Deep Tendon Reflexes, Magnesium, and Calcium: Assessments and Implications

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■ The perinatal nurse, in collaboration with physicians, can use deep tendon reflexes as a powerful tool in determining the need to start, adjust, or stop magnesium infusion. Toxicity can be detected using physical manifestations as a guide. Clinical signs may be a better indicator than serum levels of tissue levels of magnesium. Whether magnesium is given to prevent seizures or for tocolysis, patients in both situations are at risk for developing toxicity and must be assessed regularly to ensure patient safety. *JOGNN*, 33 221-230; 2004. DOI: 10.1177/0884217504263145

Perinatal nurses frequently manage patients receiving magnesium sulfate ($MgSO_4$) infusion for treatment of preterm labor or preeclampsia. The prescribed therapy requires nurses to monitor patient progress and use judgment to adjust the infusion. There is, however, a distinct lack of information in the literature on the value of using deep tendon reflexes (DTRs) as a guide to titrate the infusion. Research supports the relationship between DTR findings and serum magnesium levels but does not expound on titration methods. Nurses need to understand how to titrate $MgSO_4$ by using DTRs as a guide.

This article presents information on use of $MgSO_4$ therapy in high-risk obstetrics, outlines titration techniques with the help of DTR assessments, and emphasizes interventions for impending toxicity. Because the body's response to rising magnesium levels is predictable, the perinatal nurse can closely correlate physical manifestations with physiological, therapeutic, and toxic ranges. Using DTRs as a guide, the nurse can anticipate decisions regarding the appropriateness of starting magnesium therapy and provide recommendations on titration of the magnesium infusion.

A review of available literature on calcium as the antidote to magnesium toxicity reveals practices that vary and are not well supported by research. In this era of evidence-based practice requirements, perinatal nurses must develop interventions based on science and implement interventions based on good judgment. Suggestions for collaborative research are detailed.

Rationale for Relying on DTRs

The ability to manage patients on $MgSO_4$ therapy requires nurses to develop expert nursing judgment. Nurses use their judgment to determine who needs DTR assessments, when to perform assessments, and how often to assess. They can also provide recommendations about starting, increasing, decreasing, or ceasing magnesium therapy. Cultivating expert technique in DTR assessment is possible. The article "Deep Tendon Reflexes: The What, Why, Where, and How of Tapping" (Nick, 2003) offers a complete review of DTR assessments. The article provides information on why the term *deep tendon reflex* is a misnomer, why tendons move when tapped, where to assess DTRs, and how to assess them to obtain valid and reliable information.

The testing of DTRs, although common, can serve as a powerful tool to estimate magnesium levels and indirectly indicate changing magnesium levels in the patient. Consistency in monitoring DTRs helps nurses develop judgment regarding titration of $MgSO_4$ infusion. This method is simple, quick, inexpensive, noninvasive, and reliable. Perinatal nurses may perform DTR assessments independently and will not need an order from a physician or nurse midwife to do so. Such assessment is appropriate and within the scope of nursing practice.

When a patient is treated with $MgSO_4$ intravenously, the monitoring of DTRs is imperative. Surprisingly, reliance on serum magnesium levels as an indicator poses several problems. First, protocols for laboratory surveillance of serum magnesium levels are not consistent. Not all health care providers prescribe regular assessment of serum magnesium levels in patients receiving $MgSO_4$ infusion. Additionally, monitoring of serum levels can be prescribed at intervals of every 8 hours, every 12 hours, or less frequently. Consistency of practice does not exist. At the least, nurses can be consistent in their assessments and use the results to estimate magnesium levels in the tissue. Research supports the relationship between reflex results and tissue magnesium levels.

