Thoughts and Progress

Case Report of the First Severe Acute Respiratory Syndrome Patient in China: Successful Application of Extracorporeal Liver Support MARS Therapy in Multiorgan Failure Possibly Induced by Severe Acute Respiratory Syndrome

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Abstract: A previously healthy patient was transferred to our infectious department with a 9-day-history of continued fever. The patient was placed on assisted respiration support in addition to anti-viral medication. The diagnosis of SARS (Severe Acute Respiratory Syndrome) was made in view of the severe hypoxemia and the characteristic symptoms exhibited by the patient. Despite the best intensive therapy, he clinically deteriorated into multiorgan dysfunction syndrome (MODS) including additional dysfunction of kidney, liver, and heart. We initiated MARS therapy (extracorporeal liver support utilizing albumin dialysis) with intention to positively influence the organ functions in his MODS on the basis of recently published studies which suggested a positive impact of MARS in multiorgan failure secondary to respiratory illnesses and the possible influence on inflammatory mediators and cytokines. The application of 4 intermittent MARS treatments (8 h each, mean blood flow rate 180 ml/min) on 4 consecutive days resulted in an immediate improvement of clinical conditions within the treatment days. The further improvement of organ functions allowed withdrawing the patient from ventilatory support 13 days after start of MARS, and 44 days after admission he was discharged home with completely resolved organ functions and laboratory abnormalities. SARS is a severe form of the epidemic outbreak of atypical pneumonia which remains poorly defined regarding etiology and special therapy recommendations. However, the development and aggravation of this ARDS-like severe acute respiratory syndrome is pathologically associated with the systemic inflammatory response syndrome (SIRS) which may then mediate or cause MODS. To our knowledge, this is the first report of an application of MARS therapy in MODS which was probably induced by SARS in a patient in China which improved the clinical condition of the patient in multiorgan failure secondary to respiratory failure indicating that MARS might be an additional therapeutic option in multiorgan failure induced by SARS.

Key Words: Multi-organ dysfunction syndrome—MARS therapy—Severe acute respiratory syndrome—Systemic inflammatory response syndrome.

A previously healthy 54-year-old man was transferred to our infectious department on November 25, 2002 with a 9 day history of a continued fever of 39–40°C along with myalgias and headache, who had failed in any therapeutic improvement focusing on a primary diagnosis of typhoid fever at the local hospital. On arrival, he presented with a fever of 39.4°C, chills, a light dry cough, shortness of breath, and diarrhea. The chest x-ray indicated a mild inflammation particularly on the superior right pulmonary field. White blood cell and platelet counts were in the normal range, lactate dehydrogenase and creatine kinase were normal, and serum bilirubin levels were slightly elevated to 25 μmol/L. The Weil-Felix test, leptospiriosis-IgM, and EHF (epidemic hemorrhagic fever)-IgM were negative.

The patient was under progressive antibiotic medication applying TIENAM and vancomycin, but his medical condition failed to improve. He developed a deep cough and dyspnea on November 28, along with diffusive pulmonary inflammatory images upon X-ray detection. The diagnosis of SARS (severe acute respiratory syndrome) was made in view of his severe hypoxemia with a PaO2 of 60 mm Hg and PaO2/FiO2 of 150 mm Hg and the characteristic symptoms described above.

The patient was shifted to an intensive therapy unit to be intensively supported with assisted respiration support in addition to antiviral (Ribavirin) medication. Despite the best intensive therapy, he clinically deteriorated into multiorgan dysfunction syndrome (MODS) including additional dysfunction of kidney, liver, and heart. On November 29, he presented with proteinuria renal failure further developing to oliguria, his serum bilirubin level increased from 25 μmol/L to 56 μmol/L, and levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) appeared to increase up to 319 and 425.5 units, respectively. His body temperature remained 39–40°C, PaO2/FiO2 decreased to 120 mm Hg, heart rate was 150–160 beats/min, and mean arterial pressure (MAP) was 58 mm Hg.
We decided to initiate MARS therapy (extracorporeal liver support utilizing albumin dialysis in which enriched albumin dialysate serves as a shuttle between a blood-sided dialysis membrane on one side and a removable set of sorbent columns of charcoal and anion exchanger and a conventional dialysis unit on the other to selectively remove albumin-bound substances and reduce oxidative stress) with the intention of positively influencing the organ functions in his MODS on the basis of recently published studies which have suggested a positive impact of MARS on multiorgan failure secondary to respiratory illnesses and the possible influence on inflammatory mediators and cytokines (1–3). The Ethical Committee of the hospital approved the procedure for MARS therapy with informed consent from the patient, and the MARS treatment

