and thus reviewed medical charts of women with eclampsia from January 1997 to December 2000. This study aimed to assess age, parity, booking status, and pregnancy outcomes of women with the diagnosis. 67.8% of those diagnosed were teen-aged, and 79.8% were first time mothers. The eclampsia incidence at this hospital was 3.7% (438/11,986). MMR was 2058/100,000 (47 of 228 maternal deaths due to eclampsia). Eight women died undelivered. Vaginal deliveries were 51.0% due to presentation while in labor. Neonatal mortality due to eclampsia was 2023/100,000 (157 infants), with the following outcomes: preterm, intrauterine fetal demise (IUFD) and low birth-weight. Disease management
was not specifically noted other than stating that MgSO4 is not available in the labor and delivery unit, and that if it were available the incidence of maternal mortality would be significantly reduced. The study indicates that warning signs leading up to the first seizure were present in 91% of cases, which implies the probability for a pre-eclampsia diagnosis and course of treatment had these patients received ANC. Maternal fatality rate was 10.7% (Melah, Massa, & El-Nafaty, 2005).

Fourth, Eclampsia: ten-years of experience in a rural tertiary hospital in the Niger delta, Nigeria, Igberase, G.O., and Ebeigbe, P. N., 2006. This retrospective chart review covered cases from January 1994 - December 2003. The setting was a rural tertiary medical center serving the (south central) Nigerian Delta catchment area for more than half a century. The authors set out to assess a pattern of clinical presentation and maternal-fetal outcomes in a rural hospital setting, they referred to this as ‘highlighting the peculiarities of the experience of eclampsia in rural areas” in order to improve care (p. 414). Specific to this hospital is that it provides specialist in-patient and out-patient OB/GYN, pediatrics, and internal medicine services (p415). Upon intake of an eclamptic patient, this facility utilizes pulse oximetry, oxygen facemasks, and claims to have used MgSO4 for treating eclamptic seizures for the past fifteen years. The protocol for diagnosing eclampsia is clearly stated as using the Pritchard method (tendon reflex, urine output, respiratory rate, and hydralazine and nifedipine to control hypertension.

Eclampsia occurred in 2.3% (123 cases) of the 5,242 deliveries during the ten-year period, there were 19 maternal deaths – acute renal failure was listed as the primary cause of death. Neonatal mortality was 195/1,000 live births (24 deaths). This study reports their eclampsia rates to be more than 40 times the incidence in developed countries (p.
The women who presented in this study were mostly seen by a traditional birth attendant and brought to the hospital for eclamptic seizure. Eighty-two delivered via cesarean section, 31 vaginal delivery and 10 assisted delivery.

Patterns are described as being in agreement or disagreement with other study findings in other regions of Nigeria is as follows: authors claim a higher incidence of disease for this review compared to urban centers in Nigeria. This is attributable to access-to-care issues and more common use of traditional birth attendants (46% of women use a traditional birth attendant in this region). 80% of women were unbooked for ANC and it took over 12 hours from first seizure for 48% of the women to get to the hospital, which accounts for 66% delivering via cesarean section. There appear to have been prior symptoms of disease in 75% of women in this study. The lack of ANC which would include provider supervision and patient education contributed to this lack of early intervention. As consistent with other studies young, unbooked, primigravida women who seized prior to laboring (antepartum) were the most commonly affected group in this study. They reported the MgSO4 had not reduced the cesarean rate since it is the same as other Nigerian hospitals using diazepam, and MgSO4 use did not improved neonatal outcomes. Maternal case fatality rate was 15.4% consistent with others reported in Nigeria between 9 and 17 %. Maternal death most often resulted from renal and cardiopulmonary failure. Conversely, neonatal death resulted from preterm, asphyxia and sepsis. The use of MgSO4 cannot be identified as protective in this study due to late presentation for care. Authors’ recommend traditional birth attendant integration into formalized health services delivery (Igberase, & Ebeigbe, 2006).
Fifth, is Critical care management of eclamptics: challenges in an African setting, Okafor, U.V. and Efetie, R.E., 2008. This retrospective study focuses on the management and outcomes for eclampsia patients admitted to an intensive care unit (ICU) unit in a referral hospital in Abuja, the capital city of Nigeria. Medical chart abstraction on 38 (32 unbooked) ICU records was done between November 2001 and April 2005 for eclamptic patients. Patient demographics, booking status, parity and gestational age at delivery and at onset of seizures were documented. All patients were admitted to the ICU unit postpartum, however 20 had onset antepartum, six intrapartum and 12 postpartum. Average age of patients was 28 years (range 17-40). Twenty-three patients were first time mothers. Twenty-nine delivered via cesarean section and nine delivered vaginally. Diazepam was used to control seizures – except for one patient who received MgSO4 due to its recent availability. Hydralazine was used to control high blood pressure.