Second, serum magnesium levels have limited diagnostic value. Only 0.3% of the body's total magnesium content is located in serum (Matz, 1993). Researchers have shown that the serum level is an insensitive indicator of the tissue magnesium level (Carey, Lee, & Woeltje, 2001; Frost, Danielsen, Dorup, Kjaer, & Pedersen, 1993; Haigney et al., 1995; Romano, 1997; Shah, Santucci, & Finberg, 1994). Because tissue magnesium content determines physical manifestations, clinical manifestations are a better indicator of physiological response than serum levels. The concept that serum levels may not be valid for managing therapy may be new for those who rely heavily on laboratory values for titration. In fact, the American College of Obstetricians and Gynecologists (2001) supports using clinical symptoms as the indicator rather than serum levels and states "In most situations, clinical assessment of respirations, deep tendon reflexes, and urine output is adequate to monitor for maternal toxicity without the need to determine the actual maternal serum magnesium levels" (p. 174). Serum indicators can serve as a crude estimate of what is happening in the tissues, but it is the tissue response that is more important to determine. DTR depression can exist even when serum magnesium levels are in the therapeutic range. Therefore, although serum levels do not indicate toxicity, if physical signs of magnesium toxicity exist, interventions are required.

History of Magnesium as Therapy in Obstetrics

The effectiveness of magnesium as therapy for the prevention of seizures is well established. Before the late 1920s, traditional treatment for eclampsia included morphine injections, quiet environment, colonic enemas, venesection (bloodletting) of 500-1,000 ml of blood, and operative delivery (Alton & Lincoln, 1925; Kane, 1926; Wilson, 1925). Poor results from these treatments prompted interest in a more conservative treatment option. The first reports of magnesium as treatment for eclampsia surfaced in 1925. Lazard (1925) reported promising results with conservative management and intravenous boluses of magnesium sulfate. Alton and Lincoln (1925) reportedly controlled eclamptic convulsions by intraspinal injection of magnesium sulfate. Although intraspinal injection fell out of favor in the mid-1900s, intravenous $MgSO_4$ therapy continues as the frontline treatment for preeclampsia and eclampsia today.

Use of magnesium as a tocolytic for preterm labor is also well established. Beginning around 1980, literature first appeared on the usefulness of magnesium as therapy for preterm labor (Caritis, Edelstone, & Mueller-Heubach, 1979; Guilliams & Held, 1979; Niebyl & Johnson, 1980). High efficacy, fewer maternal side effects, and lower costs than existing therapies quickly made magnesium a favorite treatment method.

Unfortunately, literature on the neonatal benefits of using magnesium as a tocolytic provides conflicting evidence. Research has focused on in-utero exposure of magnesium on reducing risks associated with prematurity. Goldenberg and Rouse (1997) concluded magnesium could provide a protective mechanism for the fetus/newborn because they found an associated reduced incidence of cerebral palsy. Yet Cantarino et al. (1999) found no difference in the incidence of intraventricular hemorrhage or necrotizing enterocolitis in preterm infants when mothers were treated with $MgSO_4$ therapy as a tocolytic therapy. Other scientists studied the effect of magnesium as antiseizure therapy on the newborn infant. They concluded it is not the medication that provides a protective effect as much as the maternal hypertensive state that affects rates of cerebral palsy (Gray, O'Callaghan, Mohay, Burns, & King, 1998).

The efficacy of magnesium as treatment for seizures and as a tocolytic is well established for the pregnant woman. The protective effect on the infant is unsettled at this time. More interdisciplinary research is needed to determine the effect of treatment on the outcome of the newborn.

Pharmacology of Magnesium

As antiseizure therapy, elevated levels of magnesium cause a threefold effect. First, elevated magnesium levels depress the excited central nervous system (CNS) by blocking/suppressing the receptor site N-methyl-D-aspartate that produces the seizure (Lu & Nightingale, 2000). Excitation of the CNS occurs as a result of hypoxic changes in the brain, caused by cerebral vasospasm. To counteract the cerebral hypoxia, magnesium also acts as a cerebral vasodilator, increasing vascular blood flow to the brain (Naidu, Payne, Moodley, Hoffmann, & Gouws, 1996). Third, magnesium affects the neuromuscular and neurocellular signal transmission, which inhibits seizure activity ("Magnesium Sulfate," 2002). All three of these effects collectively decrease an irritable/excitable CNS, which then lowers the potential for seizures.

