J Anesth (2004) 18:118–128
DOI 10.1007/s00540-003-0222-4

Journal of
Anesthesia

Review

Monitoring magnesium to guide magnesium therapy for heart surgery

Terry L. Shirey

Nova Biomedical, 200 Prospect Street, Waltham, MA 02454-9141, USA

Key words Magnesium · Ionized · Heart · Surgery

Introduction

For many years it has been recognized that magnesium levels play an important role in morbidity associated with heart surgery. However, considerable confusion exists in the literature concerning whether Mg should be administered to these patients, and, if so, how much and when. The goals of this paper are to review (1) methods used to evaluate Mg status in patients, (2) causes and consequences of abnormal Mg levels perioperatively, (3) outcome improvements and risks with Mg supplementation, and (4) guidelines for administering Mg therapy.

Methods used to evaluate Mg status in patients

Physiological indicators

Pulse, mean arterial pressure, deep tendon reflexes, hourly diuresis, respiratory recordings, and hypotension are used to monitor Mg status in patients [1]. Significant prolongation of intraatrial and atrioventricular (AV) nodal conduction times, as seen by ECG, may also reflect Mg activity [2].

Mg measurement

Total magnesium (TMg) represents the concentration of Mg present in blood plasma or serum. TMg, a measure of all of the Mg in the plasma or serum sample, equals protein-bound Mg plus ligand-bound Mg plus ionized Mg (iMg). Measurement of TMg requires the isolation of plasma (centrifugation of blood sample) or serum (clotting and centrifugation of blood sample). Measurement is made by atomic absorption spectrophotometry or colorimetry. Reference values for plasma and serum TMg typically range from 0.66 to 1.07 $mmol \cdot l^{-1}$. There is virtually no correlation between plasma/serum TMg and intracellular TMg.

Ionized magnesium (iMg = Mg^{2+}) represents the activity of unbound Mg in whole blood plasma, plasma, and/or serum. It is the physiologically active Mg fraction, i.e., the fraction to which tissues respond. Reference values typically range from 0.45 to 0.62 $mmol \cdot l^{-1}$. The fact that it can be measured in a whole blood sample by electrode produces a rapid result (<150 s) on a small sample (<200 μl). A rapid result can be very helpful for patients (1) with arrhythmia, (2) with changes in cardiac output, (3) receiving cardiovascular drugs, (4) sustaining hypoxic damage, and (5) receiving Mg therapy. Blood plasma iMg correlates with intracellular iMg and therefore represents a better indicator of Mg status than TMg. It is typically 70% of the TMg value, but varies with the protein and small ligand concentrations in the blood. The iMg value may be substantially less than 70% of the TMg value in critically ill patients where binding ligand concentrations (heparin, citrate, lactate, phosphate, bicarbonate, etc.) have increased.

Comparisons of iMg to TMg were illustrated in nine clinical settings (hypertension, acute myocardial infarction, head trauma, noninsulin-dependent diabetes, stroke, pregnancy, ischemic heart disease, cyclosporin recipients, and asthma) [3]. Ionized magnesium was found to be a better indicator of disease than TMg. In summary, iMg (1) represents the physiologically important Mg measurement, (2) is a better indicator of disease than TMg, and (3) is a more rapid measurement.

The literature should be interpreted with caution. Frequently, if not generally, the Mg values reported in

Address correspondence to: T.L. Shirey
Received: September 4, 2003 / Accepted: December 12, 2003

the literature are TMg, even though they may be reported as Mg^{2+}. Measurement of iMg has recently been made possible (early 1990s), but this does not change the fact that many recent papers reporting Mg^{2+} really mean TMg.

Causes and consequences of abnormal Mg levels perioperatively

Presurgery

Although TMg deficiency is rare in healthy subjects, 16% of 98 heart surgery patients were hypomagnesemic [4]. Kidney disease, reduced glomerular filtration rate ($<30\,ml{\cdot}min^{-1}$) [2], reduced tubular reabsorption (frequently caused by the use of diuretics), reduced oral intake, and intravenous fluids with inadequate Mg led to abnormal Mg levels in these patients. Patients receiving digoxin for heart failure had preoperative total hypomagnesemia more frequently than patients not on digoxin (36% vs 10%) [4]. A history of high-grade ventricular dysrhythmia was associated with significantly lower preoperative mean TMg [4]. Patients who may have asymptomatic hypomagnesemia presurgery may then undergo a surgical procedure that, in the perioperative period, can cause them to progress to symptomatic hypomagnesemia [5]. Hyperaldosteronism [6] and noradrenaline [7] also promote hypomagnesemia.

During surgery

The frequency of hypomagnesemia increased to 71% (71/100 patients) following cardiopulmonary bypass (CPB) surgery [8]. Several factors reduce Mg concentration during surgery. These include hemodilution from prime volume [9], chelation of iMg by heparin and acid-citrate-dextrose when donated blood is used to prime the CPB circuit [9], and intramyocyte hypoxia [10–12]. In recently introduced off-pump coronary artery bypass grafting (CABG) surgery, many patients are not receiving Mg supplementation, and, consequently, are hypomagnesemic postsurgery (TMg averaging 0.61 mM after surgery) [13]. Magnesium administration (via cardioplegia, bolus doses, and fluid supplements) can minimize Mg depletion, if not lead to hypermagnesemia, perioperatively.

Outcome improvements and risks with magnesium supplementation

Adequate Mg levels are required for normal cardiovascular activity (conduction and contraction), tissue protection from oxygen free radicals and the inflammatory response, and blood flow. Table 1 identifies improvements in outcomes following cardiac surgery when Mg supplements were used.

Table 1. Magnesium therapy improves clinical outcomes following heart surgery

- Arrhythmia reduced, with attendant reduction in morbidity and costs [5–7,14–22]
- Fewer ischemic electrocardiograph changes [19]
- Decreased postoperative hypertension [19,23]
- Decreased creatine kinase-MB isoenzyme levels [19,24]
- Increased cardiac indices [4,19,25–27]
- Reduced postoperative pain and requirement for analgesics [19]
- Increased coronary flow [25]
- Decreased coronary vasospasms [28–30]
- Prolonged neuromuscular blockade [31]
- Reduced inflammatory response [32]
- Reduced platelet function [33]
- Reduced mortality [23,34]
- Protects ischemic myocardium from Ca overload [33]
- Reduced cell necrosis from free radicals [33]
- Reduced ventilation requirement [4,8]

MB, muscle-brain

Even though Mg supplementation provides strong benefits for the cardiac patient, the risks and complications of hypermagnesemia need to be considered. Hypermagnesemia may develop from inadequate renal function or high dosage levels of supplemented Mg. CPB surgery, itself, may cause renal failure sufficient to give hypermagnesemia with Mg therapy [35].