This facility had airway management via intubation equipment. The following monitoring measures are documented: electrocardiograph (ECG), pulse oximeter, blood-pressure, temperature, urine output and capnography, which measure carbon dioxide (CO2) production. Criteria for admission were seizure frequency, arterial oxygen saturation, and Glasgow coma scale (GCS). Atracurium or pancuronium was used for long term neuromuscular blockage as available and dependent upon the patient’s blood pressure. Outcomes were as follows: there were 11 maternal deaths (case fatality rate of 29%). 45% (17) patients were put on ventilation due to the respiratory depressive action of the diazepam sedation which lowered the GCS scores.
Authors estimate MgSO4 in lieu of diazepam would decrease the instances and need for mechanical ventilation assistance in eclamptic patients, and prevent pre-eclampsia from progressing to eclampsia. Authors attribute the death rate to use of diazepam, late management of disease, and lack of ANC. Also blamed is a lack of direct invasive arterial and venous blood pressure monitoring equipment in this ICU. Poverty and a lack of ICUs and anesthetists are noted as the cause of maternal deaths in this country (Okafor, & Efetie, 2008).

The sixth article is Anesthetic management of patients with pre-eclampsia/eclampsia and perinatal outcome, Okafor, U.V., Efetie, E.R., Igwe, W., and Okenzie, O. 2009. This study was done in a teaching hospital in Enugu. It is another retrospective chart review (1998-2006). The purpose of this study was to look at risk factors for neonatal mortality associated with anesthesia for cesarean delivery in patients with a preeclampsia or eclampsia diagnosis. Charts were reviewed for patients diagnosed with pre-eclampsia and eclampsia, for mode of delivery and outcomes specific for cesarean section. Pre-eclampsia was defined as pregnancy induced hypertension with proteinuria ≥300mg/24hour after 20 weeks gestation. Perinatal mortality in this article refers fetal demise and neonatal death within seven days postpartum. Outcomes were stillbirth, neonatal death, maternal mortality and anesthesia type. 285 women had preeclampsia/eclampsia diagnoses. 196 of the pre-eclamptic and eclamptic women delivered via cesarean. This article specifically states that a protocol for prophylactic MgSO4 is present, but because of cost (to the patient) and availability, it is not frequently used. However, the authors’ claim that a recent donation from an unnamed source of MgSO4 has ramped up use. Of the sedated patients there were 157 under general
anesthesia, 24 under spinal anesthesia, and 5 under epidural anesthesia. This study did not report on maternal morbidity, but suggested a ‘drastic’ improvement at this center attributed to improved anesthesia care. There were 19 still births and 19 perinatal deaths (PMR 180/100,000), 30 occurring under general anesthesia. Authors attribute the PMR to lack of ANC and underuse of MgSO4. They address the side effects of diazepam on the neonate referring to it as ‘neonatal withdrawal’. These withdrawal symptoms include: hypertonia, hyperreflexia, restlessness, irritability, abnormal sleep patterns, inconsolable crying, tremors or jerking of arms and legs, bradycardia, cyanosis, sucking difficulties, apnea, aspiration of milk, diarrhea, vomiting and growth restriction. These symptoms are known to last up to 3 weeks postpartum – and sometimes months. This study suggests regional anesthesia, which is spinal or epidural, to produce improved neonatal outcomes when a cesarean is needed to address pre-eclampsia and eclampsia (Okafor, Efetie, Igwe, & Okenzie, 2009).

The seventh article in this literature review is, A 5-year review of maternal mortality associated with eclampsia in a tertiary institution in northern Nigeria, Kullima A.A., Kawuwa, M.B., Audu, B.M., Usman, H., Geidam, A.D., 2009. This review spans from 2003-2007 for eclampsia related deaths in Federal Medical Centre Nguru; Nguru State borders Niger. The purpose of this study was to see if the incidence of maternal mortality from eclampsia is associated with the social demographics of patients. Outcomes were for mortality, time of eclampsia, mode and place of delivery, socio-demographics, and neonatal outcome. Fifty-two records of women who died from eclampsia were analyzed representing 46.4% of maternal deaths over the five year period. This study listed the eclampsia related maternal mortality ratio as 1322/100,000.
Maternal case fatality was 22.3%, which was higher than other parts of Nigeria: Benin (10.7%), Gombe (11.6%), Ukpoma (15.4%), and Jos (16.9%). About half of the 52 maternal deaths occurred in antepartum cases; intrapartum was 34.6% and postpartum was 15.4%. Of those who died there were nine cesarean sections, 15 assisted deliveries, and 17 vaginal deliveries. Eleven women died undelivered. Of the 52 maternal deaths 51 were illiterate and 49 did not receive ANC. Excluding the 11 mothers who died undelivered, of the 41 remaining mothers 23 babies lived and 18 were still born.