As treatment for preterm labor, elevated magnesium levels decrease levels of the neurotransmitters acetylcholine and norepinephrine (Rude, 1996), two important neurotransmitters that allow communication and transmission of information among nerve cells. Acetylcholine allows nerve cells to communicate with muscle cells, whereas norepinephrine allows communication between nerve cells and other nerve cells. Without acetylcholine, communication from nerves to muscle does not occur and muscle depression occurs (Hypermagnesemia, 2002). Because magnesium decreases acetylcholine, it is an effective uterine tocolytic.

The heart, lungs, uterus, and intestines contain smooth muscle that responds to an acetylcholine-enriched stimulus. Each organ has a different threshold for acetylcholine repression caused by magnesium. Depression and cessation of function occur at much higher magnesium levels in heart and lung tissue than in the uterine muscle (see Table 1). This, fortunately, allows practitioners to use lower magnesium levels effectively to treat preterm labor or pregnancy-induced hypertension without causing high rates of morbidity or mortality from respiratory and cardiac depression.

Reaching Therapeutic Ranges

A therapeutic range of magnesium in the bloodstream would need to be sufficient to improve a patient's condition (Thomas, 1997). Therapeutic serum magnesium levels are defined as a range from 4 to 7 mEq/L; this range simultaneously decreases CNS irritability and relaxes uterine smooth muscle ("Magnesium Sulfate," 2002). Classic studies on the pharmacokinetics of magnesium in pregnant women have shown that therapeutic levels are usually attained 6 to 8 hours after beginning infusion at a rate of 2 g per hour (Cruikshank, Pitkin, Reynolds, Williams, & Hargis, 1979; Pritchard, 1979). Because 6 to 8 hours is a long time to wait for therapeutic depression of the CNS or uterus, the physician usually prescribes a loading dose of 4 to 6 g of $MgSO_4$ intravenously. The loading dose raises the magnesium level to the high range of therapeutic levels almost immediately; the effect lasts approximately 1 hour, and then the magnesium level returns to the low end of the therapeutic range (Sibai, 1990).

Three different units of measurement for magnesium are reported in the literature. Some authors report ranges in milliequivalents per liter (Carey et al., 2001; "Magnesium Sulfate," 2002; Metheny, 2000; Rude, 1996) or in milligrams per deciliter (Sibai, 1996), whereas much of the research has been reported using millimoles per liter (Cao, Bideau, Valdes, & Elin, 1999; Haigney et al., 1995; Lu & Nightingale, 2000; Matz, 1993). Because the ranges for *therapeutic* in one unit of measurement look similar to the toxic levels using another unit of measurement, confusion exists as to cutoffs for normal, therapeutic, and toxic ranges. Table 1 presents a summary of the normal, therapeutic, and toxic ranges for magnesium in all three units of measurement. Table 1 also shows physical manifestations that correlate with serum magnesium levels—which are a better indicator of magnesium tissue content than laboratory values—and nursing interventions for titration and management of magnesium infusion.

Whether patients are receiving $MgSO_4$ infusion for tocolysis or for seizures, they are at risk for developing hypermagnesemia. For this reason, the perinatal nurse should know the normal, therapeutic, and toxic ranges of serum magnesium as well as her or his institution's reporting unit of measurement. Professional nurses who understand the pharmacodynamics of magnesium can use the information to achieve the desired therapeutic effect for the patient.

