EVALUATION OF RENAL FUNCTION IN CERVIX CANCER PATIENTS BY DOSE CISPLATIN 75 mg/m^2 WITH NaCl-MANITOL HYDRATION

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ABSTRAK

*Cisplatin merupakan sitostatika golongan platinum yang poten untuk terapi kanker solid, salah satunya adalah kanker serviks. Efek samping selama pemberian obat adalah nefrotoksisitas akut atau kronik. Studi prospektif, observasional, cross sectional dilakukan untuk mengevaluasi hidrasi NaCl Manitol pada produksi urin dan fungsi ginjal pasien kanker serviks yang mendapat kemoterapi cisplatin 75 mg/m^2. Kriteria inklusi pasien dengan eClCr Cockroft Gault > 60 mL/menit pada siklus berapapun, menerima hidrasi 1 L NaCl prekemoterapi dan 1 L hidrasi NaCl post kemoterapi dengan tambahan 30 g Mannitol, 20 mEq KCl dan 1 g MgSO4. Data laboratorium yang dikumpulkan pada saat pre kemoterapi post kemoterapi adalah BUN, serum kreatinin, albumin dan eClCr (Cockroft Gault dan MDRD). Produksi urin diukur sebelum kemoterapi, jam ke-3 dan jam ke-12 post kemoterapi. Produksi urin 21 pasien mencapai target > 100 mL/jam pada pengukuran jam ke-3 post kemoterapi. Sebanyak 8 pasien (39%) mengalami nefrotoksisitas akut yang ditandai dengan peningkatan serum kreatinin lebih dari 1,5 kali baseline.**(FMI 2014;50:226-233)***

Kata kunci: *Cisplatin, hidrasi, gagal ginjal, serum kreatinin, eClCr*

ABSTRACT

*Cisplatin is one of platinum cytostatic drug for the medication of solid cancers, one of which is cervical cancer. Adverse event that resulted during drug treatment was acute or chronic nephrotoxicity. A cross sectional, prospective, observational study was conducted to evaluate the effect of NaCl-Mannitol hydration on urine production and renal function of cervical cancer patients receiving cisplatin 75mg/m^2. Inclusion criteria were 21 pastients eClCr Cockroft Gault > 60 ml/min of any cycle, receiving 1 L of NaCl hydration pre chemoteraphy and 1 L of NaCl plus 30 g Mannitol, 20 mEq KCl, and 1 g MgSO4 for post chemoteraphy. Data obtained were BUN, SrCr, albumin and eClCr calculation (MDRD and Cockroft Gault), each was measured pre and day six post treatment. Urine production was measured before chemotherapy and 3 and 12 hours post chemoteraphy hydration. Urine production of total 21 inpatients had reached > 100 mL/hour at 3rd hour post chemotherapy. There were 8 patients (39%) who experienced acute nephrotoxicity characterized by an increase of serum creatinine by 1.5 times from the baseline. **(FMI 2014;50:226-233)***

Keywords: *Cisplatin, hydration, renal impairment, serum creatinine, eClCr*

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INTRODUCTION

Cisplatin is one of platinum cytostatic drug for the medication of solid cancers, one of which is cervical cancer. Using Cisplatin caused acute or chronic nephrotoxicity A lot of Cisplatin in the body accumulated in the kidney will damage it's function. Arany & Safirstein 2003, Yao et al 2007 suggested that accumulation of Cisplatin in the kidney induce nephrotoxicity. Due to this characteristic of Cisplatin, important to study about urine produce and renal function on patient who get Cisplatin chemotherapy.