There were a total of 224 managed cases of eclampsia reported, 80.5% delivered at the hospital. Of those 224 women 194 were illiterate and 204 did not receive ANC. Neonatal prognosis was better at antepartum diagnosis because cesarean section was possible at this tertiary facility. However, women with an eclampsia diagnosis in the antepartum stage were more likely to succumb to the disease. Diazepam was the anticonvulsant prescribed in all cases. Attributable to the high MMR in this rural northern region of Nigeria are a lack of access to emergency obstetrical care and a paucity of skilled birth attendants (Kullima, Kawuwa, Audu, Usman, & Geidam, 2009).

Last in the review is, Management of eclampsia at AKTH: before and after magnesium sulphate, Tukur, J., and Muhammad, Z., 2010. This article reviews patient records for women who delivered at Aminu Kano Teaching Hospital (AKTH) in Kano, Nigeria from January 2002- December 2004 and December 2005-December 2007 constituting the ‘before’ and ‘after’ portions of this review. Kano is located in north central Nigeria. The goal was to compare the influence of MgSO4 and diazepam on maternal outcomes. 131 maternal medical charts were reviewed out of 163 cases of eclampsia during the time period of interest. Outcomes of interest were MMR, PMR,
Apgar scores at 1 and 5 minutes, toxic effects of MgSO4, time of presentation and booking status. Thirty-eight women with an eclampsia diagnosis received diazepam, 15 (39%) of which died. 93 eclamptics received MgSO4 as treatment after it became available, 14 (15%) of which died. This was statistically significant for use of MgSO4 to reduce MMR. Total PMR was 312/1000 live births (41). The difference for PMR between the two therapies was not statistically significant; PMR for diazepam: 368/1000 and for MgSO4: 297/1000 live births. For comparing Apgar scores between the two groups the authors reported Apgar scores of six or less at one minute in 80.2% of diazepam cases and 94.7% of MgSO4 cases, and at five minutes the 6 or less in 46.2% of diazepam cases and 57.9% of MgSO4 cases. Infants in the diazepam group were likely affected by sedative properties of the drug and thus demonstrated more negative scores. Toxicity of MgSO4 was not described in detail; however, toxicity was reported as seven with renal complications and one with respiratory complications, and the outcomes were not given. Delay of care of more than 6 hours from onset of the first seizure played a significant role in maternal deaths. Out of a total of 29 deaths 25 delayed care and 4 did not delay care. The authors conclude this study is in agreement with other research in determining the MgSO4 improves maternal outcomes for eclampsia (Tukur, Muhammad, 2010).

**Interpretation of findings**

This review is meaningful for two reasons. First, within this review of Nigerian generated research articles six cite the lack of MgSO4 as a cause of elevated MMR; and one article demonstrates by comparison that MgSO4 produces lower MMR than
diazepam. There is long standing evidence from the multi-country RCT, the Magpie trial, released in 1995, and subsequent Cochrane Reviews establishing **MgSO4 as the most effective, inexpensive treatment for ceasing eclamptic seizures and protection against the progression of pre-eclampsia to eclampsia** (Woelk et al., 2009; The Eclampsia Trial Collaborative, 1995; Altman et al., 2002; Duley, Gulmezoglu, Henderson-Smart, & Chou, 2010; Duley & Henderson-Smart, 2003a; Duley & Henderson-Smart, 2003b; Duley, 2005). Second, is that it reflects a portion of continuous reports and reviews over the past 15 years that have focused on the unavailability and under use of MgSO4 therapy in Nigeria. There appears to be no significant changes in practice happening today as reported by Langer (2008), “Although magnesium sulfate has been the standard treatment in developed countries for 20 years, less effective and higher-risk drugs (eg, diazepam and phenytoin) are still widely used in most developing countries.” (Adewole, 2000; Langer, Villar, Tell, Kim, & Kennedy, 2008; Tukur, 2009).

Five of the studies gave diazepam as the anticonvulsant used to treat eclamptic patients. One stated the absence of MgSO4 as a lifesaving therapy, but did not list the anticonvulsant used. And one review completed in 2002 in southern central Nigeria stated, “Diazepam has remained the most popular regimen in the management of eclamptic fits in our hospital. It also appears to enjoy wide acceptability in other centres in Nigeria. Other regimes such as lytic cocktail, phenytoin and magnesium sulphate are not popular” (Ikechebelu & Okoli, 2002, p. 289). This is problematic because of the proven superiority of MgSO4 as management of pre-eclampsia and eclampsia. Duley, Henderson-Smart, Walker, & Chou (2010) reviewed seven RCTs, involving 1396
women. They found that for women with eclampsia, “using MgSO4 rather than diazepam reduces the [risk ratio] RR of maternal death by 41% (95% CI 8% to 62%) and of recurrence of seizures by 57% (95% CI 45% to 67%)” (p.12). Their review also reported better neonatal outcomes with better Apgar scores for babies using MgSO4 than with diazepam; however there were insignificant changes to admissions to a NICU, but the MgSO4 group had a <7day length of stay, fewer than the diazepam group.