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**TABLE 1. Change of laboratory data of endotoxin and cytokines pre- and end MARS treatment**

<table>
<thead>
<tr>
<th></th>
<th>Normal range</th>
<th>Date 29.11.02</th>
<th>Pre MARS 1</th>
<th></th>
<th>End MARS 1</th>
<th></th>
<th>Date 30.11.02</th>
<th>Pre MARS 2</th>
<th></th>
<th>End MARS 2</th>
<th></th>
<th>Date 01.12.02</th>
<th>Pre MARS 3</th>
<th></th>
<th>End MARS 3</th>
<th></th>
<th>Date 02.12.02</th>
<th>Pre MARS 4</th>
<th></th>
<th>End MARS 4</th>
<th></th>
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<tbody>
<tr>
<td><strong>TNF-α (µg/L)</strong></td>
<td>0.29–0.81</td>
<td>2.6</td>
<td>1.5</td>
<td></td>
<td>1.8</td>
<td>0.95</td>
<td>1.2</td>
<td>0.97</td>
<td></td>
<td>0.78</td>
<td>0.52</td>
<td>0.52</td>
<td>0.45</td>
<td>0.28</td>
<td>0.35</td>
<td>0.21</td>
<td>0.28</td>
<td>0.19</td>
<td>0.16</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>IL-6 (pg/ml)</strong></td>
<td>67–151</td>
<td>358</td>
<td>219</td>
<td></td>
<td>252</td>
<td>172.3</td>
<td>196.2</td>
<td>168</td>
<td></td>
<td>146.1</td>
<td>125.1</td>
<td>125.1</td>
<td>0.45</td>
<td>0.28</td>
<td>0.35</td>
<td>0.21</td>
<td>0.19</td>
<td>0.16</td>
<td>0.04</td>
<td>0.04</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>IL-8 (ng/ml)</strong></td>
<td>0.1–0.2</td>
<td>0.45</td>
<td>0.28</td>
<td></td>
<td>0.35</td>
<td>0.21</td>
<td>0.28</td>
<td>0.23</td>
<td></td>
<td>0.19</td>
<td>0.16</td>
<td>0.16</td>
<td>0–0.03</td>
<td>0.08</td>
<td>0.06</td>
<td>0.05</td>
<td>0.029</td>
<td>0.025</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>LPS (EU)</strong></td>
<td>0–0.03</td>
<td>0.08</td>
<td>0.04</td>
<td></td>
<td>0.06</td>
<td>0.029</td>
<td>0.05</td>
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<td>0.025</td>
<td>0.02</td>
<td>0.02</td>
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<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
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</table>

**FIG. 1.** Course of serum levels of TNF-α (♦), IL-6 (■), IL-8 (●), and LPS (▲) during MARS treatments 1–4.
was carried out starting November 29, the fourth day after his initial admission. The application of four intermittent MARS treatments (Molecular Adsorbents Recirculating System, Teraklin AG, Rostock, Germany; 8 hr each, mean blood flow rate 180 ml/min) on 4 consecutive days resulted in an immediate improvement of clinical conditions within the treatment days; PaO₂ continuously increased from 60 mm Hg to 90 mm Hg along with decreasing FiO₂ support from 0.5 to 0.4, heart rate decreased from 150 to 110 beats/min, and MAP increased from 58 to 72 mm Hg. This was accompanied by marked decreases of serum levels of IL-6, IL-8, endotoxin (LPS), and TNF-α (Table 1; Fig. 1) as well as by the gradual improvement of chest X-ray edema inflammatory images and urine excretion. Additionally, during each procedure, we observed a decrease in both serum bilirubin levels and transferases, which continuously decreased to 31.2 μmol/L, AST to 96, and ALT to 46 units from the peak level at initiation of MARS therapy until the end of the last MARS treatment on December 2. Further improvement of organ functions allowed withdrawing the patient from ventilation support 13 days after the start of MARS, and 44 days after admission he was discharged home with completely resolved organ functions and laboratory abnormalities.

