

## MAGNESIUM AND POTASSIUM PARENTERAL SUPPLEMENTATION DOES NOT PRODUCE SIGNIFICANT EFFECT ON MAGNESIUM AND POTASSIUM SERUM LEVEL OF CERVICAL CANCER PATIENTS RECEIVING CISPLATIN CHEMOTHERAPY

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### ABSTRAK

*Cisplatin adalah agen kemoterapi untuk pasien kanker serviks yang menerima radiasi sebagai terapi utama. Salah satu efek samping cisplatin adalah gangguan elektrolit, yang menurunkan tingkat magnesium dan kalium. Namun, efektivitas penerapan suplementasi parenteral MgSO<sub>4</sub> dan KCl sebagai hipomagnesemia dan hipokalemia profilaksis masih dipertanyakan. Penelitian ini bertujuan mengevaluasi efektivitas suplementasi magnesium dan kalium serum pada pasien kanker serviks yang menerima cisplatin 50 mg/m<sup>2</sup>. Penelitian ini merupakan penelitian observasional dengan metode cross-sectional. Kriteria inklusi adalah pasien kanker serviks stadium IIB yang akan menerima siklus keempat. Semua pasien (n = 22 pasien) menerima 1.000 cc saline normal (NS) hidrasi, tetapi hanya pasien pada kelompok perlakuan (n = 11 pasien) menerima suplemen MgSO<sub>4</sub> (0,5 g) dan KCl (10 mEq) bersama dengan hidrasi pasca-kemoterapi. Data yang diperoleh adalah kadar magnesium, kalium, kreatinin, dan serum BUN, masing-masing diukur sebelum dan sesudah kemoterapi cisplatin siklus keempat. Hasilnya, pada kelompok kontrol sebelum siklus keempat, tingkat magnesium serum adalah  $1.87 \pm 0.22$  mg/dL sedangkan kalium  $4.15 \pm 0.71$  mmol/L. Pasca siklus keempat, kadar magnesium serum  $1.75 \pm 0.19$  mg/dL sedangkan kalium  $4.21 \pm 0.67$  mmol/L. Pada kelompok perlakuan sebelum siklus keempat, kadar magnesium serum  $1.95 \pm 0.25$  mg/dL sedangkan kalium  $4.06 \pm 0.36$  mmol/L. Pasca siklus keempat, kadar magnesium serum  $1.85 \pm 0.16$  mg/dL sedangkan kalium  $4.01 \pm 0.28$  mmol/L. Simpulan, kedua kelompok menunjukkan tidak ada perbedaan signifikan pada kadar serum magnesium dan kalium. Tidak ada manifestasi klinis hipomagnesemia atau hipokalemia terjadi pada tiap pasien. (FMI 2014;50:172-178)*

**Kata kunci:** cisplatin, gangguan elektrolit, serum magnesium, serum kalium, suplementasi

### ABSTRACT

*Cisplatin is a chemotherapeutic agent for cervical cancer patients receiving radiation as the main therapy. One of cisplatin's side effects is electrolyte disturbance, which is decreasing magnesium and potassium level. However, the application of MgSO<sub>4</sub> and KCl parenteral supplementation effectiveness as the hypomagnesaemia and hypokalemia prophylaxis remained in question. This study was to evaluate magnesium and potassium parenteral supplementation effectiveness on magnesium and potassium serum level in cervical cancer patients receiving cisplatin 50 mg/m<sup>2</sup>. This was an observational study using cross-sectional method. The inclusion criteria was IIB stage cervical cancer patients who were going to receive the fourth cycle. All patients (n=22 patients) received 1000 cc normal saline (NS) hydration, but only patients in treatment group (n=11 patients) received MgSO<sub>4</sub> (0.5 g) and KCl (10 mEq) supplementation together with post-chemotherapy hydration. Data obtained were magnesium, potassium, creatinine, and BUN serum concentration, each was measured pre- and post-fourth cycle cisplatin chemotherapy. Results, in pre-fourth cycle control group, magnesium serum level was  $1.87 \pm 0.22$  mg/dL while potassium was  $4.15 \pm 0.71$  mmol/L. In post-fourth cycle, magnesium serum was  $1.75 \pm 0.19$  mg/dL while potassium was  $4.21 \pm 0.67$  mmol/L. In pre-fourth cycle treatment group, magnesium serum was  $1.95 \pm 0.25$  mg/dL while potassium was  $4.06 \pm 0.36$  mmol/L. In post-fourth cycle, magnesium serum was  $1.85 \pm 0.16$  mg/dL while potassium was  $4.01 \pm 0.28$  mmol/L. In conclusions, both groups showed no significant difference in magnesium serum and in potassium levels. No clinical manifestation hypomagnesaemia or hypokalemia appeared in any patient. (FMI 2014;50:172-178)*