Effectiveness of MgSO4 in developing, sub-Saharan African countries was shown with the inclusion of Mozambique, South Africa and Zimbabwe in the Magpie Trial. MgSO4 was proven to reduce risk of eclampsia by more than half (58%) and save maternal lives with relatively low incidence of mild side effects (headache, nausea and vomiting), which were reported in 25% of the women who participated (Duley, Henderson-Smart, Walker, & Chou, 2010; Altman et al., 2002). The articles chosen for review suggest that researchers in academic settings and providers in public hospitals in Nigeria are well aware of the superior therapeutic effects of MgSO4. There is an ongoing need for consistent provision of the first line, effective therapeutic MgSO4 for prevention of disease.

Five of the eight articles stress the importance of ANC to promote identification and proper referral and reduce the number of obstetric emergencies related to pre-eclampsia and eclampsia which lead to maternal-fetal morbidity and mortality. In Nigeria, three in five births (62%) occur at home (see Figure 1). MEASURE
Demographic Health Survey defines ANC as obstetric care “provided by a skilled health worker [which] enables: 1) early detection of complications and prompt treatment (e.g., detection and treatment of sexually transmitted infections); 2) prevention of diseases through immunization and micronutrient supplementation; 3) birth preparedness and complication readiness; and; 4) health promotion and disease prevention through health messages and counseling of pregnant women” (NPC & ICF Macro, 2009 p. 125).

Also, significant to this review is the understanding that no single improvement will change the high incidence of maternal-fetal mortality in Nigeria related to pre-eclampsia and eclampsia. In the past five years MMR has dropped by nearly 150,000 cases worldwide, but has only decreased by 92/100,000 deaths in Nigeria, according to a recent review comparing MMR in 181 countries (Hogan et al., 2010).

**Policy implications/recommendations and significance for MCH**

In order to make a significant improvement in Nigeria in maternal and neonatal morbidity and mortality related to the management of pre-eclampsia and eclampsia an assessment of the health care system and pharmaceutical market in Nigeria is needed. Also, the involvement of stakeholders with decision-making power, such as government health officials; those with funding, such as NGOs and bilateral and multilateral agencies; and those with clinical responsibilities, such as clinician-researchers, medical officers and traditional birth attendants will initiate change in current practice. Fostering alliances between providers and policy makers within the Nigerian states requires careful consideration and cultural competence, since there are 37 states divided into 774 local governments (Ladipo, 2009). Also, facilitating the identification of barriers between
practice and evidence-based medicine with the appropriate authority and stake-holders requires diplomacy, but is an effective catalyst for change. The pyramid (Figure 2) demonstrates that assessment of Nigeria’s health care infrastructure, health professionals and continued monitoring is essential to make way for use of life saving interventions like MgSO4 that are not the current standard of practice. This framework was identified by the Adverting Maternal Death and Disability Program (AMDD) as essential components to improving health services delivery (AMDD, 2010). Seven strategic steps are identified as precursors to development of community capacity to generate this change.

The first step of assessment for the implementation of new practices and policies is building alliances among stakeholders. Stakeholders need to identify the baseline of evidence-based practice culture in the health care sector in order to begin the process of changing it (Woelk, 2009). Second, is to determine the extent to which the political environment is receptive to the creation and enforcement of public health policy. A few examples of recent policy in Nigeria include: Reproductive Health Commodity Security Strategic Plan (RHCS plan2003); the Road Map for Accelerating
the Attainment of the MDGs Related to Maternal and Newborn Health in Nigeria, 2005; and Integrated Maternal, Newborn and Child Health Strategy, 2007 as reported by Ladipo in a 2009 conference presentation in Nigeria. Detailed information regarding these policies is not readily available. It may be that these recent policies address the use of MgSO4, which would reflect progressive movement.

As a part of relationship cultivation, inquiry and discussion of these policies is required. In the interest of increased provision and use of MgSO4, policies related to health professional education standards, task shifting and pharmaceutical attainment and allocation are sought. In this vein, to increase MgSO4 use stakeholders must appeal to the Nigerian Federal Ministry of Health to re-evaluate the status of drugs on the Nigerian formulary list. They must lobby for MgSO4 availability in tertiary health care centers and village dispensaries.

