

Intraperitoneal Magnesium in Peritoneal Dialysis

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Objectives

- To provide an overview of hypomagnesemia
- To review the literature on intraperitoneal magnesium replacement for the treatment of hypomagnesemia in peritoneal dialysis patients
- To present a patient case demonstrating the successful use of intraperitoneal magnesium replacement in a peritoneal dialysis patient with critical hypomagnesemia

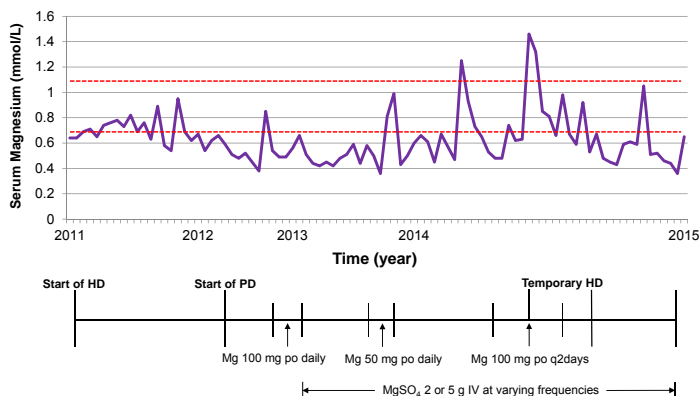
Meet Our Patient

| | |
|----------------|--|
| ID | 70 y/o female with ESRD 2° ischemic nephrosclerosis |
| HPI | <ul style="list-style-type: none"> Started HD in Nov. 2011 after ICU admission Converted to CAPD in Oct. 2012 Switched to CCPD in Jan. 2013 <ul style="list-style-type: none"> PD Prescription: Dianeal 1.5% and 2.5% or Dianeal 2.5% x 2 + Extraneal 7.5% last fill (all solutions contained magnesium 0.25 mmol/L) Temporary HD month of Apr. 2014 2° pleural effusion |
| PMHx | <ul style="list-style-type: none"> Atrial fibrillation (multiple ER visits with uncontrolled atrial fibrillation 2° low K/Mg) Celiac disease Ehlers-Danlos Syndrome Mitral valve prolapse, pulmonary artery stenosis and pulmonary HTN from above GERD (UGIB 2° duodenal ulcer) Gout HTN (low BP post dialysis initiation) Migraines Remote discectomy with L4/5 fusion Hx of central retinal artery occlusion Hx of pleural effusions and cryptogenic organizing pneumonia |
| Allergy | Allopurinol and febuxostat = whole body rash Gluten, oral magnesium and Renavite®/Replavite® = diarrhea |

Meet Our Patient

| | | |
|-------------|--|---|
| Meds | Atrial Fibrillation/ Migraines | Acebutolol 50 mg po bid Warfarin 1.5 mg po daily Acetaminophen 325-650 mg po q4h prn |
| | CKD-MBD | Alfacalcidol 0.5 mcg po daily CaCO ₃ 625 mg po bid with lunch and hs on an empty stomach |
| | Constipation | Sennosides 8.6 mg po hs prn |
| | GERD (UGIB 2° <i>H. pylori</i> duodenal ulcer) | Pantoprazole 40 mg po daily Alginate acid 200 mg/magnesium carbonate 40 mg 1 tab po daily prn |
| | Insomnia | Trazodone 12.5-25 mg po hs prn |
| | PD-related Hypokalemia Hypomagnesemia Infection Prophylaxis | Potassium chloride 16 mEq po daily MgSO ₄ 5 g IV q2 weeks Mupirocin 2% Ointment to PD cath exit site prn with dressing changes |
| | Pruritus | Urea 10% cream applied to dry or itchy skin tid prn |

Baseline Serum Magnesium Levels



Hypomagnesemia Overview

Hypomagnesemia

- **Definition:** total serum magnesium < 0.7 mmol/L
 - Normal total serum magnesium = 0.7-1.1 mmol/L
- **Prevalence:** 7-11% of hospitalized patients
 - Higher with concurrent electrolyte abnormality:
 - 40% in hypokalemic patients
 - 30% in hypophosphatemic patients
 - 23% in hyponatremic patients
 - 22-32% in hypocalcemic patients