SARS is a severe form of the epidemic outbreak of atypical pneumonia, which remains poorly defined as far as etiology and special therapy recommendations (4). However, the development and aggravation of this ARDS-like severe acute respiratory syndrome is pathologically associated with the systemic inflammatory response syndrome (SIRS), which may then mediate or cause MODS (3,5). Recently, MARS therapy has been shown to be effective in lowering endotoxins and certain cytokines, and, together with marked reduction of albumin-bound and watersoluble toxins, this leads to improved organ function and improved outcome (6,7).

To our knowledge, this is the first report of an application of MARS therapy in MODS probably induced by SARS in a patient in China. The data are similar to that of the mentioned study, which found that MARS treatments might contribute to therapeutic effects in modulating the oxygenation function in hypoxemia (1,7), alleviating lung injury and improving clinical condition in multiorgan failure secondary to respiratory failure, which indicates that MARS might be an additional therapeutic option for multiorgan failure induced by SARS (1).

REFERENCES


Use of Near-Infrared Spectroscopy to Monitor Regional Cerebral Oxygen Saturation during Infrarenal Aortic Crossclamping in Piglets

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Abstract: Purpose: The hemodynamic changes induced by infrarenal aortic crossclamping have been well documented, but the effects of such crossclamping on cerebral perfusion are unknown. To investigate these effects, we used near-infrared spectroscopy (NIRS) to monitor regional cerebral oxygen saturation (rSO₂) during infrarenal aortic crossclamping in a piglet model. Methods: The study involved 19 piglets, each weighing 7.8 ± 1 kg. The NIRS sensor was placed on each animal’s forehead. General anesthesia was induced, and the infrarenal abdominal aorta was mobilized through a laparotomy. After heparin (1 mg/kg) was administered, crossclamps were applied proximally and distally. A 2 mm segment was resected from the proximal aortic stump, and an aorto-aortic anastomosis was performed. Results: Crossclamping lasted for 30.6 ± 6.7 min. Between the time of baseline mea-
measurement and clamp application, the rSO₂ did not decrease significantly (65.4% ± 8.9% vs. 62.4% ± 7.8%). However, significant decreases in the rSO₂ occurred between baseline measurement and clamp removal (65.4% ± 8.9% vs. 55.7% ± 8.9%; P < 0.01), between baseline measurement and the end of surgery (65.4% ± 8.9% vs. 57.7% ± 7.5%; P < 0.01), and between clamp application and removal (62.4% ± 7.8% vs. 55.7% ± 8.9%; P < 0.01). At these same intervals, no intergroup differences occurred in the temperature, heart rate, or mean arterial pressure. Conclusion: Infrarenal aortic crossclamping significantly decreases the rSO₂. NIRS, which has the advantages of being non-invasive and continuous, may be useful for monitoring this variable intraoperatively. **Key Words:** Infrarenal aortic crossclamping—Near-infrared spectroscopy—Regional cerebral oxygen saturation—Piglets.

Infrarenal aortic crossclamping is required during abdominal aortic aneurysm surgery and is usually well tolerated by patients. Nevertheless, several investigators have documented the adverse effects of infrarenal aortic crossclamping on cardiac, pulmonary, liver, and renal dysfunction in some patients (1–7). In addition, adverse changes in systemic vascular resistance, stroke volume, heart rate, and mean arterial pressure associated with infrarenal aortic clamping have been well described (8–10). However, little research has been done to determine the effects of crossclamping on cerebral perfusion.