**Third is assessment of health care facilities within each state.** The Adverting Maternal Death and Disability Program (AMDD) affiliated with Columbia University has published an emergency obstetric care (EmOC) needs assessment field guide and data collection modules in response to the need to improve health systems in developing countries. These modules cover

<table>
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<th>Basic EmOC include:</th>
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<td>Treatment for sepsis</td>
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<td>Treatment for eclampsia</td>
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<tr>
<td>Treatment for prolonged or obstructed labor</td>
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<tr>
<td>Post-abortion care (PAC)</td>
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<td>Treatment for incomplete miscarriage</td>
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<tr>
<td>Removal of the placenta</td>
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<tr>
<td>Assisted delivery using forcepsor suction</td>
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<tr>
<th>Comprehensive EmOC services include the services listed above, and also:</th>
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<tr>
<td>Surgery (specifically, Caesarean section)</td>
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<tr>
<td>Anesthesia</td>
</tr>
<tr>
<td>Safe blood transfusion observing universal HIV</td>
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</table>

![Figure 3. Emergency Obstetric Care](image-url)
Identification of Facility and Infrastructure; Human Resources; Essential Drugs, Equipment, and Supplies; EmOC Signal Functions and Other Essential Services; Provider Knowledge and; Cesarean Delivery Review; and a Maternal Death Review (AMDD, 2010). These validated data collection instruments will take a current snapshot of facilities to further demonstrate gaps in care for women with pre-eclampsia and eclampsia and other obstetric complications in each Nigerian state (WHO, 2009). This information can be compared and supplemented by a similar 2003 report of health facilities in 12 Nigerian states where 4.2% of health care facilities met the Basic Essential Obstetric Care (BEOC) and 1.2% met Comprehensive Essential Obstetric Care (CEOC) criteria (see Figure 3) (Fatusi & Iiadunola, 2003; Raise Initiative, 2007).

Fourth is understanding the complex motivations of health care providers and the factors that may influence use or demand for MgSO4, which seem to stem from historical drug access, experience-based practice, cost, and fear of side effects (Sevone et al., 2005; Laing, 2003). A paper recently presented at the 2009 Nigerian National Health Conference by M.S.I Ohuabunwa addresses the challenges of essential drug availability in the country. Dr. Ohuabunwa sites corruption, poverty, budgetary restrictions, and a poorly supported pharmaceutical industry as the reasons for lack of appropriate therapeutics such as MgSO4. He explains that once drugs reach clinics and pharmacies they are pocketed or re-sold; also, that competition with India and China make it difficult for national pharmaceutical companies to thrive. This is true especially in an inadequate industrial environment as is the case in Nigeria. Ohuabunwa faults recent World Trade Organization (WTO) policy for making Nigeria an open door for pharma trade and the influx of fake drugs (Ohuabunwa, 2009). Moreover, a study of perinatal care providers
lack of use of evidence-based reproductive health interventions in neighboring Cameroon suggests the provider related barriers are: a lack of continued medical education (CME), inadequate formal training, insufficient access to learning resources e.g., journals, newsletters, and data, and a culture that does not promote self-learning (Tita, 2005). Another barrier specific to Nigeria is widespread use of other anticonvulsant therapy (diazepam) that can be used for other health indications e.g. sedation, pain relief, anxiety, insomnia, seizures, and muscle spasms (Duley, Henderson-Smart, Walker, Chou, 2010).

**Fifth, educating the public and health sectors** through health promotion efforts and continuing medical education (CME). Special attention must be paid to traditional birth attendants on the importance of antenatal care and basic emergency obstetric care practices (See Figure 3). Already the WHO has advocated that in resource-limited settings only tests that are proven to impact maternal-fetal outcomes be offered at the antenatal care visit. These tests have been determined as blood pressure, urine tests for bacteria and protein, and blood tests for syphilis and anemia (WHO, 2001; Osungbade, Oginni & Olumide, 2008). Consideration towards task-shifting and training traditional birth attendants in these basic skills would likely increase antenatal care throughout the country, but particularly in the rural areas.

Improved access and patient acceptance of antenatal care is needed in the case of pre-eclampsia and eclampsia for early detection, birth preparedness and complication readiness as stated in the DHS Nigeria Report for 2008. Again, integration of traditional birth attendants into the antenatal care and referral system for these same lines of defense is needed. Particular emphasis should be put on the higher risk young primigravida women have of to developing this disease. Also, because antenatal care and diagnostic
testing cannot necessarily predict the onset of pre-eclampsia or eclampsia women have to have awareness about where to go for basic and comprehensive emergency obstetric management.