**Keywords:** cisplatin, electrolyte disturbances, magnesium serum, potassium serum, supplementation

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### INTRODUCTION

Cancer of the cervix can be defined as the malignant transformation of the cervix uteri. The most common cause is human papilloma virus (HPV) infection

(Cherath et al 2005, DeCherney et al 2007). Treatment for cervical cancer can be either surgery, radiation, or chemotherapy according to the stage and tissue metastases (Cherath et al 2005). National Cancer Institute recommend cisplatin-based as the

chemotherapy given concurrently with radiation therapy for cervical cancer (Monk & Tewari 2007). Cisplatin nephrotoxicity is dose-related, cumulative, and usually reversible. Acute nephrotoxicity caused by cisplatin is characterized by decreased mitochondrial function, decreased ATPase activity; altered cell cation content, altered solute transport; persistent losses of sodium, magnesium (Mg), potassium (K), calcium, water; decreased renal blood flow (RBF) and glomerular filtration rate (GFR); increased serum creatinine (SCr); and increased blood urea nitrogen (BUN). These events precede renal architectural alterations (Stewart et al 1985, Cornelison & Reed 1993, Tiseo et al 2007, Arunkumar et al 2011). The major site of cisplatin-induced damage in the kidney is generally felt to be the part of proximal and distal tubule, but collecting duct sometimes can also be affected. This impairment of the tubule is believed to cause the occurrence of body electrolyte imbalance (Stewart et al 1985, Zekri et al 2009). According to a study, the most common manifestation of nephropathy is mild hypomagnesaemia grade 1 which occurs significantly after fourth or fifth cycle of chemotherapy (Anvari et al 2010, Mashhadi et al 2013). Hypomagnesaemia occurs because of elevated magnesium excretion as the result of decrease Mg reabsorption in the proximal tubule and collecting duct (Cornelison & Reed 1993). It is known that cisplatin treatment can cause up to 90% Mg deficiency in patient who does not acquire Mg supplement as prophylaxis (Gaby 2009). In the beginning, Obstetric and Gynecologic ward Dr. Soetomo Hospital applies only 75 mg/m<sup>2</sup> cisplatin-based chemotherapy together with 2000 cc normal saline (NS) hydration.

Then 50 mg/m<sup>2</sup> dose is also used as a combined therapy while the patient is waiting for radiotherapy, because radio-therapy device is limited. This fact makes a large amount of cisplatin dose 50 mg/m<sup>2</sup> chemotherapy usage. The protocol used is based on BC Cancer Agency (BCCA) that is dose 40-60 mg/m<sup>2</sup> needs 1000 cc NS hydration for more than 1 hour with parenteral supplementation of MgSO<sub>4</sub> 0.5 g and KCl 10 mEq (BC Cancer Agency Drug Manual 2008). This was an observational, cross-sectional study for evaluating the effect of parenteral supplementation of MgSO<sub>4</sub> 0.5 g and KCl 10 mEq towards magnesium and potassium serum level in cervical cancer patients receiving cisplatin single dose 50 mg/m<sup>2</sup> as neo-adjuvant chemotherapy which had never been held before.