Clin Biochem Rev Vol 2003;24:47-66

Causes of Hypomagnesemia

- **Redistribution of magnesium:**
 - Refeeding and insulin therapy
 - Hungry bone syndrome
 - Correction of acidosis,
 - Catecholamine excess
 - Massive blood transfusion
- **GI causes:**
 - Reduced intake (Mg free IV fluids, dietary deficiency)
 - **Reduced absorption (celiac disease)**
- **Renal loss:**
 - Reduced sodium reabsorption
 - Saline infusion
 - Diuretics

Clin Biochem Rev Vol 2003;24:47-66

Causes of Hypomagnesemia

- **Renal disease:**
 - Post obstructive nephropathy
 - Post renal transplantation
 - **Peritoneal Dialysis (use of low Mg PD solution)**
 - Diuretic phase of acute renal failure
 - Inherited disorders (Bartter's and Gitelman's Syndromes)
- **Endocrine causes:**
 - Hypercalcemia
 - Hyperthyroidism
 - Hyperaldosteronism
- **Miscellaneous:**
 - Diabetes mellitus
 - Alcoholism
 - **Drugs (Proton Pump Inhibitors)**

Clin Biochem Rev Vol 2003;24:47-66

Clinical Features of Hypomagnesemia

- **Electrolyte disturbance:**
 - **Hypokalemia, hypocalcemia**
- **Neuromuscular and central nervous system:**
 - Carpopedal spasm, convulsions, **muscle cramps**, **muscle weakness**, fasciculations, tremors, vertigo, nystagmus, depression, psychosis, athetoid and choreiform movements
- **Cardiovascular:**
 - Atrial tachycardias, **atrial fibrillation**, supraventricular arrhythmias, ventricular arrhythmias, torsade de pointes, digoxin sensitivity

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Treatment of Hypomagnesemia

- **Replete magnesium!!!**
 - Target total serum magnesium: 0.7-1.1 mmol/L
- **Reverse underlying causes:**
 - Diet-related
 - Medication-related
- **Check other electrolytes and replete if needed:**
 - Potassium (Target: 3.5-5.0 mmol/L)
 - Calcium (Target: 2.10 -2.55 mmol/L)

Treatment of Hypomagnesemia

| | Oral | IV | IP |
|------------|---------------------------------|--|----|
| Efficacy | Poorly absorbed (~30%) | 100% absorbed Fluctuating serum Mg levels with intermittent administration | ? |
| Safety | Diarrhea, stomach upset | IV-related (flushing, ↓ BP) Infection risk Damage to blood vessels → loss of potential vascular access | ? |
| Compliance | Poor 2° diarrhea Pill burden | Difficult 2° need for hospital visits | ? |
| Cost | \$ | \$\$\$ | ? |

Question from Nephrologist:

- Is there any literature on the use of intraperitoneal magnesium for magnesium replacement in peritoneal dialysis patients?

Literature Review on Intraperitoneal MgSO₄

| Non-PD Patient Case | | |
|---------------------------------------|---|--|
| Bastani B, Pandurangan G | Intraperitoneal route of magnesium sulphate supplementation in a patient with severe renal magnesium wasting | Nephrol Dial Transplant 2001;16:2086-9 |
| PD Patient Cases | | |
| Amirmokri P, Morgan P, Bastani B | Intra-peritoneal administration of potassium and magnesium: A practical method to supplement these electrolytes in peritoneal dialysis patients | Ren Fail 2007;29:603-5 |
| Egan G, Lange DB, Messenger S, et al. | Intermittent intraperitoneal administration of magnesium sulphate in an elderly patient undergoing dialysis | Can J Hosp Pharm 2014;67:157-9 |