Educating providers to best practices is as essential as providing them with the therapies that are known to produce the better outcomes. **Sixth is the assurance of drug availability.** MgSO4 has been on the WHO essential medicines list (EML) since 1996, one year after the dissemination of the Magpie trial evidence. It is categorized under **anticonvulsants/antiepileptics** with the caveat: “For use in eclampsia and severe pre-eclampsia and not for other convulsant disorders” (WHO, 2010). It is also listed in the latest 2003 version of the EML for Nigeria published by the Federal Ministry of Health and WHO (Sevene et al. 2005). In the Nigerian EML the therapeutic appears under the ‘List of Essential Drugs” heading, yet is not present in “The Primary Health Care List” under the anticonvulsant category (diazepam injection, paraldehyde injection, and phenobarbitone tablet are listed). This primary health care list is meant for drugs which are considered essential for specialist and tertiary health care facilities. However, it is listed for use as a **purgative drug** or laxative under “Products to be Stocked and Sold by Patent Medicine Dealers/vendors.” The patent medicine vendors are much like corner drugstores in the U.S. and not likely to sell prescription medications. Notably, there is no anticonvulsant medication listed for **Level B – Village Dispensaries** (Federal MOH Abuja Nigeria, 2003). At thirty five cents per dose (ampoule (40ml of 10% MgSO4) there is an unnecessary breakdown in availability of this life-saving therapy as is evident in the literature reviewed above. Simon, Gray & Duley (2006) conducted a economic evaluation of use of MgSO4 and found that in low gross national income countries like...
Nigeria administering MgSO₄ adds $11 to hospital costs. They also report an institutional savings of $456 for one missed case of eclampsia. This included cost savings for all aspects of antenatal and postnatal care for both mother and baby: administrative costs, treatment costs and facility costs (high dependency, ICU, neonatal ICU, ventilation, medications, dialysis and transfusions) (Simon, Gray & Duley, 2006).

**And seventh, implementing WHO guidelines and recommendations,** which use evidence-based clinical criteria, will improve pre-eclampsia/eclampsia management. The most compelling strategy to address poor outcomes for patients presenting with pre-eclampsia and eclampsia are criteria published in a 2000 Bulletin of the World Health Organization by Graham, W., et. al. A short and easy-to-follow set of criterion for the optimal management of eclampsia:

- Senior Medical Staff takes responsibility of formulating a management plan for the patient.
- Anti-hypertensive treatment is given to patients with severe hypertension.
- The treatment and prophylaxis of seizures is with MgSO₄.
- Respiratory rate and tendon reflexes are monitored when MgSO₄ is used (to test for toxicity).
- Antepartum/intrapartum fluid balance chart is maintained.
- Hematological and renal investigations are done at least once: clotting time, platelet count, and urine albumin test.
- Delivery is achieved within 12 hours of the first convulsion.
- Monitoring of blood pressure and urine output continues for at least 48 hours after delivery (Graham, 2000).

More importantly, these criteria were evaluated for use in a clinical setting in southwestern Nigeria in 2002-2003. Original research conducted in the Federal Medical Centre in Abeokuta described results of a pre-test and post-test of implementation of the above criteria by clinical staff. Researchers assessed quality of care before criteria were instated by a discreet audit of patient records for documentation of activities related to...
care and outcomes. They then met with nursing staff to discuss their findings and institute the new criteria. The second phase of the study which implemented the new criteria lasted for six months. This study is remarkable because clinic staff identified a specific need for the provision of MgSO4 in the feedback session before implementation of Phase II. Indicating awareness of the inadequacy prior to implementation of a protocol which called for MgSO4 use. Also, adherence to the criteria was based on a score of one per unit criteria, if criteria were only partially fulfilled a half point was given.

Significant to this study was the total care score prior to implementation for eclampsia of 54.3% and 90% post implementation; Figure 4 demonstrates percent change in the uptake and adherence to each criterion by clinic staff for care for eclamptic patients (Hunyinbo, Fawole, Sotilove, Otolorin, 2008).

Other WHO generated resources for training health care providers and traditional birth attendants can be adapted to suit urban and rural Nigerians at different literacy levels and according to experience. These guides provide illustrations, definitions, risk factors, didactic exercises and checklists for understanding onset of disease (WHO, 2005;
Traditional birth attendants can be taught how to administer basic antenatal testing as recommended by the WHO (blood pressure, urine tests for bacteria and protein, and blood tests for syphilis and anemia) and referral routes for women who need more specialized care. Early recognition of the characteristics related to pre-eclampsia and eclampsia is likely to hasten administration of the appropriate treatment regime. Herein, engagement of the array of stakeholders previously mentioned is key to gain trust and buy-in for use and to determine functionality of such resources.