Cardinal Reasons to Assess DTRs in Obstetric Patients

When a patient receives $MgSO_4$ infusion, the obstetric nurse must assess DTRs frequently. Information from DTRs will help nurses develop judgment about titrating the infusion. Three cardinal reasons to perform DTRs are

DTRs can be used to determine need for magnesium therapy, evaluate efficacy of magnesium therapy, and prevent toxicity from magnesium therapy.

to (a) determine the client's *need* for $MgSO_4$ therapy, as evidenced by hyperreflexia; (b) evaluate the *efficacy* of

Levels	mmol/L	mEq/L	mg/dL	Physical Manifestations	Nursing Action
Physiologic	0.65-1.1	1.3-2.1	(1.6-2.7)[c]	Couples with adenosine triphosphate (ATP) to increase ATP utilization. Activates numerous enzyme systems, facilitates nerve conduction and potassium ion transport.	—
Initial response to loading dose	(1.5-2.5)[b]	3-5	(3.6-6)[d]	Peripheral vasodilation with facial flushing, sense of warmth, nausea and vomiting. These signs and symptoms occur with overly rapid administration.	Dilute to at least a 20% concentration and administer by infusion pump over 20 minutes. Educate patient.
Therapeutic	2-3	4-6	4.9-7.3	Depression: CNS and uterine smooth muscle Arrest: Uterine smooth muscle	Verify patient has reached therapeutic range as evidenced by uterine quiescence and normo-reflexia. If uterine contractions or hyperreflexia persist, dosage needs to be increased.[a]
Toxic	(3.5-4)[b] 4-5 (5-6)[b] 6-7.5 7.5-10 >10	7-8 8-10 10-12 12-15 15-20 > 20	(8.5-10)[c] 9-12 (12-15)[c] 15-18 (18-24)[c, d] 25-35	Depression: Deep reflexes Arrest: Deep reflexes Depression: Respiratory Arrest: Respiratory Depression: Arrhythmia, bradycardia, heart block Arrest: Cardiac	Dosage should be decreased.[a] Discontinue magnesium.[a] Discontinue magnesium.[a] Administer diluted calcium gluconate (not calcium chloride, $CaCl_2$). Monitor electrocardiograph changes before and after calcium administration. Have emergency equipment available.

Note. Serum magnesium levels that affect body systems are approximate. There is wide variation in reports of levels at which signs and symptoms occur. Focus on generalizations and patterns in the data.

[a]Notify physician.

[b]Magnesium levels not reported in the literature but computed mathematically and rounded appropriately using the equation: y mmol/L = x(mEq/L) * 0.5.

[c]Magnesium levels not reported in the literature but computed mathematically and rounded appropriately using the equation: y mg/dL = x(mmol/L) * 2.43.

[d]Magnesium levels not reported in the literature but computed mathematically and rounded appropriately using the equation: y mg/dL = x(mEq/L) * 1.21.

$MgSO_4$ therapy in depressing the CNS, as evidenced by normoreflexia; and (c) prevent the *development* of toxicity, as evidenced by hyporeflexia or areflexia. Remembering these three cardinal reasons enhances clinical practice and benefits patients.

Determining Need

When caring for patients diagnosed with preeclampsia, it is important to know the status of the CNS. In essence, DTRs function as a window into the CNS. Therefore, DTR assessment can be useful in providing information on the patient's need for magnesium sulfate. The National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health developed a DTR scale for practitioners (see Table 2) (Hallet, 1993). For a full discussion on issues related to the different DTR rating scales, refer to Nick (2003).

When hyperreflexia or brisk reflexes (3 or 4 on NINDS scale) are present, the nurse should notify a health care provider who can prescribe magnesium infusion. Hyperreflexia is a sign that the disease has affected the cortex, and the patient should be managed with $MgSO_4$ therapy.