## MATERIALS AND METHODS

This observational cross-sectional study is conducted for 4 months (June - September 2013). Population subject were cervical cancer patients who were

hospitalized in Obstetric & Gynecologic ward in Dr. Soetomo Hospital. Patients were elected by consecutive sampling, we took every patient who fulfills the criteria. Later they were divided into 2 groups, which are control (patients did not acquire MgSO<sub>4</sub> 0.5 mg and KCl 10 mEq supplementation after obtained each cycle of chemotherapy) and treatment (patients acquired MgSO<sub>4</sub> 0.5 mg and KCl 10 mEq supplementation after obtained each cycle of chemotherapy). Patients got chemotherapy once a week. Prior to the fourth cycle, patients' Mg and K serum level were evaluated as a pre data and one week afterward they were evaluated again as a post data. Each group consists of 11 patients.

Inclusion criteria for this study were IIB stage cervical cancer patients treated with single dose cisplatin 50 mg/m<sup>2</sup> who were ready for the fourth cycle and always got the same chemotherapy regimen since the first cycle; women more than 21 years old who were willing to sign informed consent. While exclusion criteria included patients whose respiration rate less than 16 times/min; hypotensive patients (blood pressure < 90/60 mmHg); patients with decreased or without patella reflex; and patients suffer from diabetes mellitus.

## Data Analysis and Statistics

For analyzing the alteration of Mg and K serum level between pre and post data, we used paired t-test for normal distribution and Wilcoxon test for the other one. While to compare effect supplementations on Mg and K serum level between two groups, we used independent t-test if the distribution is normal and Mann-Whitney test if it is not normal. We used the differences between pre and post data as parameters.

## RESULTS

Number of samples who fulfill inclusion criteria from June until September 2013 were 22 patients, divided into 11 patients for control group and 11 patients for treatment group. Sample of study characteristics are shown in Table 1.

Pre-data was collected before patients endured fourth cycle chemotherapy, because a study concluded that the most significant decline of Mg and K serum level because of cisplatin-based chemotherapy occurred after the third cycle, while post-data was collected a week after patients endured the fourth cycle. Data of Mg and K serum level are shown in Table 2.

Statistical analysis used to compare Mg and K serum level between pre-data and post-data is paired t-test. The results of this test are shown in Table 3. There was no

significant change between pre- and post-data in control group either for Mg serum level ( $p = 0.065$ ) or K serum level ( $p = 0.705$ ). In treatment group there was also no significant change between pre- and post-data either for Mg serum level ( $p = 0.104$ ) or K serum level ( $p = 0.574$ ).

Table 1. Sample of study characteristics

Patients' Characteristics	Number of Patients (N = 22)	%
Age (years)		
Average = 48.7 (36-64)		
Range 30-40	2	9.09
Range 41-50	14	63.64
Range 51-60	4	18.18
Range 61-70	2	9.09
Range of GFR Level		
60 cc/min	16	72.73
50-59.99 cc/min	6	27.27
< 50 cc/min	—	—
Range of Body Mass Index		
18.5-22.9 kg/cm <sup>2</sup>	10	45.45
23-24.9 kg/cm <sup>2</sup>	3	13.64
25 kg/cm <sup>2</sup>	9	40.91

Meanwhile, we calculated the difference of pre- and post-data for both Mg and K serum level to compare the change between control and treatment group. Statistical analysis used to compare these groups is independent t-test. Table 4 showed the result of statistical test to evaluate the effect of MgSO<sub>4</sub> (0.5 g) and KCl (10 mEq) parenteral supplementation between control and treatment group which did not statistically give any significant difference, for either Mg serum level ( $p = 0.914$ ) or K serum level ( $p = 0.539$ ).