The incidence of stroke after abdominal aortic surgery is only 0.6%–1.1% (11,12). However, 10%–15% of patients undergoing aortic reconstruction have a history of preoperative cerebral ischemia, and 21% have carotid stenosis exceeding 50% (11). The ability of preoperative diagnosis and correction of asymptomatic, severe internal carotid artery stenosis to prevent perioperative stroke after aortic surgery remains unproven, and the optimal approach remains controversial (13,14).

The goals of this study were (1) to characterize the effects of infrarenal aortic crossclamping on regional cerebral oxygen saturation (rSO₂) using near-infrared spectroscopy (NIRS), and (2) to determine whether NIRS is effective in this setting. Because NIRS is both noninvasive and continuous, it is a novel tool for monitoring cerebral perfusion. Real-time monitoring may alert physicians that cerebral oxygenation is falling and may allow them to treat the cause of cerebral malperfusion before irreversible damage occurs.

**MATERIALS AND METHODS**

Nineteen piglets, weighing 7.8 ± 1.0 kg, were used. All experiments were performed in the Cullen Cardiovascular Surgical Research Laboratories of the Texas Heart Institute at St. Luke’s Episcopal Hospital. All animals received humane care as described in the “Guide for the Care and Use of Laboratory Animals” of the National Academy of Sciences, published by the National Institutes of Health (NIH Publication No. 85-23, 1985).

The piglets were premedicated with a cocktail consisting of atropine (0.04 mg/kg), acepromazine (0.25 mg/kg), and ketamine (20 mg/kg). This cocktail was administered intramuscularly to achieve adequate sedation. Both the oral and nasal airways were masked with 1.0%–3.0% isoflurane for induction of anesthesia and for intubation with an appropriate endotracheal tube. General anesthesia was maintained with 1.0%–2.5% isoflurane throughout the procedure. Cefuroxime (Kefurox) was given intravenously (500–750 mg, depending on the animal’s weight). Pancuronium bromide (Pavulon; 0.1 mg/kg) was administered intravenously to achieve adequate muscle paralysis. Pain was managed with buprenorphine (Buprenex; 0.1 mg, intramuscularly).

**Experimental design**

In each case, the NIRS sensor was positioned on the piglet’s forehead. After general anesthesia was induced, a laparotomy was performed. The infrarenal abdominal aorta was exposed. After intravenous heparin was administered (1–3 mg/kg), the aorta was clamped below the renal arteries and above the iliac bifurcation. After transecting the aorta, a 2 mm segment was excised from the proximal stump. The aorta was then repaired via an end-to-end anastomosis using interrupted polypropylene sutures.

**rSO₂ measurements**

For continuous monitoring of the rSO₂ of the mixed arterial and venous blood in the brain cortex, we used a pediatric near-infrared spectroscope (INVOS Model 5100, Somanetics Corporation, Troy, MI, U.S.A.). This device passed low-intensity, near-infrared light into the subject’s forehead, through the skull and the cerebral cortex. The degree of spectral absorption by the cerebral circulation was indicated by the intensity of the reflected light 3 and 4 cm from the light source (Fig. 1). Light absorption data were collected 15 times/s and were stored on a diskette for computer analysis. Further details concerning the NIRS system have been published elsewhere (15).

**Statistical analysis**

A two-way ANOVA for a randomized complete block design with a post-hoc test was used for statistical analysis. A P value < 0.05 was considered statis-
RESULTS

There were no intergroup differences in the hematocrit, arterial oxygen tension, or arterial carbon dioxide tension at any of the experimental stages. The heart rate was 115 ± 20 bpm at baseline, 105 ± 23 bpm during crossclamp application, 107 ± 27 bpm during clamp removal, and 110 ± 21 bpm at the end of surgery. At these same periods, the temperature was 34.8 ± 0.9°C, 34.3 ± 0.8°C, 34.4 ± 0.9°C, and 33.8 ± 0.8°C, respectively. The mean arterial pressure was 53 ± 4 mm Hg, 55 ± 9 mm Hg, 50 ± 11 mm Hg, and 51 ± 4 mm Hg at baseline, during crossclamp application, clamp removal, and at the end of surgery, respectively. There were no statistically significant intergroup differences in the heart rate, temperature, or mean arterial pressure at any of the experimental stages.