**Conclusions**

Upwards of 10,000 women are dying from pre-eclampsia/eclampsia in Nigeria each year and the use of MgSO4 could cut this in half. For each death it is estimated there are 30 cases of morbidity. In the case of pre-eclampsia and eclampsia it is somewhat likely a woman will have hypertension after her pregnancy or later in life. Complications related to hypertension and history of pre-eclampsia/eclampsia includes cardiomyopathy, retinopathy, renal damage, and incidence of stroke and heart attack (Oyati, 2008). This disease puts a tremendous strain on the public health status of the country, resulting in an array of economic consequences to the individual and society.

It has been established within this review that MgSO4 is not currently available in teaching hospitals and medical centers in all geographic regions in Nigeria. Provision of essential medicine was established in the 1978 Alma Ata Declaration as one of eight key components of basic health care in article VII *Primary Health Care* (Laing, 2003). Evidence-based criteria for drug inclusion on the EML is that there must be public-health relevance, established efficacy, safety, and cost effectiveness. Although MgSO4 is on the
PRE-ECLAMPSIA AND ECLAMPSIA MANAGEMENT IN NIGERIA

Nigerian EML it is not on “The Primary Health Care List” or properly categorized on the “Products to be Stocked and Sold by Patent Medicine Dealers/vendors” list, nor is it available in village dispensaries (Federal MOH Abuja Nigeria 2003). These failures to list appropriately are likely a primary cause of drug unavailability within the country.

Health care providers of all types need access to therapeutics which offer the most favorable outcomes for their clients. This includes traditional birth attendants who require training in recognizing pre-eclampsia, administration of MgSO4 and patient monitoring. Also, women need access to facilities and providers that are both nearby their homes and adequately equipped to manage obstetric emergencies for optimal health outcomes for them and their babies.
References


for the treatment of eclampsia and pre-eclampsia in Mozambique and Zimbabwe.

**BMJ (Clinical Research Ed.),** *331*(7519), 765-769.


Acknowledgments

I would like to thank Marcia S. Roth, MPH as the first reader and D. Michael Armstrong, MD as the second reader on this paper. Marcia was exceptionally generous with her time and supportive of me as I found my way to the end of this project. Dr. Armstrong lent his expertise in the subject of hypertension in pregnancy to this review, and has provided invaluable feedback regarding content. Also, my family and my sister, Luree Holt, RN, CRNA, who has endured the discomforts of breast cancer this year.
Appendix A

Critical Reading of the Medical Literature: Format for Review of Articles

1) What was the purpose of the study?
2) List the study’s hypothesis and comment on whether they are directly stated or implied.
3) Basic description of study design:
   a. What kind of study was it
   b. Describe the study population (use of sampling, defined eligibility criteria, etc.)
   c. Identify potential problems with design (selection bias, inappropriate comparison groups, etc.)
4) Describe the intervention(s) or treatment(s), if any:
5) Data collection
   a. What was measured
   b. How and when were data collected?
   c. Identify any problems with data and data collection (factors measured, factors poorly measured, subjects lost to follow-up, etc.)
6) Is the plan for data analysis clear and reasonable?
7) Results:
   a. Discuss the presentation of the data (content and clarity of tables and text).
   b. List and discuss important result:
   c. Discuss the investigators’ interpretations and conclusions:
8) Overall critique of the study:
   a. Did the investigators accomplish what they set out to do?
   b. Summarize both successes/innovations and fatal flaws/major problems in design, methodology, or interpretations. What would you do differently?
9) Is the study relevant for clinical practice?
10) Are the results generalizable?
11) Overall summary rating of the paper
   3-4    Severe limitations in interpreting results of drawing conclusions
   5-6    Questionable confidence in results or conclusions
   7-8    Worth reading, but some limitations
   9-10   Outstanding contribution
12) Justification:
### Appendix B: Articles reviewed for management of pre-eclampsia/eclampsia in Nigeria, 2000-2011.