## DISCUSSION

Cisplatin is an antineoplastic drug used in the treatment of many solid-organ cancers, including those of the head, neck, lung, testis, ovary, and breast (Miller et al 2010). According to the protocol used in Obstetric-Gynecologic Department in Dr. Soetomo Hospital, single dose cisplatin 50 mg/m<sup>2</sup> regimentation is applied as neo-adjuvant therapy (NAC) for cervical cancer stage IB2 or more, which is given weekly. This study was conducted since June until September 2013, involving woman patients with cervical cancer stage IIB who acquired single dose cisplatin 50 mg/m<sup>2</sup> chemotherapy as NAC. Inclusion criteria were patients had received 3 chemotherapy cycles and were going to endure the fourth cycle. This was an observational with cross-sectional assessment study.

Table 2. Magnesium and Potassium Serum Level

Observation	Average Control Group (n = 11)		Average Treatment Group (n = 11)	
	Pre 4 <sup>th</sup> Cycle	Post 4 <sup>th</sup> Cycle	Pre 4 <sup>th</sup> Cycle	Post 4 <sup>th</sup> Cycle
Mg (mg/dL)	1.87 ± 0.22	1.75 ± 0.19	1.95 ± 0.25	1.85 ± 0.16
K (mmol/L)	4.15 ± 0.71	4.21 ± 0.67	4.06 ± 0.36	4.01 ± 0.28
S <sub>Cr</sub> (mg/dL)	0.95 ± 0.08	1.00 ± 0.17	0.88 ± 0.17	0.92 ± 0.17
BUN (mg/dL)	11.00 ± 3.77	12.45 ± 4.76	14.00 ± 7.17	12.09 ± 3.59

Table 3. Statistical Analysis between Pre- and Post- Fourth Cycle Chemotherapy

Parameter	Control Group			Treatment Group		
	Average ± Sd	T-Count	Significant Value	Average ± Sd	T-Count	Significant Value
Mg Level	0.118 ± 0.189	2.076	0.065	0.109 ± 0.202	1.789	0.104
K Level	-0.064 ± 0.541	-0.390	0.705	0.055 ± 0.311	0.582	0.574

Table 4. Statistical Analysis of the Difference of Magnesium and Potassium Serum Level between Control and Treatment Groups

Group	Magnesium Serum Level			Kalium Serum Level		
	Average ± Sd	T-Count	Significant Value	Average ± Sd	T-Count	Significant Value
Control	-0,118 ± 0,189	-0,109	0,914	0,064 ± 0,541	0,628	0,539
Treatment	-0,109 ± 0,202			-0,055 ± 0,311		

We chose patients with cervical cancer stage IIB as an inclusion criterion because they would receive cisplatin chemotherapy weekly. The range of patients' ages which involved in this study was between 36-64 years old (average = 48.7 years old), with the most common incidence occurred in range 41-50 years old. In this case, age was not one of the risk factors affecting the development of cervical cancer disease (Parra et al 2006, Beckmann et al 2010, Dizon & Campos 2011). Besides, age also did not affect any Mg metabolism in plasma (Lajer et al 2003). But, according to the data acquired by Asia Oceania Research Organization in Genital Infection and Neoplasia (OAGIN), it is known that commonly this disease occurs in 40-50 years old women, with incubation period estimated approximately 7-10 years. It means that the patients began to be infected by human papilloma virus (HPV) in productive age about 30-40 years old.

This study focused on the evaluation of the effectiveness application of MgSO<sub>4</sub> (0.5 g) and KCl (10 mEq) for patients who acquiring cisplatin chemotherapy, with Mg and K serum level as measuring parameters. Evaluation was conducted when patients were going to endure the fourth cycle chemotherapy (pre-data) and after patients got the fourth cycle chemotherapy (post-data).