The aortic crossclamp time was 30.6 ± 6.7 min. No significant decrease in the rSO₂ occurred between the time of baseline measurement and crossclamp application (65.4% ± 8.9% vs. 62.4% ± 7.8%; \( P = \text{NS} \)). However, statistically significant decreases in the rSO₂ occurred between baseline measurement and clamp removal (65.4% ± 8.9% vs. 55.7% ± 8.9%; \( P = 0.0001 \)), between baseline measurement and the end of surgery (65.4% ± 8.9% vs. 57.7% ± 7.5%; \( P = 0.0001 \)), and between crossclamp application and removal (62.4% ± 7.8% vs. 55.7% ± 8.9%; \( P = 0.0002 \)).

DISCUSSION

Several investigators have shown that a decrease in regional cerebral oxygen saturation (rSO₂) is a predictor of cerebral injury (16–20). The particular near-infrared spectroscopy (NIRS) system used in our study monitors the critical balance between the rSO₂ and cerebral oxygen consumption. Factors that affect the rSO₂ include cerebral blood flow, arterial oxygen saturation, and hemoglobin concentration. The cerebral oximeter used in our study has already compared favorably with other valid techniques such as transcranial Doppler imaging, electroencephalography (EEG), and evaluation of somatosensory evoked potentials (SSEPs) for determining cerebral malperfusion. Williams and colleagues (16) have demonstrated that there is a good correlation between the decrease in the rSO₂ and the percentage of change in the peak transcranial Doppler velocity in patients with contralateral carotid stenosis and occlusion. Levy and associates (17) have shown that, in patients undergoing tests for automatic defibrillator placement, EEG changes are correlated with changes in cerebral oxygenation. In a separate study (18), the decreased rSO₂ in carotid endarterectomy patients was correlated with the amplitude of SSEPs. The decreased rSO₂ may be due to embolic events in carotid endarterectomy patients. Using NIRS during pediatric cardiac surgery, Daubeney and coworkers (19) identified vulnerable periods for cerebral oxygenation. These authors suggested that a cerebral oximeter using NIRS is useful for monitoring oxygen supply/demand relationships during circulatory arrest. In our previous study, we showed that NIRS is a superb tool for continuously monitoring the rSO₂ during cardiopulmonary bypass (15).

Liu and associates (20) have investigated the effects of infrarenal crossclamping on the middle cerebral artery flow velocity and cerebral oxygenation during infrarenal crossclamping in adults. These researchers showed that cerebral oxygen saturation and middle cerebral artery flow velocity decreased significantly during crossclamping. Our results support their observations and suggest that NIRS is an effective tool for monitoring these changes. In addition, Liu noticed that changes in the cardiac output paralleled those in cerebral oxygen saturation and cerebral blood velocity.

Our study documented profound changes in the rSO₂ levels during and after infrarenal crossclamping. Between the time of baseline measurement and clamp application, the rSO₂ deficiency was only −4%. However, significant increases in rSO₂ deficiency occurred between baseline measurement and
clamp removal (−15%) and between baseline measurement and the end of surgery (−11%). Figure 2 gives a detailed analysis of rSO$_2$ deficiency.

We observed a 10-point transient decrease (from 65% to 55%) when we compared the baseline measurement with that obtained at clamp removal; this difference was statistically significant. Although this decrease seems small, Cho and associates (18) have clearly shown that a 10-point decrease in rSO$_2$ is enough to cause cerebral ischemia in carotid endarterectomy patients. To the best of our knowledge, we and Liu (20) were the first to use NIRS to investigate the effects of infrarenal aortic cross-clamping on rSO$_2$. Therefore, no clinical data (other than Liu’s) are available with which to compare our experimental results. Certainly, our findings correlate very well with Liu’s data. Based on these findings, further clinical studies are warranted to investigate the effects of infrarenal crossclamping on cerebral dysfunction.