Hypermagnesemia can cause excessive flushing, sweating, warm sensations, hypotension, and vasodilation [5]. Magnesium may act as a laxative [1]. As an anticoagulant, Mg inhibits platelet aggregation, P-selectin expression, and fibrinogen binding to platelet GP IIb/IIIa receptor in vitro [36]. The number and energy of direct-current shocks to initialize and to sustain defibrillation was greatest in patients who received Mg therapy before bypass and in those whose plasma TMg was greater than $0.93\,mmol{\cdot}l^{-1}$ [37].

Table 2 presents a rough guideline correlating Mg values and clinical observations. Mg therapy in the immediate postoperative period following cardiac surgery can result in hypotension and bradycardia [5]. In one study, St. Thomas II cardioplegia solution, containing 16 mM $MgCl_2$, was infused ($10\,ml{\cdot}kg^{-1}$ every 30 min) during aortic cross-clamping [44]. Ionized magnesium levels of $1.5–1.58\,mmol{\cdot}l^{-1}$ were noted after unclamping. After discontinuation of extracorporeal circulation, vascular resistance decreased by 40%, while 78% (14/18) of patients required atrial or ventricular pacing in order to maintain a physiological level of heart rate for obtaining better hemodynamics. The hypotension and bradycardia extended the time for extracorporeal circulation.

Table 2. Magnesium levels and clinical correlates[a]

TMg (mM)	iMg (mM)	Clinical observations
0.66–1.07	0.44–0.61	Normal range
1.5		Mild hypotension, feelings of warmth, flushed appearance, nausea and vomiting
2		Patient becomes symptomatic, muscle weakness, reduced deep tendon reflexes
2.5	1.5	Bradycardia, hypotension, electrocardiogram changes, somnolence
3.5		Loss of deep tendon reflexes
4		Respiratory compromise
5		Respiratory failure
6		Heart block, coma
7.5		Respiratory arrest
10		Cardiac arrest

TMg, total magnesium; iMg, ionized magnesium (Mg^{2+})
[a] Data obtained from multiple references: Polancic [38], Kasaoka [39], Brusco [5], Greenway [40], Springhouse [41], Burtis [42], Hoshino [43], Pages [1], Noronha [2]

Hypotension following cardiac surgery may be unresponsive to pressors [5].

Magnesium therapy also poses risk when used with other medications. In CPB patients receiving nitrate (another vasodilator) or an angiotensin-converting enzyme inhibitor, Mg therapy is not currently justified [36]. Considering that Mg is a natural calcium channel blocker, individuals with low ionized calcium levels may experience compromised contraction. Magnesium also affects the properties attributed to quinolones, tetracyclines, aminoglycosides, and vancomycin [1]; neuromuscular blocking agents; and volatile anesthetics [19].

Guidelines for administering Mg therapy

Magnesium supplementation is generally considered to be safe and has resulted in few side effects [2]. While there is documentation for people/equipment-related overdoses, inadequately functioning kidneys pose the most serious risk. Consequently, it is recommended that kidney function be assessed prior to the use of Mg therapy [2]. Outcomes may differ depending on the variables that follow, making it very difficult to tie outcomes to Mg therapy based on dosage and timing considerations.

Mg salt

Many reports in the literature quantify the magnesium salt used in grams. Considering that multiple hydrates of Mg salts are available, the molar concentrations of Mg administered should always be stated. $MgSO_4$ is the traditional formulation used in cardioplegic solutions and i.v. bolus infusions [1]. $MgCl_2$ provides higher bioavailability than other commercial Mg preparations [45]. It is more advantageous pharmacologically and toxicologically than $MgSO_4$ [1], and it avoids the reduction of Ca^{2+} seen with the use of $MgSO_4$ [46]. Mg-ATP improves organ blood flow, microcirculation, energy balance, and immune competence, leading to survival. It is a fast-acting vasodilator used for the management of acute pulmonary hypertensive crises, for maintenance of blood pressure during aortic cross-clamping, and as a therapeutic adjunct in patients with multiple organ failure [47]. It has been shown to improve organ function and survival time in a variety of animal models of oligemic shock, ischemia, and sepsis, and in human volunteers and patients with shock [48]. Mg oxide is better absorbed from the intestine than other commonly available compounds for oral Mg repletion [49].

Routes of Mg administration

Oral Mg therapy may be used to maintain Mg levels under conditions associated with chronic Mg loss, e.g., use of diuretics [2]. It resulted in arterial pressure decreasing from 91 to 87 mm Hg, and a significant reduction in all classes of arrhythmia (VPBs, couplets, and nonsustained ventricular tachycardia) [50,51]). Taking 16 mmol $MgCl_2 \cdot day^{-1}$ (~400 mg elemental Mg) orally as tablets raised TMg from 0.87 mM to 0.92 mM after 6 weeks, and was accompanied by a large increase in urine excretion [50].

Intravenous Mg therapy provides greater bioavailability than oral Mg therapy [52], acutely increasing intracellular Mg levels [53]. While a 30-mmol oral dose of Mg gave a 4.4% increase in TMg (0.91 to

0.95 mM) and a 6.3 % increase in iMg (0.48 to 0.51 mM) 2 h after ingestion, 15 mmol of Mg by i.v. gave a 50% increase in TMg (0.88 to 1.32 mM) and a 44% increase in iMg (0.48 to 0.69 mM) at 4 h [52].

Cardioplegia solution with 15 mM Mg offered maximum recovery of myocardial function after an ischemia-reperfusion sequence. This is the concentration used in the St. Thomas II cardioplegia solution [53]. Using three cardioplegia solutions (3–4 mM Mg, 8–10 mM Mg, and 16–18 mM Mg), it was found that the 8- to 10-mM Mg cardioplegia solution yielded higher auto-resuscitation following surgery, shorter mechanical ventilation, shorter intensive care unit (ICU) stays, and the lowest creatine kinase MB isoenzyme (CK-MB) and troponin I levels [54]. The addition of Mg to warm blood cardioplegia resulted in a lower incidence of intraoperative and postoperative arrhythmias in patients undergoing urgent CABG for unstable angina [55].