Based on the routine procedure, every patient acquiring 50 mg/m<sup>2</sup> dose cisplatin with GFR 60 cc/minute would also receive NS hydration 500 cc each pre- and post-chemotherapy. Together with hydration after chemotherapy, patients also received 0.5 g MgSO<sub>4</sub> and 10 mEq KCl supplementation. This protocol refers to the BC Cancer Agency (BCCA). The hydration was given to prevent cisplatin ligand exchange and advance damage caused by platinum-protein bond. Besides, NS 'hydration also applied in purpose to shorten the contact time between drug and renal tubule. NS hydration becomes the most important strategy to protect and maintain renal function (Cornelison & Reed 1993).

Cisplatin chemotherapy toxicities include ototoxicity, gastrotoxicity, allergic reaction, myelosuppression, and the main dose-limiting side effect, nephrotoxicity (Miller et al 2010). Acute renal failure can be occurred even in low-dose cisplatin which is given routinely. This condition is caused by free cisplatin which does not bond with plasma protein will be infiltrated freely in glomerulus (because of the low molecular weight), accumulated, and finally injured renal function (Launay-Vacher et al 2008, Moon et al 2011). Besides, necrosis on major nefron can also disturb electrolyte balance (Arunkumar et al 2011). Cisplatin is known as cytotoxic agent which often cause electrolyte imbalance (Zekri et al 2009). Direct injury at loop of Henle, either

in ascending or descending is believed as the mechanism causing hypomagnesaemia. While hypokalemia can be occurred because of increase renal reabsorption capacity as a respond of decrease potassium absorption in intestinal (Arunkumar et al 2011).

Magnesium serum level in both control and treatment group decreased after patients got the fourth cycle chemotherapy. But statistically no difference shown by paired t-test analysis between pre-data and post-data. Although both of them endured the same decrease, Mg serum level in treatment group was higher than in control group. However, according to the independent t-test analysis, there was no significant difference between Mg serum level in control and in treatment group. Uncontrollable patients' intake while they were at home became one of the factors affecting this condition, besides the degree of nausea/vomiting which happened in patients. Degree of nausea/vomiting could affect Mg serum level because excessive vomiting will cause Mg deficiency (Zekri et al 2009). According to the patients' assessments, it was known that nausea/vomiting happened more frequently in treatment group (9 patients) than in control group (5 patients). A literature stated that body Mg surplus can cause vomiting and constipation (Lang 2000).

In the other hand, severe nausea/vomiting occurred in most patients may also because of cisplatin is high emetogenic drug. That severe nausea/vomiting (> 90%) could occur immediately or delayed. Risk of nausea/vomiting because of cisplatin increase in woman patients, young patients, high-dose cisplatin application, and rapid infusion. Nausea/vomiting could also affect patients' intake by decreasing their appetite. Most of patients complained for 3-5 days decrease of appetite after chemotherapy.

A study concluded that plasma Mg cannot be the only reliable parameter used to measure total body Mg reserved, Mg depletion, and supplementation treatment, because most Mg is stored in intracellular element and only about 0.3% of total body Mg appears in plasma (Lajer et al 2003, Anvari et al 2010). In his study, Macaulay et al (1982) also met progressively decrease of Mg serum level even in group of patients who received supplementation either orally or intravenously.

Meanwhile, hypokalemia is a common condition occurred in cisplatin-based chemotherapy because of incline renal reabsorption capacity as a result of decrease K absorption in intestine (Arunkumar et al., 2011). Based on statistical analysis used in this study, there was no significant difference in K serum level between post- and pre-fourth cycle chemotherapy.

Increased K excretion was caused by increasing K secretion (via sodium-load dependent potassium mechanism) by means to increase sodium, potassium, and water concentration in distal segment of renal, because of the decrease sodium reabsorption in proximal tubule. Furthermore, loss of renal potassium and calcium is the secondary result of Mg deficiency (Cornelison & Reed 1993).