Our study may be clinically relevant in two ways: (1) because reduced cerebral perfusion may precipitate a stroke in patients with preexisting carotid stenosis, our documentation of impaired cerebral perfusion/oxygenation during infrarenal clamping supports the practice of screening for, and correction of, significant carotid stenosis before elective aortic surgery, and (2) NIRS may be useful in patients with an uncertain carotid status or with known carotid disease that cannot be corrected before aortic repair, including patients who present with symptomatic aneurysms that require urgent/emergent repair. If rSO$_2$ decreases, strategies for improving cardiac output may enhance oxygen delivery and increase rSO$_2$, reducing the chance of stroke in patients with uncorrected significant carotid stenosis.

In summary, infrarenal crossclamping significantly decreases rSO$_2$—most likely due to reduced cardiac output and changes in cerebral perfusion patterns—and NIRS may be useful for monitoring this variable intraoperatively.

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REFERENCES
Magnesium Homeostasis in Patients Undergoing Continuous Ambulatory Peritoneal Dialysis: Role of the Dialysate Magnesium Concentration


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Abstract: We carried out this retrospective study to examine the magnesium status of our chronic ambulatory peritoneal dialysis (CAPD) patients dialyzed with 0.75 mmol/L (group I) or 0.50 mmol/L (group II) magnesium peritoneal dialysis solution. A total of 34 anuric patients on CAPD (age: 31–72 years; duration of CAPD: 7–74 months) were studied. None of them received magnesium-containing phosphate binders or vitamin D. Biochemical parameters including magnesium, calcium, phosphate, parathormone, and albumin were measured in all patients. The corrected for hypoalbuminemia serum magnesium concentration in group I was significantly higher compared to that found in group II. However, there were no significant differences in the other measured parameters between the two groups of CAPD patients, though iPTH levels were somewhat increased in group II patients. Serum magnesium levels were weakly correlated with serum prealbumin levels in both groups of CAPD patients (r = 0.16, P = 0.08 and r = 0.17, P = 0.07). The incidence of hypermagnesemia was significantly higher in group I patients versus those in group II (13/19 [68.4%] vs. 2/15 [13.3%], P < 0.01). On the other hand, no patient developed hypomagnesemia (corrected total magnesium <0.65 mmol/L), despite the trend toward decreased magnesium levels in group II patients. Our results point out that serum iPTH levels and nutritional parameters, such as prealbumin levels, should be taken into account in the choice of the magnesium concentration of the peritoneal dialysis fluid. Key Words: Chronic ambulatory peritoneal dialysis—Magnesium homeostasis—Hypermagnesemia—Prealbumin—Parathormone.

Magnesium is the fourth most abundant cation in the body and is involved in many cell functions. Magnesium levels depend on the rate balance of intake and excretion. Thus, the kidney plays a prominent role in determining serum magnesium homeostasis, and patients with advanced chronic renal failure often have an increased serum magnesium concentration (1,2). Dialysis is the main route of magnesium removal in patients with end-stage renal disease, and subsequently the magnesium status depends on the concentration gradient between serum and dialysis fluid in both hemodialysis (HD) and chronic ambulatory peritoneal dialysis (CAPD) patients (3–5). In contrast to HD patients, only few data have been reported on magnesium concentration in patients undergoing CAPD (6,7). We undertook this study to evaluate magnesium homeostasis in CAPD patients in relation to the dialysate magnesium concentration as well as to other factors.
potentially influencing magnesium homeostasis, such as iPTH levels.