Intramuscular Mg therapy, by attaining a higher and more sustained serum Mg concentration, converted multifocal atrial tachycardia to normal sinus rhythm more rapidly (1–2 h) than i.v. Mg therapy (4–8 h) [56].

Speed of Mg infusion

The pharmacologic effect of supplemented Mg is quite rapid, while the replenishment of body stores is much more gradual and slow [57]. Slower infusions (32–48 mmol $Mg \cdot 24\,h^{-1}$) are appropriate unless cardiac arrhythmias or seizures are present [2]. Usually, at least 50% of an infused dose is wasted in the urine, even in patients who are profoundly Mg-depleted [5]. Replacement over 12–24 h will cause the plasma level of Mg to exceed Tmax (plasma TMg ~1.2 mM, the plasma level at which the kidney tubule resorbs less Mg from the glomerular filtrate) less often and will lead to less wasting [5]. Eight millimole Mg by i.v. over 1–2 min, followed by an additional 40 mmol over the next 5 h, is considered safe and probably effective for arrhythmias [2].

In patients with normal renal function it is very difficult to induce hypermagnesemia with commonly used regimens. Treatment of mild hypomagnesemia with 50 ml of 4 mmol $MgSO_4$ over 1 h or 25 mmol $MgSO_4$ over 6 h was acceptable [5]. For severe hypomagnesemia (life-threatening emergencies with known hypomagnesemia complicated by seizures, unremitting cardiac dysrhythmias, etc.), 8–12 mmol Mg over 5–10 min was found acceptable [5]. Rapid administration of Mg preparations can cause excessive flushing, sweating, warm sensations, hypotension, and vasodilation [5].

Timing of Mg infusion perioperatively

Preoperative Mg supplementation protects the heart from anoxic and toxic challenges [14]. Preoperative treatment of patients undergoing mitral valve replacement with a slow-releasing oral $MgCl_2$ showed a decrease in dysrhythmias postoperatively [5]. Extreme caution should be employed when Mg is given in combination with drugs that act synergistically, such as nitrates.

Intraoperative Mg infusion is as effective as preoperative infusion in decreasing the rate of new-onset atrial fibrillation [7]. Cardioplegia containing Mg yielded CABG patients with higher Mg levels, fewer ischemic ECG changes, and fewer ventricular arrhythmias postoperatively [19].

Postoperative Mg supplementation for several days may be used to maintain Mg levels. This may be important, considering that atrial arrhythmias frequently occur 2–3 days following surgery. One recommendation for postoperative Mg supplementation is 48 mmol for the first 24 h postsurgery, followed by 12 mmol of $Mg \cdot day^{-1}$ for the next 3 days (provided that kidney function is adequate; i.e., creatinine $<2\,mg \cdot dl^{-1}$). Monitoring TMg daily is recommended [19].

Dynamics of serum/plasma Mg perioperatively

Plasma Mg levels decrease during heart surgery. With no Mg supplementation, 18% (18/99) of patients were hypomagnesemic (TMg <0.80 mM) preinduction, going to 71% (71/100) following CPB [8]. Table 3 describes several studies in which TMg was measured at various times over the perioperative course when no Mg was administered. Five studies giving preoperative TMg values and those measured 1 day after surgery suggest that the median TMg decrease is 27%, ranging from 13% to 34% [4,15,24,60,61]. The lowest serum/plasma TMg values are generally seen after surgery and on day 1 postsurgery, gradually returning to their normal ranges over the next several days. Ionized magnesium activity also drops during surgery, but recovers more quickly than TMg after surgery, returning to its normal range within 48 h [31,62].

Perioperative plasma Mg levels depend on the dosage and timing of Mg supplements. Table 3 tracks TMg in patients receiving Mg supplements. Predictably, TMg values obtained on the day of surgery will depend on the amount of Mg administered, when it was administered, and when samples were obtained (e.g., after CPB, ICU entry). Dose regimens in Table 3 include best estimates from the articles cited, including Mg present in cardioplegia solutions (volumes delivered) and molar estimates when solutions were reported in terms of grams of salt used (neglecting to mention water of hydration). Values obtained on the days following surgery will depend on the Mg status preoperatively, Mg administered during surgery, and on subsequent additions. Without the addition of Mg postsurgery, TMg levels were lower the day after surgery [4].

Table 3. TMg (mM) levels following various dose regimens of magnesium therapy

Dose regimen	Preop	After CPB	ICU entry	Day 1	Day 2	Day 4	Reference
No Mg therapy	0.84		0.58	0.57			England [4]
No Mg therapy	0.95	0.58		0.63	0.72	0.93	Fanning [15]
No Mg therapy	0.82	0.56		0.67			Harris [58]
No Mg therapy	0.82	0.74		0.71	0.74	0.9	Karmy-Jones [24]
No Mg therapy	0.81			0.59			Togashi [59]
~10 mmol? (2 g MgCl2) bolus after CPB	0.84		0.85	0.68			England [4]
~16 mmol by end of surgery		1.12		0.87			Harris [58]
~16 mmol·day^{-1} for 14 days				1.03	1.03	1.03	Van den Bergh [60]
~22 mmol over day 1 + 6 mmol over day 2	0.82		0.98	1	0.87		Wistbacka [35]
~30 mmol·day^{-1} for 14 days				1.1	1.1	1.1	Van den Bergh [60]
~48 mmol·24 h^{-1} (+12 mmol·day^{-1} for 3 days)	0.95	0.61		1.22	1.15	1.04	Fanning [15]
~60 mmol·24 h^{-1} (6–9.6 mmol boluses)	0.82	1.1		1.49	0.96	0.9	Karmy-Jones [24]
~64 mmol·day^{-1} for 14 days				1.38	1.38	1.38	Van den Bergh [60]
~86 mmol over day 1 + 27 mmol over day 2	0.82		1.5	1.6	1.2		Wistbacka [35]

CPB, cardiopulmonary bypass; preop, preoperative; ICU, intensive care unit

Urine Mg levels rose in all patients following CPB no matter when or if they received supplementary Mg [61]. Subjects with normal Mg balance and renal function excrete most of a parenterally administered Mg load within 24 h [2].