Vacher et al 2008 has reported that nephrotoxicity by cisplatin can be prevented by modification method giving aggressive hydration, nephro-protection drug and other development analog platinum repaired therapeutic index. Miller et al 2010 suggested that hydration Sodium Chloride (NaCl) in large number become a major strategy decrease effect Cisplatin nephrotoxicity. However there is no information how does urine produce and renal function on cancer patients who got chemotherapy Cisplatin with hydration NaCl-Manitol.
Adequate hydration during giving Cisplatin (up to 12 hours after) induced diuresis at least 100 mL/hour. Frick et al 1978 and Vacher et al 2008 have reported that mannitol dan furosemid decrease concentration of platinum in the urine by increasing diuresis so it will be shorten the time contact drug with renal tubular which expected decrease nephrotoxic effect by Cisplatin and

decrease toxin metabolite formation. Although, there are many article inform accumulation Cisplatin in the renal tubular, there are limited reports about evaluation urine produce and renal function due to Cisplatin therapy with NaCl-Mannitol hydration. The aim of this study was to evaluate the effect of NaCl-Mannitol hydration on urine production and renal function of cervical cancer patients got cisplatin 75 mg/m^2 was conducted in the Department of Obstetrics Gynecology RSUD Dr. Soetomo.

MATERIALS AND METHOD

This is an observational study with cross sectional approach held in SMF Obstetrics Gynecology Dr. Soetomo Hospital, Surabaya. It was to evaluate renal function of 21 cervix cancer patients before and after giving chemotherapy cisplatin 75 mg/m^2 with NaCl-Mannitol hydration. Inclusion criteria is patient with cervix cancer who gave single cisplatin dose 75 mg/m^2, age > 21 years old, eClCr Cockroft Gault > 60mL/minute, liver function, heart and lung is normal and ready to sign informed consent study. The exclusion criteria consist of patient with allergy of cisplatin, patient with nefrotoxicity inducer drugs as aminoglikosida, siklofosfamid, ifosfamid, metotreksat, etc. Whereas patient will be dropped out if they experience hypersensitivity to cisplatin during period of study, and patient died when study is held. This study has received an approval or ethics approval by Ethic Health Study Committee Dr. Soetomo Hospital Surabaya for method which submitted (313/Panke. KKE/I/2013) on Januari 18th 2013.

Patient with cervix cancer who give chemotherapy by cisplatin 75 mg/m^2 and appropriate inclusion criteria asked to fill informed consent and examined in pre-chemotherapy laboratory involved as: Complete Blood Count (CBC), albumin, creatinine serum, BUN, and count estimation ClCr with MDRD and Cockroft-Gault formula (baseline data/pre-chemotherapy). Other data that needed in this study are age, weight (kg), height (cm), body surface area (m^2), cancer stage, history of chemotherapy, other complication, history of allergy and history of therapy.

Subject are given cisplatin 75 mg/m^2 on 500 mL during 3 hours that preceded with hydration NaCl 1000 mL during 2 hours and post cisplatin get NaCl hydration 1000 mL with mannitol 30 gr, elektrolit MgSO4 1 g and KCl 20 mEq for 2 hours. Then, urine are collected and measured for 12 hours post-chemotherapy (available in pre-chemotherapy urine produce, average per hour in first 3 hours period and 3-12 hours after chemotherapy finished).

Liver function evaluation (creatinine serum, BUN, eClCr) was done in sixth day post chemotherapy and third week post chemotherapy. Acute renal interference defined by criteria of Kidney Disease Improving Global Outcomes (KDIGO 2012) is level of one enhancement creatinine serum 1.5-1.9 times from baseline, level of two enhancement creatinine serum 2.0-2.9 times from baseline, and level of three enhancement creatinine serum 3.0 times from baseline. Recovery function is evaluated by comparing creatinine serum, BUN, and eClCr in sixth day and third week.

Evaluation of NaCl-Mannitol hydration about urine produce and liver function are done analysis test different t-test in urine produce, creatinine serum pre and post chemotherapy, BUN pre and post chemotherapy, eClCr (Cockroft Gault dan MDRD) pre and post chemotherapy. To analyze relative risk between urine production and acute nefrotoxicity incident we carried out prevalence analysis with table 2 x 2 in every type of cross sectional study.