Evaluating Efficacy

A second reason to conduct DTR assessments is to determine magnesium efficacy. Once the nurse starts the

TABLE 2
NINDS Scale for Tendon Reflex Assessment

Description	Score
Reflex absent	0
Reflex small, less than normal; includes a trace response, or a response brought out only by reinforcement	1
Reflex in lower half of normal range	2
Reflex in upper half of normal range	3
Reflex enhanced, more than normal; includes clonus if present, which can be noted in an added description of the reflex	4

Note. From "NINDS Myotatic Reflex Scale," by M. Hallett, *Neurology*, *43*, p. 2723. Copyright 1993 by the National Institutes of Health. Reprinted with permission.

prescribed $MgSO_4$ infusion, therapeutic levels can be validated by observing for uterine relaxation or normoreflexia. Reflex assessment cannot help evaluate efficacy of treatment for preterm labor but can assist the nurse in evaluating the effect on the CNS.

When the goal of treatment is to depress the CNS, DTR assessments can assist nurses in evaluating the efficacy of treatment. Hyperreflexia occurs as a result of CNS irritability secondary to the vasospasms caused by preeclampsia. Once CNS irritability decreases (as a result of magnesium therapy), the cerebral cortex produces sufficient dampening signals and sends them down the spinal cord. Hence, normoreflexia (2 on NINDS scale) resumes. If, however, the patient continues to have brisk reflexes, the nurse should confer with the physician, because the dosage is inadequate and should be increased. When hyperreflexia (3 or 4 on NINDS scale) changes to normoreflexia, proper dosing has been achieved and the treatment is effective. The nurse should maintain the infusion at the rate that achieves treatment goals while maintaining normoreactive or slightly hyporeactive reflexes.

Preventing Toxicity

The third cardinal reason to perform DTR assessment is to prevent magnesium toxicity from developing in the patient. Toxicity develops from overdosing the patient with the medication. DTR assessments are helpful for developing clinical judgment and detecting impending toxicity.

Use of DTR findings has been shown to be an inexpensive indicator of magnesium levels. In retrospective studies, Chinayon (1998) and Raman and Rao (1995) found that DTR response was a reliable indicator of tissue magnesium levels when coupled with respiratory and urine output indicators. Because the body excretes mag-

nesium via the kidneys, urine output must be sufficient to process the continuous infusion (i.e., ≥ 30 mL/h). When output drops below this level, the patient can rapidly develop toxicity. But as long as DTR response, respiratory rate, and urinary output are normal, practitioners are reassured of attaining therapeutic levels.

Hypermagnesemia occurs primarily in two instances: with impaired renal function or when a large magnesium load is given to the patient (Agus & Lau, 1995). Because the kidneys are the principal organ involved with magnesium excretion, patients diagnosed with preeclampsia may have renal impairment as a result of the disease process and are, therefore, at particular risk for developing hypermagnesemia (Rude, 1996). Magnesium toxicity can develop rapidly in this instance if renal function decreases suddenly. Thus, if a patient is receiving $MgSO_4$ infusion and her urine output decreases, she should be assessed for hyporeflexia or areflexia more frequently. If depression of reflexes occurs, the nurse should notify the physician and request new medication orders, because decreasing the magnesium should be considered. For patients with a compromised renal system, nurses should develop judgment to determine how frequently to assess DTR and urinary output to prevent hypermagnesemia.

Patients in preterm labor may not have impaired renal function but often require high dosages to achieve uterine quiescence. Additionally, such patients may be receiving

> **I**f a patient is receiving $MgSO_4$ infusion and her urine output decreases, she should be assessed for hyporeflexia or areflexia more frequently.

$MgSO_4$ intravenously for extended periods of time, which places them at risk for developing hypermagnesemia. It is helpful to employ diligence in assessing DTRs in patients receiving $MgSO_4$ as a tocolytic.

Vigilant practitioners can, in many cases, prevent toxicity from developing by using information provided from DTR assessment. When normoreflexia turns into hyporeflexia or areflexia, the nurse should recognize these as signs of developing toxicity and notify the physician in a timely manner. A collaborative relationship between physician and nurse is crucial to patient safety in this situation.