Plasma TMg does not correlate with myocardial TMg. Hypomagnesemia predated decreases in myocardial TMg by 2 to 6 weeks in patients with heart failure who commonly have persistent hypomagnesemia. Repletion of myocardial TMg occurred some weeks later than normalization of serum TMg levels [63]. Low myocardial TMg may contribute to the high incidence of fatal arrhythmic events [11]. Myocardial TMg is lower in patients with postoperative arrhythmia compared to those without arrhythmia [7]. Myocardial calcium levels are particularly high in Mg-depleted subjects [63].

Dose-time approach to guiding Mg therapy

Table 4 illustrates observations of arrhythmias, made by several authors who related their findings to dose and time of Mg administration. The studies included in Table 4 were chosen because each made mention of a TMg measurement either on the day of surgery or the day following, giving more information than simply dose and time. Generally, the incidence and intensity of the arrhythmias decreased with increasing Mg levels. A general impression one gets from the literature is that ventricular arrhythmias are of greater concern for the first 24 h after surgery, while atrial arrhythmias tend to develop during the second and third postoperative days [6,7,19,20,66]. While higher levels of Mg supplementation favorably reduce the danger of arrhythmias, bradycardia may become a concern [35].

In some dose-time studies, Mg supplementation was made via cardioplegia, only. Cardioplegia solution that was 15 mM in $MgSO_4$ reduced the ischemic electrocardiographic changes, the frequency of ventricular ectopia, and the number of patients with ventricular arrhythmia relative to the control group. Atrial fibrillation occurred in 5/25 patients receiving Mg, compared to 8/25 not receiving Mg [16]. The addition of Mg to warm blood cardioplegia resulted in a lower incidence of intraoperative and postoperative arrhythmias [55].

An interoperative bolus of 2 g $MgCl_2$ (value in millimoles not given) in 100 ml normal saline, given over 30 min after termination of CPB, halved the frequency of postoperative ventricular dysrhythmias. It also increased the stroke volume, and thereby the cardiac index, in the early postoperative period. Magnesium therapy also reduced the need for drugs to combat arrhythmias, and shortened the time patients spent on respirators [4]. Magnesium, given before cardioversion in patients suffering atrial arrhythmias following mitral and/or aortic valve surgery, diminished repolarization abnormalities and ventricular arrhythmias [67].

An 8 mmol bolus of Mg after surgery reduced ventricular ectopia and lowered its grade, as categorized by a modified Lown classification [65].

Intravenous Mg delivery during surgery and for the first 24 h after surgery [23] reduced ventricular arrhythmias and helped control hypotension. Fifty patients, receiving 16 mmol $MgSO_4$ by i.v. from induction to aortic cross-clamping and a second dose (32 mmol) starting at release of cross-clamp until 24 h later, were

Table 4. Comparing magnesium dosage, TMg values, and arrhythmias

Mg dose/time	TMg (mM)	Arrhythmia	References
No Mg therapy		AF 26% (27/102) at a mean of 2.7 days po	Zaman [6]
No Mg therapy	0.58 (Day after Sx)	Ventricular dysrhythmia: 34% (17/50)	England [4]
No Mg therapy	0.70 (Day after Sx)	Ventricular tachyarrhythmia: 52% VT episodes/patient: 1.4	Karmy-Jones [24]
No Mg therapy		Atrial tachyarrhythmia: 38%	Bert [64]
No Mg therapy	0.62 (Day after Sx)	Atrial arrhythmia: 45 episodes/50 patients	Fanning [15]
No Mg therapy	0.65 (Day after Sx)	Ventricular arrhythmia: 63%	Harris [58]
No Mg therapy	0.69 (Day after Sx)	Higher requirement for internal defibrillation AF: 34%	Yeatman [55]
~8 mmol bolus after Sx		Ventricular ectopia: marked reduction to lower grade	Yurvati [65]
~10 mmol? (2 g $MgCl_2$) bolus after CPB	0.86 ICU entry 0.68 (Day after Sx)	Ventricular dysrhythmia: 16% (8/50)	England [4]
~12 mmol over day 1		Atrial tachyarrhythmia: 38%	Bert [64]
(Mg in cardioplegia, dose not calculated)	0.80 (Day after Sx)	Lower requirement for internal defibrillation AF: 19%	Yeatman [55]
~16 mmol by end of surgery	1.12 End of CPB 0.87 (Day after Sx)	Ventricular arrhythmia: 22%	Harris [58]
~20 mmol bolus	1.28 End of bolus		Pinard [31]
~22 mmol over day 1 + 6 mmol over day 2	1.0 (Day after Sx)	VF: 10% (4/40) and 5/40 needed temp. pacemaker Vent. ectopic beats during 1st 24 h: 71% (27/38) AF: 25% (10/40) over 48 h po AF episodes: 4% (18/40) had 41 during 1st po week Bradycardia: 5% (2/40) req. pacemaker w/i 24 h	Wistbacka [35]
~48 mmol/24 h (+12 mmol·day^{-1} for 3 days)	1.22 (Day after Sx)	Atrial arrhythmia: 12 episodes/49 patients	Fanning [15]
~60 mmol/24 h (6–9.6 mmol boluses)	1.09 Postoperative 1.49 (Day after Sx)	Ventricular tachycardia: 17% VT episodes/patient: 0.3	Karmy-Jones [24]
~86 mmol over day 1 + 27 mmol over day 2	1.60 (Day after Sx)	VF: 2% (1/41) Vent. ectopic beats during 1st 24 h: 43% (17/40) AF: 7% (3/41) over 48 h po AF episodes: 24% (10/41) had 19 during 1st po week Bradycardia: 17% (7/41) req. pacemaker w/i 24 h	Wistbacka [35]

Sx, surgery; AF, atrial fibrillation; VT, ventricular tachycardia; VF, ventricular fibrillation; po, postoperative; temp., temporary; vent., ventricular; req., required; w/i, within

compared to 48 control patients who received no Mg. The patients receiving Mg had a lower incidence of ventricular arrhythmias (2% [1/50] vs 29% [14/48]) and were hypotension-free more frequently (4% [2/50] vs 33% [16/48]) [23].

Continuous Mg infusion after surgery (no Mg in cardioplegia or prime) reduces atrial fibrillation. It was shown that 48 mmol Mg over the first 24 h followed by 12 mmol·day^{-1} for the next 3 days reduced the number and severity (requiring less cardioversion and multiple drug intervention) of episodes of atrial fibrillation, with no recognized adverse effects [15].