There is a related link between hypomagnesaemia and hypokalemia: the decrease of intracellular Mg which is caused by Mg deficiency will mediate renal outer medullary potassium (ROMK) channel inhibition by Mg and increase K secretion. Besides, Mg deficiency will disturb Na-K-ATPase regulation and decrease uptake K<sup>+</sup> into cells. Decrease of cellular K<sup>+</sup> uptake if occurs concomitantly with increase either gastrointestinal excretion or urinary will cause K<sup>+</sup> loss and hypokalemia. About 50% hypokalemia incidence occurs together with Mg deficiency. Mg and K are the most abundant cations in intracellular which function to stabilize potential membrane and decrease cell excitation. Mg plays an important role in K intracellular balance. Hypokalemia affecting tissue will be more severe and refractory if preceded by Mg deficiency (Huang & Kuo 2007, Zekri et al 2009).

Evaluation of the effectiveness MgSO<sub>4</sub> and KCl supplementation in patients receiving cisplatin chemotherapy was conducted by comparing between 2 groups of patients. In control group, patients receiving cisplatin did not acquire MgSO<sub>4</sub> (0.5 g) and KCl (10 mEq) supplementation at all during enduring all four cycles of chemotherapy, while treatment group consisted of patients who received MgSO<sub>4</sub> (0.5 g) and KCl (10 mEq) supplementation in each cycle of chemotherapy during enduring 4 cycles of cisplatin chemotherapy. After conducting statistical analyzes using independent t-test, we gained a conclusion that MgSO<sub>4</sub> and KCl supplementation gave a significant difference neither in Mg nor in K serum level in patients who received that supplementation when compared with patients who did not.

A study stated that although Mg supplementation appears to be beneficial for all patients, it is likely that the greatest benefit will be to patients with large volume metastatic disease who may require prolonged treatment with cisplatin (Wilcox et al 1986). Study conducted by Lajer et al. in 26 patients with cisplatin treatment results a significant difference in Mg plasma measurement between before and after chemotherapy, and also for intracellular K in skeletal muscle biopsy. But there was no significant difference in K plasma between before and after chemotherapy. This study also showed that there was a correlation between Mg and K plasma

which each was measured after chemotherapy (Lajer et al 2003). In other hand, a study conducted by Macaulay et al (1982) concluded that supplementation applied intravenously in a short time could not compensate variable patients' food intake for a long time. On the contrary, that supplementation will lead to increasing urinary Mg loss while maintaining Mg serum level in the normal range. It seems that urinary Mg loss happened in patients was resulted from the large amount of liquid given besides from renal injury because of cisplatin (Macaulay et al 1982).

Although there was no statistically significant result in this study, the results showed that there was an increasing K serum level after fourth cycle chemotherapy in control group. This condition may be caused of decreasing renal function which was showed from much lower GFR value (calculated with Cockcroft-Gault formula) in control group than in treatment group. Decreasing renal function until renal impairment becomes the most common cause of hyperkalemia, because K excretion by renal is an important defense mechanism towards chronic K disturbance (Freshwater-Turner et al 2008). This depends on the glomerular free filtration, huge amount of reabsorption in proximal tubule, also secretory regulation process in distal convoluted tubule, cortical collecting duct, and outer medullary collecting duct.

Cortical collecting duct and outer medullary collecting duct consist of at least 2 types of different cells, termed principal cells and intercalated cells. Principal cells, which comprise approximately 70-75% of collecting duct cells, mediate sodium reabsorption and potassium secretion and are targets for angiotensin II, aldosterone, aldosterone receptor antagonists, and potassium-sparing diuretics. Principal cells exploit the electrochemical gradient established by sodium entry into the cell through a sodium channel at the luminal membrane and the basolateral membrane Na-K-ATPase to drive potassium secretion through 2 classes of luminal membrane potassium channels. The other collecting duct cell type, intercalated cells, mediate acid-base transport but upregulate expression of luminal H,K-ATPases during potassium depletion to enhance potassium reabsorption (Greenlee et al 2009). Renal impairment will disturb K homeostasis regulation (Freshwater-Turner et al 2008).