Intraperitoneal route of magnesium sulphate supplementation in a patient with severe renal magnesium wasting

| | |
|-------------|---|
| ID | 43 y/o Caucasian female with hypomagnesemia (Mg 0.33-0.37 mmol/L) 2° renal magnesium wasting Symptoms: severe lethargy, left-side numbness and hemiparesis, palpitation, and severe agitation |
| HPI | <ul style="list-style-type: none"> • Neuroendocrine benign pancreatic tumour → Whipple's procedure • Consequences: severe hypomagnesemia, mild hypokalemia, borderline hypocalcemia, low bicarbonate levels |
| PMHx | <ul style="list-style-type: none"> • MI x 2 • Right parietal stroke with left-side hemiparesis • Hypothyroidism 2° • Hashimoto's thyroiditis • HTN • Iron deficiency anemia • Uterine fibroid • Liver hemangioma • DMII • Recurrent sinusitis |
| FHx | Mother, sister, daughter, and grandson have some degree of hypomagnesemia |
| Meds | Calcium carbonate, levothyroxine, magnesium oxide, omeprazole, potassium chloride, spironolactone |

Nephrol Dial Transplant 2001;16:2086-9

Intraperitoneal MgSO₄ Administration

| Mg Regimen | Serum Mg Level | Side Effects |
|--|--|---------------------------------|
| Baseline • MgSO ₄ 10 g IV over 8-10 h/day • Mg oxide 400 mg, 4 tabs po tid (241.3 mg elemental Mg/tab) | • 0.33 – 0.37 mmol/L (nadir) | • Infections ↓ QOL |
| • MgSO ₄ 4 g IV over 8 h/day • Mg-Tab SR®, 2 tabs po tid (84 mg elemental Mg/tab) | • 0.53 – 0.78 mmol/L | • Infections ↓ QOL |
| • Mg-Tab SR®, 4 tabs • MgSO ₄ 4 g IP in 500cc D5W over 20 min | • 0.66 mmol/L (6 h post PO) • 0.99 mmol/L (4 h post IP) • 0.74 mmol/L (14 h post IP) • 0.41 mmol/L (20 h post IP) | • Lower abdo pain (Rated 10/10) |
| • MgSO ₄ 4 g IP in 500cc D5W over 30 min* | • 1.19 mmol/L (2 h post IP) • 0.66 mmol/L (23 h post IP) | • Lower abdo pain (10/10) |
| • MgSO ₄ 2 g IP in 500cc D5W over 20 min daily* | • Not reported | • Lower abdo pain (8/10) |
| • MgSO ₄ 1 g IP in 500 cc D5W over 20 min BID* | • 0.58-0.62 mmol/L | • Lower abdo pain (1/10) |

*No information provided on oral magnesium supplementation

Nephrol Dial Transplant 2001;16:2086-9

Author's Conclusions

- IP MgSO₄ administration may be beneficial to patients requiring IV magnesium replacement
 - Freedom from long hours of IV MgSO₄ infusion
 - Gradual slow absorption of magnesium with maintenance of adequate levels over 18-24 hours

Nephrol Dial Transplant 2001;16:2086-9

Intra-peritoneal administration of potassium and magnesium: A practical method to supplement these electrolytes in peritoneal dialysis patients

| | |
|---------------------|--|
| Objectives | <ul style="list-style-type: none"> • To report on the prevalence of hypokalemia and hypomagnesemia in CCPD patients • To report on the efficacy and safety of IP KCl and MgSO₄ administration in this population |
| Patients | <ul style="list-style-type: none"> • 5/27 CCPD pts with 1-year lab data and persistently low serum K and Mg concentrations despite supplementation or intolerance to supplementation due to side effects • Baseline characteristics: 4 males/1 female; mean age 49 yrs (range 29-69 yrs); PD x 2-5 yrs • Causes of CKD: obstructive uropathy, DM, HTN, congenital malformation, failed renal transplant |
| Intervention | MgSO ₄ 4 g ± KCl 60-80 mEq in Dianeal 2.5% 2 L as last dwell **1 pt received only KCl as serum Mg normal** |
| Outcome | Serum K and Mg concentrations measured at 2, 4, and 6-8 hour intervals during dwell and 20-24 hours after fluid drained |