Mg supplementation along with other drugs may alter clinical effects. Magnesium infusion with low doses of lidocaine is more effective for ventricular arrhythmia than lidocaine alone [1]. Magnesium and a low-dose beta-blocker were key to an aggressive atrial fibrillation prophylaxis regimen, cutting the atrial fibrillations in half (20% to 10%) [68]. Administration of $MgSO_4$, resulting in iMg levels of 1.3 mM, prolonged neuromuscular blockade by 30–35 min (from 42 to 74 min) using cisatracurium [31].

Risks associated with the dose-time approach to guiding Mg therapy

Perioperative Mg levels depend on the Mg status of the patient preoperatively, the amount of Mg administered, the rate of Mg delivery, kidney function, hemodilution, binding ligands, pH, and intraoperative hypoxia. Outcomes appear to depend on Mg levels at specific times over the postoperative period, making it difficult to predict outcomes from Mg therapy solely on dosage and timing.

Contradictory dose-time outcomes have been documented. For example, one study reports that, of 100 patients receiving 12 mmol $MgSO_4$ over 2 h preoperatively, perioperatively, and on postoperative days 0, 1, 2, and 3, 15% developed atrial fibrillation. Of the 100 patients not receiving the $MgSO_4$, 16% also developed atrial fibrillation. This led to the conclusion that Mg infusion alone was not sufficient for the prophylaxis of atrial fibrillation [69]. Another study reports that 100 patients who received 6 mmol $MgSO_4$ in 100 ml of 0.9% NaCl solution over 4 h the day before surgery, just before CPB, and once daily for 4 days after surgery, were compared to 100 control patients who received the saline solution only. Intermittent 16-mM Mg cardioplegia was given to both the Mg and the control patients. Of the patients in the Mg group, 2% (2/100) had postoperative atrial fibrillation; 21% (21/100) had atrial fibrillation in the control group. It was concluded that the use of Mg in the preoperative and early postoperative periods is highly effective in reducing the incidence of atrial fibrillation after CABG [7].

Other evidence demonstrates that the dose-time approach to Mg therapy may be inadequate. The efficacy of Mg therapy for ventricular arrhythmias has been debated [1,15]. In addition, the prevention of atrial fibrillation could not be attained with only routine (dose-time) administration of $MgSO_4$ [69].

Monitoring TMg as an approach to guiding Mg therapy

Giving Mg supplements before or during CPB surgery, or not giving it at all, did not affect the incidence of arrhythmias and ventricular fibrillation after aortic unclamping; however, the plasma TMg levels did [19]. Even then, the correlation between serum TMg levels and clinical outcomes is poor [7,70], in part because a normal serum Mg level may coexist with tissue Mg deficiency [7]. Clinical signs of hypomagnesemia lag considerably behind falling total serum levels. Therefore, early treatment of serum Mg changes may be important in preventing or reducing clinical dysfunction [71].

Table 5 suggests that once TMg drops near the lower limit of its reference range (~0.75 mmol·l^{-1}), the frequency of atrial and supraventricular arrhythmias increases dramatically. The combination of signal-averaged P wave duration before surgery, along with low serum TMg on the first postoperative day, identified the majority of patients with atrial fibrillation after coronary artery bypass surgery [6]. Of the patients with lower TMg (<0.8 mM) persisting into day 1 (66% of patients), 35% (22/63) required prolonged ventilatory

Table 5. Arrhythmias develop at lower TMg concentrations

Postop TMg (mM)	Arrhythmia	References
>0.74	2.66 × the risk of atrial fibrillation (AF)	Kaplan [69]
0.72 ± 0.02 On day 1	Patients in whom AF developed	Yeatman [55]
0.76 ± 0.02 On day 1	Patients in whom AF did not develop	
<0.75 Postoperative	Supraventricular dysrhythmia: 37% (19/52)	England [4]
>0.75 Postoperative	Supraventricular dysrhythmia: 17% (8/48)	
<0.80 Postoperative	Atrial dysrhythmia: 31% (22/71)	Aglio [8]
>0.80 Postoperative	Atrial dysrhythmia: 10% (3/29)	

support (mechanical ventilation >24 h after surgery), in contrast to 12% (4/33) of the normomagnesemic patients [4,8]. Maintaining TMg between 1.5 and 3.0 mmol·l^{-1} is generally considered to be the level required to prevent and treat arrhythmia [31]. Only 4% (2/50) of patients with high Mg administration (TMg > 2 mM) had ventricular arrhythmias [23].

Monitoring iMg as an approach to guiding therapy

Magnesium therapy during CPB should be based on iMg rather than TMg values [36,72]. Postoperatively, Mg supplementation should be continued despite normal serum TMg levels, because iMg hypomagnesemia may occur [19]. A large drop in iMg (but not in TMg) 24 h after CPB was seen in patients receiving 16 mM $MgCl_2$ at bypass. The iMg drop correlated highly with preoperative iMg ($r = 0.96$) [73]. In addition, the risk of hypermagnesemia from giving Mg to heart patients with kidney disease (e.g., creatinine >2 mg·dl^{-1}) might be reduced with careful monitoring of iMg.

Samples ($n = 237$), collected from 31 patients before, during, and after cardiac surgery, during which Mg-containing cardioplegia was used, were monitored for both TMg and iMg [74]. Scatter about the regression line between iMg and TMg (Sy·x = 0.0914) suggested that the iMg value could vary between 0.54 and 0.92 mM in patients having a TMg value of 1.0 mM. In some instances, even greater differences were noted (e.g., in one sample, iMg was 0.3 mM and TMg was 1.1 mM). It was suggested that the scatter about the regression line reflects the differences in Mg bound to protein and small ligands from sample to sample. Most of the samples with elevated iMg had values ranging from 0.7 to 1.1 mM; 3% (7/237) of samples were in the 1.2- to 1.3-mM range. The slope of the least-squares line comparing iMg to TMg was 0.71; suggesting that, on average, 71% of the Mg in the samples was unbound (ionized). Interestingly 2 of the 31 patients maintained a high iMg/TMg ratio for all samples following the addition of the cardioplegia, while 1 of the 31 maintained a low iMg/TMg ratio. As time progressed, both sets of Mg values (iMg and TMg) dropped, but, surprisingly, maintained either continuously high or low iMg/TMg ratios for each of the 3 patients. These 3 patients illustrate that iMg and TMg cannot be used interchangeably. It is not clear whether or not the iMg/TMg ratio may suggest the underlying Mg status in the patients.