MATERIALS AND METHODS

We reviewed the medical records of all patients (a total of 34 patients, 19 male, 15 female) who had been on CAPD for the last 6 (range 8–120) months. Renal failure was due to glomerulonephritis in 16 patients, chronic interstitial nephritis in 7 patients, and hypertension in 3 patients. The cause was unknown in the remaining 8 patients. None of them received magnesium-containing phosphate binders or any form of vitamin D therapy. All patients were dialyzed with 2L of dialysate four times a day. In all cases, urine volume was less than 100 ml/day. The calcium concentration of the dialysis fluid was 1.75 mmol/L, while the magnesium concentration was 0.75 mmol/L in 19 patients and 0.50 mmol/L in 15 patients (patients were randomly selected). The dialysate concentrations of electrolytes were sodium 132 mmol/L, chloride 102 mmol/L, lactate 35 mmol/L, glucose 1.35 g/dl, and pH 5.5. The osmotic pressure was 347 mosm/L.

Patients were considered as hypermagnesemic if they had increased (>1.1 mmol/L) and hypomagnesemic if they had decreased (<0.65 mmol/L) serum total magnesium concentration corrected for hypoalbuminemia according to Kroll’s proposed formula: corrected serum magnesium (mmol/L) = measured total serum magnesium (mmol/L) + 0.005 + (40-serum albumin (g/L)) (8).

Additionally, we attempted to correlate the patients’ magnesium status with duration of dialysis, serum levels of total proteins, parameters of calcium metabolism (serum levels of calcium, inorganic phosphorus, and parathormone), dialysis adequacy (Kt/V), and nutritional status (serum levels of albumin and prealbumin, as well as nPCR). The values represented the mean of two measurements.

Serum samples were analyzed for calcium, phosphorus, and magnesium by photometric assays. Serum total protein concentrations were measured by the Biuret method and serum albumin by the BCG method. Serum prealbumin was determined using a nephelometric method (Beckman Array Protein System, Beckman Instruments Inc., Richmond, CA, U.S.A.; Brea A). Parathormone levels were estimated by the immunoradiometric assay (Cisbio International, Cedex, France), which can determine the intact biological chain of 84 amino acids of iPTH in human sera. The intra- and interassay coefficients of variation (CV) were 7.5% and 6.8%, respectively. Detection limit was 0.7 pg/ml (normal values 11–62 pg/ml). The 24 hr Kt/V was determined by standard methods and expressed as weekly Kt/V (9). The Randerson formula was used for the determination of protein catabolic rate (PCR) and PCR normalized by standard weight (nPCR) (10).

Data are generally expressed as mean ± SD. The statistical significance of differences and differences of mean were tested by Student’s t test (for normally distributed data) or nonparametric methods (Mann Whitney U test). Intercorrelations of variables were described by Pearson’s product-moment correlation coefficients or by Spearman’s rank-order correlation coefficients where appropriate. A P value below 0.05 was regarded as significant.

RESULTS

The clinical and laboratory parameters of the study population are shown in Table 1. The corrected serum magnesium was 1.07 ± 0.18 mmol/L (95% confidence intervals 0.80–1.40 mmol/L), which was increased compared to that observed in 58 age- and sex-matched controls (0.95 ± 0.08 mmol/L, P = 0.03). The corrected serum magnesium concentration of the patients dialyzed with a 0.75 mmol/L magnesium solution was significantly higher compared to that found in patients dialyzing against fluids containing magnesium at 0.50 mmol/L (Table 1). Fifteen patients experienced increased corrected total serum magnesium levels (>1.1 mmol/L). The incidence of hypermagnesemia was significantly increased in patients dialyzed with a 0.75 mmol/L versus those dialyzed with a 0.50 mmol/L magnesium peritoneal dialysis solution (13/19 [68.4%] vs. 2/15 [13.3%], P < 0.01). However, there were no significant differences in the other measured parameters between the two groups of CAPD patients, though iPTH levels were somewhat higher in patients dialyzed with a 0.50 mmol/L magnesium peritoneal dialysis solution (P = 0.09 by Mann Whitney U test; see Table 1). Serum total magnesium levels were not correlated to patients’ age, body weight, BMI, Kt/V, nPCR, and dialysis duration, or to the levels of parathormone, lipid parameters, calcium, phosphorus, and albumin in both groups of patients. However, they were weakly correlated with serum prealbumin levels in both groups (r = 0.16, P = 0.08 and r = 0.17, P = 0.07).