<table>
<thead>
<tr>
<th>Source</th>
<th>Location and type of study</th>
<th>Management/therapy</th>
<th>Observation</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Tukur, J., Muhammad, Z., 2010</td>
<td>Aminu Kano Teaching Hospital, North Central Nigeria. Retrospective chart review of diazepam vs MgSO4. Jan 2002 - Dec 2004 and Jan 2005 - Dec 2007. N=131</td>
<td>Diazepam compared to MgSO4</td>
<td>Maternal and perinatal mortality, APGAR scores @ 1 and 5 minutes, toxic effects, delay at presentation and unbooked for ANC.</td>
<td>Significant for: 38 tx w/ diazepam, 39% (15) died. 93 tx w/ MgSO4, 15% (14) died. 41 babies’ stillbirth. Total 29 deaths: 25 delayed care; 26 had no ANC.</td>
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<tr>
<td>Okafor UV, 2009</td>
<td>Enugu, Nigeria. University of Nigeria Teaching Hospital. Central Nigeria Retrospective chart review of anesthetic management and perinatal outcomes. 1998-2006. N=196,</td>
<td>General anesthesia, spinal and epidural anesthesia management for preeclampsia/eclampsia for cesarean section.</td>
<td>Demographics, stillbirths, early neonatal deaths, maternal mortality and type of anesthesia administered.</td>
<td>73 mothers w/ PE, 123 mothers with severe PE or eclampsia-all had cesarean; 157 delivered under general anesthesia (30 perinatal deaths), 34 spinal anesthesia (8 perinatal deaths), 5 epidural (0 deaths). 154 &gt;32 weeks, 38 26-31 weeks. Inadequate management of anesthesia to reduce PMR. Use of MgSO4 may have reduced cesarean rate by lowering incidence of eclampsia.</td>
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<tr>
<td>Authors</td>
<td>Location</td>
<td>Study Type</td>
<td>Interventions</td>
<td>Patient Demographics and Findings</td>
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<td>Okafor, U.V., and Efetie, R.E. 2008</td>
<td>Abuja, Nigeria, Central Nigeria</td>
<td>Retrospective chart review of eclampsia patients in the ICU. Nov 2001 - April 2005. n=38</td>
<td>Diazepam and MgSO4</td>
<td>Patient demographics, booking status, parity and gestational age at delivery and at onset of seizures. 38 ICU admissions postpartum. 20 onset antepartum, 6 intrapartum and 12 postpartum. Age range 17-40. 23 primigravida. 29 cesarean, 9 vaginal. 37 diazepam 1 MgSO4. Antihypertensive was hydralazine control. 11 deaths, 17 ventilated from diazepam sedation.</td>
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<tr>
<td>Igberase, G. O. and Ebeigbe, P.N. 2006</td>
<td>Eku, Delta State, Nigeria. Southeastern Coast. Ten year retrospective chart review of eclampsia outcomes in rural areas Jan 1994 - Dec 2003. N = 123</td>
<td>MgSO4</td>
<td>Age, parity, booking status, clinical presentation, maternal-fetal outcomes. 43% age 20-25, 59% primigravida, 86% unbooked, 53% full term. 2.3% eclampsia in ten yrs. 19 maternal deaths, 24 neonatal deaths. 82 cesarean, 31 vaginal, 10 assisted delivery. 12+ hrs from first seizure for 48% of the women to get EmOC. Untimely MgSO4 administration negated protective effects.</td>
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<tr>
<td>Melah, G.S., Massa, A.A., El-Nafaty, A.U. 2005</td>
<td>Gombe, Nigeria. Rural eastern central Nigeria. Retrospective chart review Jan 1997 - Dec 2000. N=438.</td>
<td>Therapy was not specifically noted other than stating that MgSO4 is not available in the labor and delivery unit.</td>
<td>Age, parity, booking status, and pregnancy outcomes 3.7% dx eclampsia, 67.8% teen-aged, 79.8% primigravida. 47 of 228 maternal deaths and 157 neonatal deaths due to eclampsia. 91% women had warning signs. Supporting the hypothesis that ANC would have prevented mortality.</td>
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<td>Ikechebelu, J.I., and Okoli, C.C. , 2002</td>
<td>Nnamdi Azikiwe University Teaching Hospital, Nnewi, Southern Nigeria Retrospective chart review Jan 1996-Decr 2000. N=43.</td>
<td>Diazepam for convulsions and hydralazine for hypertension</td>
<td>Dx of eclampsia, age, parity, booking status, time of onset, mode of delivery and outcomes. .75% (43) incidence of eclampsia, 32.6% age 21-25, 65% primigravida, 84% received no ANC and more likely to be eclamptic antepartum (55.8%). 86% cesarean. 9.3% maternal deaths. 16.3% neonatal deaths.</td>
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<tr>
<td>Conservative management of pre-eclampsia: bed rest, alpha-methyldopa or hydallazine as anti-hypertensive. Diazepam for seizures,</td>
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<td>Compared early onset (case) to late on-set controls for outcomes using conservative management. Other variables: age, parity, booking status, SES, family history of hypertension and other medical disorders.</td>
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<td>175 cases: onset of disease before 30 weeks gestation; 574 controls: onset after 30 weeks. Cases: 91 pure pre-eclampsia, 84 superimposed pre-eclampsia; 21 developed eclampsia and 7 died. Controls: 98 developed eclampsia, 7 died. Cases: avg 31 yrs-old, primigravida, 68% booked, 52% &gt;$100/month, 52% tertiary education, 64% no family hx of hypertension, 68% bp≥170/100, 92% no other medical disorders. Controls: avg 29 yrs-old, primigravida, 66% booked, 37% ≥$100/month, 46% tertiary education, 73% no family hx of hypertension, 57% bp≥170/100, 94% had no other medical disorders.</td>
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