Of 186 pediatric patients undergoing congenital cardiac surgery augmented with Mg in cardioplegia, 34% had low iMg (2 SD below the mean of the age-adjusted reference range) before surgery, 40% during CPB (particularly during cooling), 30% post-CPB, and 21% on admission to the ICU. Intraoperative ionized hypomagnesemia was more prevalent in patients who took furosemide before surgery. Patients with low iMg had higher mean lactate levels and required 1.65 × the mechanical ventilation time of normomagnesemic patients. Low-iMg patients had longer cardiac ICU (CICU) stays that correlated most strongly with presurgical iMg values. Among the 14 patients who died during hospitalization, 12 (86%) had ionized hypomagnesemia during CPB [9,75].

In one study, cardioplegia (St. Thomas II cardioplegia solution) containing 16.0 mmol·l^{-1} of $MgCl_2$ was infused at 10 ml·kg^{-1} every 30 min during aortic cross-clamping into 18 patients. This amounted to an average of 38 ± 9 mmol of Mg administered per patient. For the first 20 min after unclamping, iMg values averaged around 1.55 mM (ranging from 1.2 to 2.0 mM). Vascular resistance dropped by 40%, and 14/18 patients required atrial or ventricular pacing. Hypotension and bradycardia after unclamping delayed weaning from extracorporeal circulation. It was concluded that monitoring iMg was needed to avoid side effects of a high Mg concentration when Mg-rich cardioplegia solutions were used [44].

Reflections and recommendations

The dynamics of Mg metabolism suggest that myocytes store Mg, 90% to 99+% of which is bound to ATP, protein, and other ligands in the cytosol. Intracellular iMg, the remaining small percentage of the intracellular TMg, may pass through the cell membrane, and appears to establish equilibrium with extracellular iMg over a time span of minutes to hours, depending on the intra- to extracellular iMg gradient [3]. Chronic Mg wasting presurgery would result in low levels of intracellular TMg. An acute decrease in blood plasma iMg during cardiac surgery would reduce further the intracellular iMg. An acute bolus of Mg from supplementation would start to reverse the intracellular loss, but the kidneys rapidly void much of the added Mg. Unless the intracellular shortage of Mg is made up over the time following surgery (days), intracellular Mg may remain low. This could explain why extracellular Mg might drop, even after bolus Mg supplementation. Reduced myocardial iMg likely plays a major role in the clinical consequences following cardiac surgery.

A target range for plasma iMg, which should provide therapeutic value without significant risk during the time surrounding heart surgery, might be 0.60–1.0 mmol·l^{-1}. This range is based on the following considerations: (1) the clinical observations detailed in Tables 2, 4, and 5 are reported as a function of TMg, (2) on average, iMg in 70% of the TMg value, (3) iMg is a more clinically relevant value than TMg, (4) there is a delay in intracellular iMg equilibration with plasma

iMg, and (5) plasma iMg changes with time. The suggested range needs to be confirmed

Summary

Many factors affect the activity of the physiologically important ionized Mg fraction, iMg, in patients who undergo heart surgery. These factors include the use of diuretics before surgery; hemodilution, binding ligands, and hypoxia introduced during surgery; and the administration of Mg via pump prime, cardioplegia, or injection perioperatively. The consequences of abnormal Mg in these patients range from arrhythmia and respiratory complications when the patients are hypomagnesemic, to hypotension and bradycardia when they are hypermagnesemic.

While Mg supplements are helpful for these patients, their clinical effects are best predicted by measurements of blood plasma iMg rather than by dosing schedules.