Meanwhile, there was decreasing in K serum level in treatment group. Nausea/vomiting incidents occurred longer and more common in patient in the treatment group. Vomiting can cause decrease body K level. This is not because of loss K from vomiting, but because of loss H<sup>+</sup> and water which leads to metabolic alkalosis and aldosterone increasing. When extracellular body pH

increases, the cells release  $H^+$  in exchange for  $Na^+$  ( $Na^+/H^+$  exchangers) and pump the  $Na^+$  out again in exchange for  $K^+$  ( $Na^+-K^+$ -ATPase). This  $K^+$  uptake by the cells causes hypokalemia (Lang 2000). Meanwhile, aldosterone plays a role to increase  $Na^+-K^+$ -ATPase activity in distal tubule and collecting duct (Freshwater-Turner et al 2008).

There was also a chance that intracellular  $K^+$  was not in balance state during cisplatin treatment. When hypokalemia occurs, body activates some mechanisms to maintain body  $K^+$  level, especially by renal role. Besides, skeletal muscle and liver can also be a buffer toward alteration of plasma  $K^+$  concentration by means of transcellular  $K^+$  redistribution and feedback control for renal  $K^+$  excretion.  $Na^+-K^+$ -ATPase actively pumps  $K^+$  into cells and maintains extracellular electrochemical gradient in normal range between 3.5-5.0 mmol/L and intracellular  $K^+$  concentration around 150 mmol/L, which is very important for excitable cells function.  $\beta$ -catecholamines, aldosterone, insulin, pH, and osmolality can also affect transcellular  $K^+$  distribution. By that function, they help to restabilize alteration of  $K^+$  concentration which ever occurred in plasma (Greenlee et al 2009).

Measurement of hyperkalemia severity can be determined by its symptoms, plasma  $K^+$  concentration (although this value is not representative enough), and electrocardio-graphy abnormality. But to determine more precisely the cause of  $K^+$  loss from renal, trans-tubular potassium concentration gradient (TTKG) can be conducted. TTKG is calculated by comparing  $K^+$  concentration in lumen of cortical collecting duct with  $K^+$  concentration in peri-tubular capillary or plasma. The validity of measurement is affected by the number of solute reabsorbed in medullary collecting duct, neither secreted nor reabsorbed  $K^+$  in medullary collecting duct, and the amount of liquid osmolality in the edge of cortical collecting duct. Hypokalemia state with TTKG value  $> 4$  indicates that loss of renal  $K^+$  is a result from increasing distal  $K^+$  secretion.

Hypomagnesaemia may become symptomatic, with muscle irritability or cramps, clonus, tremor, carpopedal spasm and/or tetany (BC Cancer Agency Drug Manual 2008, Jahnen-Dechent & Ketteler 2012), while, excessive  $Mg$  concentration in body can lead to  $Mg$  intoxication with such symptoms as constipation, vomiting, hypotension, neuromuscular dysfunction, hypotonia, atonia, even respiratory depression (Lang 2000, Jahnen-Dechent & Ketteler 2012). These symptoms often occur in eclampsia treatment with  $MgSO_4$  as seizure prophylaxis.

In this study, we also observed patients' clinical condition after chemotherapy was given together with its hydration and supplementation, but there was none of them showed these symptoms. A literature stated that even in a patient with severe hypomagnesaemia, clinical symptoms related to  $Mg$  deficiency do not likely appear (Jahnen-Dechent & Ketteler 2012).

Besides  $K^+$ ,  $Mg$  existence in the body can also affect body calcium regulation. Then to precisely determine electrolyte imbalance, calcium serum level may become an alternative measurement, considering that  $Mg$  existence in extracellular fluid is not quite amount enough. Uncontrollable patients' food intake while they were at home became a limitation for this study, because it might affect  $Mg$  and  $K^+$  serum level when the patients returned to the hospital a week later.

## CONCLUSION

Magnesium and potassium parenteral supplementation does not produce significant effect on magnesium and potassium serum level of cervical cancer patients receiving cisplatin chemotherapy.

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