Physical Manifestations of Toxicity

The consequences of magnesium toxicity can be grave. With mild magnesium toxicity (serum levels between 6

> **M**any obstetric personnel see the importance of assessing DTRs in preeclamptic patients but fail to assess DTRs regularly in preterm labor patients treated with intravenous magnesium therapy.

and 8 mEq/L), magnesium functions as a neuromuscular blockade. Physical manifestations of neuromuscular blockade include muscle dysfunction such as lethargy, muscle weakness, slurred speech, and decreased DTRs. At higher levels of toxicity, magnesium secondarily functions as an effective calcium channel blocker (Agus & Lau, 1995). Signs of calcium channel blockade include hypotension and arrhythmia, such as bradycardia, prolonged P-R interval, widened QRS interval, and heart block (serum levels estimated at 15–20 mEq/L).

If the patient receives too much elemental magnesium, or the kidneys cannot handle the excretion load, the serum magnesium level will rise past the therapeutic range and vital systems will be affected. Fortunately, the signs of magnesium toxicity are easily detected. There is a predictable progression from alteration (i.e., depression) of the CNS to alteration then arrest of the deep reflexes, followed by alteration then arrest of the respiratory system, followed by alteration then arrest of the cardiac system. Because of this linear progression, tissue magnesium levels can be estimated using tendon reflexes as the guide.

Management Techniques With Magnesium

With hyporeflexia (0 or 1 on NINDS scale), the magnesium infusion should be decreased or discontinued, which requires an updated medication order from the physician. However, if respiratory alteration occurs, the nurse should not hesitate to turn off the infusion before notifying the physician. A delay could cause respiratory alteration to progress to respiratory arrest. Quick action with the magnesium infusion may prevent further problems. With normoreflexia (2 on NINDS scale), the infusion should remain constant. With hyperreflexia (3 or 4 on NINDS scale), the infusion should be increased, which again necessitates collaboration with the physician. Because nurses are at the bedside providing continuous care, the nurse's frequent monitoring can detect signs of toxicity and help the physician fine-tune the dosing requirements for each patient (see Table 1). Interventions for overdosing include decreasing or stopping the infusion and administering calcium to reverse the effects of magnesium.

For mild magnesium toxicity (hyporeflexia or areflexia), slowing the rate of or discontinuing the intravenous magnesium should be a first priority. Working closely with the physician, the nurse can titrate the magnesium infusion and enhance patient well-being.

After achieving distribution into the extracellular-extravascular space, moving magnesium out of this space is more difficult. Unfortunately, the elimination half-life for magnesium is rather slow—about 4 hours (Chen, Li, & Guo, 1991, as cited in Lu & Nightingale, 2000; Hall, 1957). That is, in patients with normal renal function, if the therapy were discontinued, in about 4 hours the serum level would be about half what it was initially. Twenty-four hours after magnesium infusion is discontinued, 90% of the extra magnesium is excreted from the body (Cruikshank, Pitkin, Donnelly, & Reynolds, 1981). For patients with abnormal renal function, such as those with preeclampsia, the elimination half-life is even greater (Belfort & Moise, 1992). Therefore, because of the slow elimination, if signs of moderate toxicity are apparent, discontinuing the magnesium may not be sufficient. Calcium reversal is required. Signs of moderate toxicity include respiratory depression and cardiac arrhythmia. Intravenous calcium, which quickly reverses the effects of magnesium toxicity, may be required when moderate to severe toxicity occurs (Agus & Lau, 1995; Metheny, 2000).

Calcium as Antidote

Since the beginning of the last century, scientists have known about the effect of calcium on hypermagnesemia (Meltzer & Auer, 1907). However, only sporadic information can be found on calcium antidosing (Bryant, Lehman, & Knoefel, 1939; Mordes, Swartz, & Arky, 1975).

Calcium counteracts the effects of magnesium intoxication by simply undoing what magnesium has done. It increases acetylcholine and norepinephrine release during each depolarization (Rubin, 1970). Early on, authors demonstrated that calcium antidosage directly relates to magnesium dosage, and the magnesium-to-calcium ratio is important (Bryant et al., 1939). The higher the magnesium overload, the more calcium will be required to counteract the effect.