There were no significant differences in all studied parameters between hypermagnesemic and normomagnesemic patients of both groups (data not shown). It should be mentioned, however, that prealbumin levels were somewhat increased and iPTH levels somewhat decreased in hypermagnesemic patients dialyzing against solution containing magnesium at 0.75 mmol/L (Table 1). On the other hand,
no patient developed hypomagnesemia (corrected total serum magnesium levels <0.65 mmol/L), despite the trend toward decreased magnesium levels in patients with the lower (0.50 mmol/L) magnesium peritoneal dialysis solution.

It has been pointed out that dialysis patients need a serum iPTH between two and four times the upper limit of the normal range to maintain normal bone remodeling (120–240 pg/ml) (11). When patients were divided into two groups based on their iPTH levels (group A [n = 15], patients with inadequate iPTH [<120 pg/ml, range 15–84 pg/ml] and group B [n = 19], patients with adequate iPTH levels [>120 pg/ml, range 129–902 pg/ml]), in eleven of them with iPTH >240 pg/ml, there were no significant differences between the two groups in all parameters including serum magnesium levels.

**DISCUSSION**

In agreement with previously published data, our study showed that serum magnesium levels are elevated in CAPD patients dialyzed against fluid containing magnesium at 0.75 mmol/L (12–14). However, hypermagnesemia observed in about two thirds of these patients was of modest degree, which is unlikely to have any adverse effects. Additionally, it has been suggested that mild hypermagnesemia can retard the development of arterial calcification in CAPD patients and can also suppress parathyroid gland activity, thus rendering it beneficial in the amelioration of secondary hyperparathyroidism (15,16). Regarding our patients, no apparent calcification was observed. In fact, our cohort serum iPTH levels were lower (0.50 mmol/L), despite the trend toward decreased magnesium levels in patients with the lower (0.50 mmol/L) magnesium peritoneal dialysis solution.
Of special interest is the relation of serum magnesium concentration with parathyroid gland function in uremic patients. Navarro et al. have recently showed that patients with hypermagnesemia had inappropriately low serum iPTH levels, while a negative linear relationship between iPTH and magnesium levels was demonstrated (22,23). The authors suggested that hypermagnesemia may have a negative influence on parathyroid gland function, and, in this way, could be a potential risk factor for the development of adynamic bone lesion. However, in our cohort, even though patients dialyzing against 0.75 mmol/L had somewhat decreased iPTH levels compared to those dialyzing against 0.50 mmol/L and hypermagnesemic patients tended to exhibit decreased iPTH levels compared to normomagnesemic ones, these differences were not statistically significant. Moreover, the slightly decreased serum PTH levels observed in patients dialyzed with 0.75 mmol/L magnesium solution could also be the result of the significantly increased serum calcium concentration (Table 1). Additionally, no correlation between serum magnesium and iPTH concentration was found, whereas, in contrast to the findings of Navarro et al., no evidence of increased serum magnesium levels was revealed in patients with inadequately low iPTH concentration. The reasons for the observed discrepancies are not clear cut but they may relate to a number of factors, such as the small number of patients studied, the variability of serum magnesium concentrations, or to other poorly understood factors. In this context, it should be mentioned that variations in dietary intake from food and water may also play a prominent role in magnesium homeostasis in CAPD patients and may, in part, account for the observed variability in serum magnesium concentration as well as for some of the differences in the literature concerning magnesium status. It has been suggested that the dietary intake of magnesium is less than the recommended amount, leading to a frank or borderline hypomagnesemia in much of the population (24–26). The value of nutrition and subsequently of dietary magnesium intake in the magnesium homeostasis is shown from the fact that the hypermagnesemic patients had higher serum prealbumin levels, whereas a weak correlation between serum prealbumin levels and magnesium concentration was found in both groups of CAPD patients.

**CONCLUSION**

Our results point out that serum iPTH levels and nutritional parameters, such as prealbumin levels, should be taken into account in the choice of the magnesium concentration of the peritoneal dialysis fluid.

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**REFERENCES**