References

1. Pages N, Guiet-Bara A, Bac P, Bara M, Dupont C, Durlach J (2001) Pharmacological properties and indications of magnesium. In: Rayssiguier Y, Mazur A, Durlach J (eds) Advances in magnesium research: nutrition and health. John Libbey, Eastleigh, England, pp 453–458
2. Noronha JL, Matuschak GM (2002) Magnesium in critical illness: metabolism, assessment, and treatment. Intensive Care Med 28: 667–679
3. Shirey TL (2000) Ionized magnesium (iMg): clinical importance and measurement [1]. Life Support and Anesthesia 7:265–270
4. England MR, Gordon G, Salem M, Chernow B (1992) Magnesium administration and dysrhythmias after cardiac surgery. JAMA 268:2395–2402
5. Brusco L (1994) Magnesium homeostasis in the operating room and intensive care unit. In: Eisenkraft JB (ed) Progress in anesthesiology VIII, chapter 3. WB Saunders, Philadelphia, pp 47–56
6. Zaman AG, Alamgir F, Richens T, Williams R, Rothman MT, Mills PG (1997) The role of signal averaged P wave duration and serum magnesium as a combined predictor of atrial fibrillation after elective coronary bypass surgery. Heart 77:527–531
7. Toraman F, Karabulut EH, Alhan HC, Dagdelen S, Tarcan S (2001) Magnesium infusion dramatically decreases the incidence of atrial fibrillation after coronary artery bypass grafting. Ann Thorac Surg 72:1256–1262
8. Aglio LS, Stanford GG, Maddi R, Boyd JL, Nussbaum S, Chernow B (1991) Hypomagnesemia is common following cardiac surgery. J Cardiothorac Vasc Anesth 5:201–208
9. Munoz R, Laussen PC, Palacio G, Zienko L, Piercy G, Wessel D (2000) Whole blood ionized magnesium: age-related differences in normal values and clinical implications of ionized hypomagnesemia in patients undergoing surgery for congenital cardiac disease. J Thorac Cardiovasc Surg 119:891–898
10. Kirkels JH, van Echteld CJA, Ruigrok TJC (1989) Intracellular magnesium during myocardial ischemia and reperfusion: possible consequences for postischemic recovery. J Mol Cell Cardiol 21: 1209–1218
11. Millane TA, Ward DE, Camm AJ (1992) Electrophysiology, pacing, and arrhythmia: is hypomagnesemia arrhythmogenic? Clin Cardiol 15:103–108
12. Satur CMR, Anderson JR, Jennings A, Newton K, Martin PG, Unikrishnan N, Walker DR (1994) Magnesium flux caused by coronary artery bypass operation: three patterns of deficiency. Ann Thorac Surg 58:1674–1678
13. Huss MG, Wasnick JD (1999) Magnesium and off-pump coronary artery bypass. J Cardiothorac Vasc Anesth 13:374–375
14. Birch RFH, Lake CL (1991) Magnesium therapy in cardiac surgery: Pro: magnesium is a valuable therapy in the cardiac surgical patient. J Cardiothorac Vasc Anesth 5:518–521
15. Fanning WJ, Thomas CS, Roach A, Tomichek R, Alford WC, Stoney WS (1991) Prophylaxis of atrial fibrillation with magnesium sulfate after coronary artery bypass grafting. Ann Thorac Surg 52:529–533
16. Shakerinia T, Ali IM, Sullivan JA (1996) Magnesium in cardioplegia: is it necessary? Can J Surg 39:397–400
17. Dorman BH, Sade RM, Burnette JS, Wiles HB, Pinosky ML, Reeves ST, Bond BR, Spinale FG (2000) Magnesium supplementation in the prevention of arrhythmias in pediatric patients undergoing surgery for congenital heart defects. Am Heart J 139:522–528
18. Roscoe A, Ahmed AB (2003) A survey of peri-operative use of magnesium sulphate in adult cardiac surgery in the UK. Anaesthesia 58:363–365
19. Gomez MN (1998) Magnesium and cardiovascular disease. Anesthesiology 89:222–240
20. Soucier RJ, Mirza S, Abordo MG, Berns E, Dalamagas HC, Hanna A, Silverman DI (2001) Predictors of conversion of atrial fibrillation after cardiac operation in the absence of Class I or III antiarrhythmic medications. Ann Thorac Surg 72:694–698
21. Creswell LL, Schuessler RB, Rosenbloom M, Cox JL (1993) Hazards of postoperative atrial arrhythmias. Ann Thorac Surg 56:539–549
22. Lowe JE, Hendry PJ, Hendrickson SC, Wells R (1991) Intraoperative identification of cardiac patients at risk to develop postoperative atrial fibrillation. Ann Surg 213:388–392
23. Caspi J, Rudis E, Bar I, Safadi T, Saute M (1995) Effects of magnesium on myocardial function after coronary artery bypass grafting. Ann Thorac Surg 59:942–947
24. Karmy-Jones R, Hamilton A, Dzavik V, Allegreto M, Finegan BA, Koshal A (1995) Magnesium sulfate prophylaxis after cardiac operations. Ann Thorac Surg 59:502–507
25. Altura BT, Altura BM (1991) Measurement of ionized magnesium in whole blood, plasma and serum with a new ion-selective electrode in healthy and diseased human subjects. Magnes Trace Elem 10:90–98
26. Reynolds TR, Geffin GA, Titus JS, O'Keefe DD, Daggett WM (1989) Myocardial preservation related to Mg content of hyperkalemic cardioplegic solutions at 8°C. Ann Thorac Surg 47:907–913
27. Storm W, Zimmerman JJ (1997) Magnesium deficiency and cardiogenic shock after cardiopulmonary bypass. Ann Thorac Surg 64:572–577
28. Sjogren A, Edvinsson L, Fallgren B (1989) Magnesium deficiency in coronary artery disease and cardiac arrhythmias. J Intern Med 226:213–222
29. Finlayson DC (1991) Mg: its time has come. J Cardiothorac Vasc Anesth 5:199–200
30. Altura BM, Altura BT (1995) Magnesium and cardiovascular biology: an important link between cardiovascular risk factors and atherogenesis. Cell Mol Biol Res 41:347–359
31. Pinard AM, Donati F, Martineau R, Denault AY, Taillefer J, Carrier M (2003) Magnesium potentiates neuromuscular blockade with cisatracurium during cardiac surgery. Can J Anaesth 50:172–178
32. Rayssiguier Y, Malpuech C, Nowacki W, Rock E, Gueux E, Mazur A (1997) Inflammatory response in magnesium deficiency. In: Smetana R (ed) Advances in magnesium research. John Libbey, London, pp 415–421