Unfortunately the literature does not specify how often to give calcium to reverse magnesium toxicity or how many doses are required to reverse hypermagnesemia. Authors state that reversal is transient and repeated doses may be required (Carey et al., 2001; Metheny, 2000; Mordes & Wacker, 1978; Rude, 1996). Tissue response such as normal cardiac rhythms (determined via electrocardiography) and normal reflexes will need to serve as

the guide for repeated doses until further research establishes quantitative guidelines.

Calcium administration warrants careful attention, because injecting the medication intravenously as a bolus dose can cause tissue necrosis, hypotension, bradycardia (Hypermagnesemia, 2002), or, worse, ventricular fibrillation (Auerbach & Langenberg, 1985; Chin, Garmel, & Harter, 1995). For this reason, it would be prudent to attach an electrocardiograph to the patient for monitoring purposes before, during, and after administration.

Calcium Dosing Information

There is wide variation in the literature regarding calcium antidosing and rate of administration required for magnesium reversal. Agus and Lau (1995) and Rude (1996) recommended 100 to 200 mg of elemental calcium over 5 to 10 minutes. Interestingly, those authors used Mordes and Wacker (1978) as their supporting reference, but that reference only stated, "Immediate but transient reversal of toxicity may be effected with calcium," and no dosing recommendations were given.

Sibai (1996), a leading expert on pregnancy-induced hypertensive disorders, recommends 1 g of 10% solution of calcium gluconate administered over 3 minutes. Sisson and Sauer (1995) recommend 1 g of calcium gluconate given over 1 to 2 minutes. Metheny (2000) recommends 10 to 20 mL of 10% calcium gluconate (equal to 1–2 g of calcium) but cautions to give the antidote over 10 minutes. Nursing textbooks specify 1 g of intravenous calcium gluconate to be given over 3 minutes as a bolus dose (Dickason, Silverman, & Kaplan, 1998; Olds, London, Ladewig, & Davidson, 2004). The American College of Obstetricians and Gynecologists (1996) recommended 1 g of calcium gluconate intravenously over 2 minutes. In more recent publications by ACOG, there is either no mention of calcium as antidote (2001) or there are no dosing recommendations given, and it is stated only that "if toxic serum levels or side effects are encountered, magnesium sulfate infusion must be discontinued, and calcium gluconate may be administered to reverse these effects" (American Academy of Pediatrics and American College of Obstetricians and Gynecologists, 2002, p. 174).

The well-known electronic pharmacologic database MICROMEDEX recommends either calcium *chloride*, 350 to 700 mg intravenously over 10 minutes or calcium *gluconate*, 500 to 800 mg over 2 minutes (Hypermagnesemia, 2002). Although calcium chloride is an acceptable antagonist for magnesium, it tends to be more caustic and will extravasate into tissues, thus causing tissue damage. Therefore, calcium chloride must be given over a longer period of time than calcium gluconate.

Many believe that the causticity of calcium chloride is related to the chloride ion forming hydrochloric acid.

Heckler and McCraw (1979) found this to be erroneous, however. They demonstrated that the causticity and necrosis were not caused by pH changes but, rather, were caused from the concentration of free calcium once disassociation occurs in the bloodstream. Whereas calcium chloride immediately disassociates, calcium gluconate disassociates over a period of time and is thus not as caustic to vessels. After their own experience with calcium chloride causing severe tissue damage, Semple and Booth (1996) recommended administering calcium solutions into central veins (i.e., subclavian, internal jugular, or femoral), increasing the dilution before infusion, and using gluconate instead of chloride, which is less irritating to tissues.

Areas for Future Research

Although magnesium therapy and calcium countertherapy have historical precedence, knowledge gaps still exist in perinatal nursing. Independent nursing studies and interdependent research between disciplines can be accomplished in this area of research. A well-thought-out research project has the potential to impact the profession of nursing positively, increase the validity of interventions, and improve patient health.