Ren Fail 2007;29:603-5

Serum Mg Concentrations at Different Time Intervals after MgSO₄ 4 g Intraperitoneal Administration

| Patient | Baseline Serum Mg | 2 h | 4 h | 6-8 h | 20-24 h |
|-----------|-------------------|-------------|-------------|-------------|-------------|
| 1 | 0.74 | 1.23 | N/A | 1.40 | 0.86 |
| 2 | 0.58 | 1.03 | 1.19 | 1.11 | 0.78 |
| 3 | 0.58 | 0.90 | 0.99 | 1.07 | N/A |
| 4 | 0.53 | N/A | N/A | 0.86 | 0.82 |
| Mean (SD) | 0.62 (0.08) | 1.03 (0.16) | 1.19 (0.21) | 1.07 (0.04) | 0.82 (0.04) |

- MgSO₄ 4 g IP qweekly x 12-16 months demonstrated good results in correcting hypomagnesemia
- No adverse effects reported (abdominal pain or peritoneal irritation)

Ren Fail 2007;29:603-5

Ren Fail 2007;29:603-5

Author's Conclusions

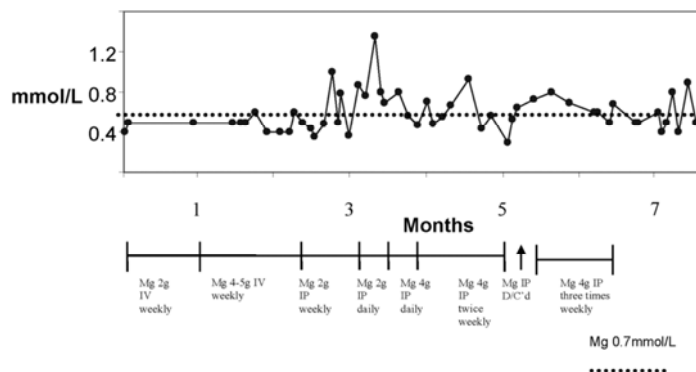
- "IP administration is a safe, practical, and effective method to supplement K and Mg in PD patients"

Intermittent Intraperitoneal Administration of Magnesium Sulphate in an Elderly Patient Undergoing Dialysis

| | |
|---------------------|---|
| ID | 81 y/o female with CKD Stage 5 on CAPD 2° recurrent renal calculi and possible renal oxalosis (hx of jejunioleal bypass procedure) |
| HPI | <ul style="list-style-type: none"> • Fatigue and weakness post initiation of CAPD • Before CAPD initiation: serum Mg = 0.7 mmol/L • Post CAPD initiation: serum Mg= 0.4 mmol/L • CAPD Prescription: <ul style="list-style-type: none"> - Nutrineal (2 L) + Dianeal (2 L) + Extraneal (3 L) - All solutions contained Mg 0.25 mmol/L • Tried oral Mg supplementation and Dianeal with Mg 0.75 mmol/L but symptoms persistent and serum Mg < 0.7 mmol/L • Inconsistent effectiveness with IV Mg and difficulty with maintaining IV access and scheduling |
| Intervention | • Trial IP Mg in Nutrineal daytime dwell |

Can J Hosp Pharm 2014;67:157-9

Course of Therapy: IV and IP MgSO₄



Can J Hosp Pharm 2014;67:157-9

Author's Conclusion

- "IP Mg corrected hypomagnesemia and did not result in hyermagnesemia or other adverse effects such as chemical peritonitis or bacterial peritonitis"