33. Benzer W (1997) Significance of supraphysiologic administration of magnesium after myocardial infarct. Wien Klin Wochenschr Suppl 2:38–41
34. Brown PS, Holland FW, Parenteau GL, Clark RE (1991) Magnesium ion is beneficial in hypothermic crystalloid cardioplegia. Ann Thorac Surg 51:359–366
35. Wistbacka J-OM, Koistinen J, Karlqvist KEV, Lepojarvi MVK, Hanhela R, Laurila J, Nissinen J, Pokela R, Salmela E, Ruokonen A, Nuutinen LS (1995) Magnesium substitution in elective coronary artery surgery: a double-blind clinical study. J Cardiothorac Vasc Anesth 9:140–146
36. Grigore AM, Mathew JP (2000) Con: magnesium should not be administered to all coronary artery bypass graft surgery patients undergoing cardiopulmonary bypass. J Cardiothorac Vasc Anesth 14:344–346
37. Hecker BR, Lake CL, Kron IL, Mentzer RM, Crosby IK, Nolan SP, Crampton RS (1985) Influence of magnesium ion on human ventricular defibrillation after aortocoronary bypass surgery. Am J Cardiol 55:61–64
38. Polancic JE (1991) Magnesium: metabolism, clinical importance, and analysis. Clin Lab Sci 4:105–108
39. Kasaoka S, Tsuruta R, Inoue T, Yamamoto M, Ueda S, Sadamitsu D, Tateishi A, Maekawa T (1994) Evaluation of a new ion selective electrode for ionized magnesium. J Jpn Soc Inten Care Med 2:119–121
40. Greenway DC, Hindmarsh JT, Wang J, Khodadeen JA, Hebert PC (1996) Reference interval for whole blood ionized magnesium in a healthy population and the stability of ionized magnesium under varied laboratory conditions. Clin Biochem 29:515–520
41. Springhouse (1997) Fluids and electrolytes made incredibly easy. Springhouse Corp., Springhouse, PA, p 123
42. Burtis CA, Ashwood ER (1999) Tietz textbook of clinical chemistry (3rd edn). WB Saunders, Philadelphia, p 1825
43. Hoshino K, Ogawa K, Hishitani T, Kitazawa R (2001) Characteristics of improved NOVA magnesium ion-selective electrode: changes of ionized magnesium values and reference interval in healthy children. Magnes Res 14:203–210
44. Ohashi Y, Uchida O, Kuro M (1996) The effect of magnesium rich cardioplegic solution upon blood ionized magnesium level during open heart surgery. Anesthesiology 85(3A):A138
45. Rodrigues-Moran M, Guerrero-Romero F (2003) Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects. Diabetes Care 26:1147–1152
46. Wilson RF, Binkley L, Sabo FM, Wilson JA, Munkarah MM, Dulchavsky SA, Diebel LN (1992) Electrolyte and acid-base changes with massive blood transfusions. Am Surg 58:535–545
47. Nalos M, Asfar P, Ichai C, Rademacher P, Leverve XM, Froba G (2003) Adenosine triphosphate-magnesium chloride: relevance for intensive care. Intensive Care Med 29:10–18
48. Soliman HM, Mercan D, Lobo SSM, Melot C, Vincent J-L (2003) Development of ionized hypomagnesemia is associated with higher mortality rates. Crit Care Med 31:1082–1087
49. Salem M, Munoz R, Chernow B (1991) Hypomagnesemia in critical illness: a common and clinically important problem. Crit Care Clin 7:225–252
50. Bashir Y, Sneddon JF, Staunton HA, Haywood GA, Simpson IA, McKenna WJ, Camm AJ (1993) Effects of long-term oral magnesium chloride replacement in congestive heart failure secondary to coronary artery disease. Am J Cardiol 72:1156–1162
51. Feyertag J, Laimer H, Herglotz P, Douglas T, Boettcher E, Ekmekcioglu C, Marktl W (1995) Effect of an oral magnesium supplementation on magnesium status and on ventricular arrhythmias. Magnes Res 8[Suppl 1]:27–28
52. Meludu SC, Castillo MJ, Scheen AJ, Lefebvre PJ (1995) Magnesium retention tests: marked differences in intravenous and oral magnesium administration. Magnes Res 8[Suppl 1]:52
53. Boyd WC, Thomas SJ (2000) Pro: magnesium should be administered to all coronary artery bypass graft surgery patients undergoing cardiopulmonary bypass. J Cardiothorac Vasc Anesth 14:339–343
54. Ji B, Feng Z, Liu J, Long C (2002) Myocardial protection related to magnesium content of cold blood hyperkalemic cardioplegic solutions in CABG. J Extra Corpor Technol 34:107–110
55. Yeatman M, Caputo M, Narayan P, Lotto AA, Ascione R, Bryan AJ, Angelini GD (2002) Magnesium-supplemented warm blood cardioplegia in patients undergoing coronary artery revascularization. Ann Thorac Surg 73:112–118
56. Cohen L, Kitzes R, Shnaider H (1995) Mg in cardiac arrhythmias—digoxin-induced non-paroxysmal atrioventricular junctional tachycardia and multifocal atrial tachycardia responsive to parenteral magnesium sulphate. Magnes Res 8[Suppl 1]:18
57. Foley C, Zaritsky A (1998) Should we measure ionized magnesium? Crit Care Med 26:1949–1950
58. Harris MNE, Crowther A, Jupp RA, Aps C (1988) Magnesium and coronary revascularization. Br J Anaesth 60:779–783
59. Togashi H, Kasuda H, Inoue S, Hotta Y, Fukuda H (1997) Serum and urinary magnesium during and after cardiac surgery. Masui 46:1336–1341
60. Van den Bergh WM, Albrecht KW, Berkelbach Van Der Sprenkel JW, Rinkel GJ (2003) Magnesium therapy after aneurysmal subarachnoid haemorrhage: a dose-finding study for long term treatment. Acta Neurochir 145:195–199
61. Skerrett PJ (1992) Magnesium touted for preventing arrhythmia complications following open heart surgery. Anesthesiology News 5:22
62. Hoshino K, Ogawa K, Hishitani T, Kitazawa R (2003) Influence of heart surgery on magnesium concentrations in pediatric patients. Pediatr Int 45:39–44
63. Millane T (1993) Studies of magnesium in heart transplantation: further insights into magnesium and cardiac physiology. Magnes Res 6:361–368
64. Bert AA, Reinert SE, Singh AK (2001) A beta-blocker, not magnesium, is effective prophylaxis for atrial tachyarrhythmias after coronary artery bypass graft surgery. J Cardiothorac Vasc Anesth 15:204–209
65. Yurvati AH, Sanders SP, Dullye LJ, Carney MP, Archer RL, Koro PP (1992) Antiarrhythmic response to intravenously administered magnesium after cardiac surgery. South Med J 85:714–717
66. Rubin DA, Nieminski KE, Reed GE, Herman MV (1987) Predictors, prevention, and long-term prognosis of atrial fibrillation after coronary artery bypass graft operations. J Thorac Cardiovasc Surg 94:331–335
67. Szyszka A, Baszynska-Wachowiak H, Paluszkiewicz L, Tomczyk J (1995) Magnesium sulphate diminishes abnormalities of repolarization and ventricular arrhythmias after electrical cardioversion. Magnes Res 8[Suppl 1]:70
68. Gott JP, Cooper WA, Schmidt FE, Brown WM, Wright CE, Merlino JD, Fortenberry JD, Clark WS, Guyton RA (1998) Modifying risk for extracorporeal circulation: trial of four antiinflammatory strategies. Ann Thorac Surg 66:747–754
69. Kaplan M, Kut MS, Icer UA, Demirtas MM (2003) Intravenous magnesium sulfate prophylaxis for atrial fibrillation after coronary artery bypass surgery. J Thorac Cardiovasc Surg 125:344–352
70. Zaloga GP (1989) Interpretation of the serum magnesium level. Chest 95:257–258
71. Marcus JC, Valencia G, Altura BM, Altura BT, Jean-Baptiste D, Sinha K (1998) Serum ionized magnesium (iMg) levels in premature and full-term infants. Pediatr Neurol 18:311–314
72. Salem M, Stacey J, Chernow B (1993) Ionized magnesium values in critically ill patients—a novel ion selective electrode for determining free extracellular magnesium concentrations. Crit Care Med 21 [Suppl]:S256
73. Brookes CI, Fry CH (1993) Ionised magnesium and calcium in plasma from healthy volunteers and patients undergoing cardiopulmonary bypass. Br Heart J 69:404–408

74. Altura BT, Shirey, TL, Young CC, Dell'Orfano K, Hiti J, Welsh R, Yeh Q, Barbour RL, Altura BM (1994) Characterization of a new ion selective electrode for ionized magnesium in whole blood, plasma, serum, and aqueous samples. Scand J Clin Lab Invest Suppl 217:21–36

75. Munoz R, Laussen PC, Zienko L, Palacio G, Piercy G, Wessel D (1999) Ionized hypomagnesemia in patients undergoing congenital cardiac surgery: frequency and clinical implications. J Am Coll Cardiol 33:Abstract 530A