Potential Research for Magnesium

Perinatal patients may receive $MgSO_4$ therapy for long periods of time. Studies need to answer questions regarding appropriate length of treatment and elucidate short-term and long-term effects on maternal and fetal health. After the patient has been on $MgSO_4$ infusion for weeks, are physical manifestations still a reliable indicator? Do tissues build up a tolerance to $MgSO_4$ over time? Or, possibly, are tissues more sensitive to $MgSO_4$ over time? Could tolerance or sensitivity account for the wide variation in reports of levels at which signs and symptoms first occur? With the increased autonomy of the nurse, developing titration protocols would seem appropriate. Nurses titrate other medications on the basis of patient parameters, yet protocols do not exist for titrating magnesium first then notifying the physician after altering the dosage. Has nursing judgment developed enough to work toward developing protocols for magnesium titration? Can this action be changed from a dependent nursing action to an interdependent action? Research would need to demonstrate the safety and effectiveness of such a service.

Because serum levels are not a reliable indicator of intracellular content, there may be other indicators or parameters that nurses can use. Do all deep reflexes respond similarly to beginning toxicity, or is one more sensitive than another? How do superficial reflexes respond to magnesium overload? Do they become depressed at similar levels as the deep reflexes? Does sali-

va contain magnesium? Could saliva become another indicator? Because magnesium causes peripheral vasodilation, would peripheral skin temperature monitoring prove useful in estimating magnesium load? These are questions that can be answered by nurse researchers.

Potential Research for Calcium

Although it is known that a ratio between magnesium and calcium exists, and a certain magnesium level requires a certain calcium level to counteract the effects, specific guidelines for calcium dosing do not exist. For example, how many calcium dosages are required when the serum magnesium level is 12 mEq/L? How many dosages are required to reverse the effects when the magnesium level is 15 mEq/L? Is tissue response the best indicator, or would guidelines help practitioners manage patients with hypermagnesemia?

There are several options recommended for calcium as antidote, which makes developing protocols difficult. The dosage ranges from 100 mg to 2 g of elemental calcium, the counter-ions can be either chloride or gluconate, and the rate of administration ranges from 1 to 10 minutes. Why do these variations exist? How many doses are required to effectively reverse hypermagnesemia? After an exhaustive search of databases including the Cochrane Library, MICROMEDEX, CINAHL, and MEDLINE (using both Silver Platter and PubMed) for the years 1966 to 2002, this author found no research-based articles relating to dosage and rate of administration of calcium for magnesium toxicity reversal. Although magnesium therapy as treatment for eclampsia has been used since the mid-1920s (Alton & Lincoln, 1925; Kane, 1926; Lazard, 1925), treatment for hypermagnesemia did not appear until 15 years later (Bryant et al., 1939). The Cochrane Library has future plans for a meta-analysis of treatment options for pregnancy-induced hypertension and preterm labor, but the compiled information is not available yet. How can nurses evaluate practice if the supporting references are not research based? This topic clearly is an area for interdisciplinary research among nurses, physicians, and pharmacologists.

Conclusions

Regardless of the purpose of $MgSO_4$ therapy (anticonvulsant or tocolytic), the goal of treatment is to achieve a therapeutic situation without creating toxicity. Too much or too little magnesium compromises the maternal/fetal condition. Magnesium underdosing results in continued brisk reflexes or an irritable uterus. Overdosing results in diminished or absent reflexes. Because of the linear progression of magnesium toxicity, DTR assessment can be used as a tool to indicate or estimate the serum magnesium level and to decide on titration needs. Necessary interventions for hypermagnesemia include slowing the infusion, turning off the intravenous magnesium, and, if patient condition warrants, administering calcium. Although the literature provides instruction for calcium reversal, there is wide variation of protocols and they do not seem to be research based. Magnesium sulfate and calcium use would benefit from further research, allowing nurses to practice in a more evidence-based manner.

Acknowledgments

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