Can J Hosp Pharm 2014;67:157-9

Back to our Patient

70 y/o female with ESRD 2° ischemic nephrosclerosis on CCPD since Jan. 2013

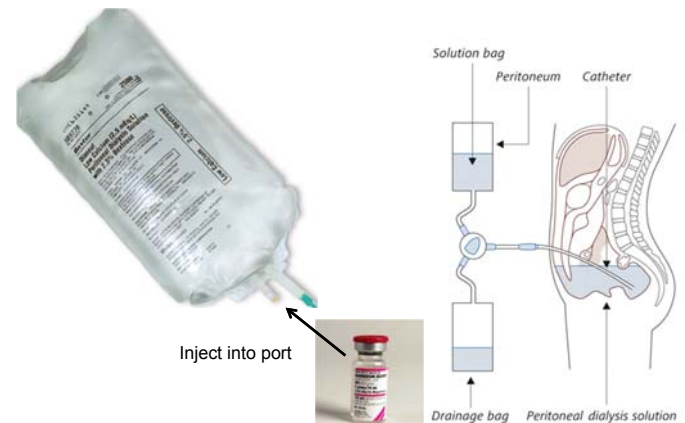
- Critical hypomagnesemia – lowest Mg 0.36
- Uncontrolled atrial fibrillation → multiple ER visits
- Intolerance to oral magnesium supplementation
- Fluctuating serum Mg levels and inconvenience of IV MgSO₄ administration
 - IV access, staffing and time (administration/travel)

Back to our Patient

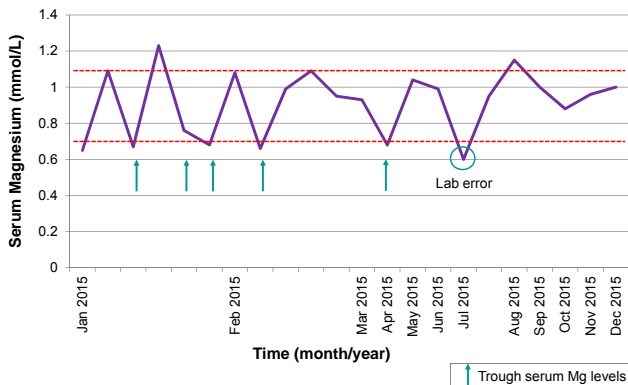
Intervention:

1. Stop $MgSO_4$ 5 g IV q2weeks on Jan 7/15
2. Start $MgSO_4$ 4 g IP qweekly in a daytime dwell of Dianeal 2.5% 2L for 6 hours on Jan 12/15
(Based on regimen from 2nd case series)
3. Peak (1 day post-dose) and trough (4 days post-dose) serum Mg levels until levels stable within normal range (0.7-1.1 mmol/L)

IP Magnesium Administration



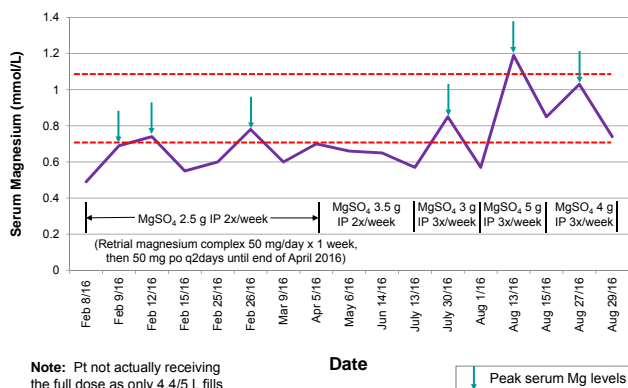
One-Year Serum Magnesium Levels Post $MgSO_4$ 4 g IP qweekly in Daytime Dwell



Back to our Patient

- Patient returns to PD clinic on Jan. 22, 2016 complaining of muscle cramping similar to when she previously had low Mg levels
- Trough serum Mg level drawn on Jan. 25, 2016 immediately pre-dose = 0.50 mmol/L
- Plan: increase $MgSO_4$ dose and trial administration through CCPD machine

Serum Magnesium Levels Post IP $MgSO_4$ Administration Through CCPD Machine



Conclusion

- IP $MgSO_4$ is an effective and safe option for magnesium replacement in PD patients
- Consider in PD patients with severe, persistent hypomagnesemia unresponsive to and/or intolerant of dietary and oral magnesium supplementation

Note: Pt not actually receiving the full dose as only 4.4/5 L fills