RESULTS

This study lasted from January to April 2013. The sample were 21 patients who met inclusion criteria. The average age of patients was 47.1 years with range 30-57 years old. Type of cervical cancer based on anatomic pathology examination grouped into keratinized carcinoma squamous cell (n = 4), non-keratin carcinoma squamous cell (n = 12), and adenocarcinoma (n = 5) were dispersed in several stages namely stage 1b to Iva (Table 1).

Urine Production Monitoring

Urine production pre-Chemotherapy hydration and post chemotherapy hydration (Table 2) urine production in the most patients reached ≥ 100 mL/hour. However, there were 2 patients pre chemotherapy and 6 patients 12nd hours post-chemotherapy hydration measured urine output < 100 mL/hour. There were 100% patients achieving urine production target > 100 mL/hour which were measured at 3rd hour post-chemotherapy hydration. Different test t-test between urine capacity measurement period showed that there were statistically significant differences ($p < 0.05$), where the highest urine production occurs in the 3rd hour period caused by the diuretic effect of mannitol.

Table 1. Characteristic of cervical cancer patients

Patients Characteristics	Amount of Patient (n=21) (%)	Range
Age (years old)		
Average	47.1	30 - 57
Kind of cancer according to histology		
Keratin Squamous Cell	4 (19)	
Non Keratin Squamous Cell	12 (57)	
Adenocarcinoma	5 (24)	
Characteristic of Cervix Cancer (FIGO)		
Stadium I b	1 (4.8)	
Stadium II a	1 (4.8)	
Stadium II b	7 (33.3)	
Stadium III a	1 (4.8)	
Stadium III b	10 (47.6)	
Stadium IV	1 (4.8)	
Chemotherapy *Neoadjuvant**		
Cycle I	3 (14.3)	
Cycle II	6 (28.6)	
Cycle III	6 (28.6)	
Cycle IV	1 (4.8)	
Cycle V	4 (19)	
Cycle VI	1 (4.8)	
Baseline Clinic Parameter		
BUN (mg/dL)		9.71 ± 3.24 (4 - 15)
Creatinine Serum (mg/dL)		0.86 ± 0.19 (0.5 – 1.2)
eClCr Cockroft Gault (mL/menit)		78.7± 20.54(60.2 – 142.7)
Stage 1 : >90	4 (19)	
Stage 2 : 60 – 89	17 (80.9)	

Table 2. Urine Production Monitoring Pre and Post Chemotherapy Cisplatin 75mg/m^2

Urine Production	Amount of Patient (%) (n = 21)	Average Value (range)
Pre Chemotherapy (mL/ hour)		212± 119 (10 - 506)
<100 mL/hour	2 (9.5)	
>100 mL/hour	19 (90.5)	
3rd hour post chemotherapy hydration (mL/ hour)		275± 86 (136 - 433)
<100 mL/hour	-	
>100 mL/ hour	21 (100)	
12nd hour post chemotherapy hydration(mL/ hour)		131± 44 (75 - 230)
<100 mL/ hour	6 (28.5)	
>100 mL/ hour	15 (71.5)	

Table.3 Renal Function Monitoring Pre dan Post Chemotherapy Cisplatin 75 mg/m^2

Patients (Total N = 21)	Baseline				6th Day Post Chemotherapy			
	BUN (mg/dL)	SK (mg/dL)	eClCr CG (mL/minute)	eClCr MDRD (mL/minute)	BUN (mg/dL)	SK (mg/dL)	eClCr CG (mL/ minute)	eClCr MDRD (mL/ minute)
Average ± SD	9.71 ± 3.24	0.86 ± 0.19	78.7 ± 20.54	86.7 ± 22.94	20.86 ± 16.54	1.13 ± 0.40	62.6 ± 27.58	65.9 ± 24.66
Average	4-15	0.5 – 1.2	60.2–142.7	55.1–140.8	6–65.69	0.6–2.4	23.5–134.1	20.71-120.36

6th day Renal Function Evaluation Post Chemotherapy

On the sixth day creatinine serum increased from baseline by an average score increase of 0.272 mg/dL (p = 0.003), which was followed by a decrease eClCr Cockroft Gault and MDRD each with an average value decrease -16.127 mL/minute/1.73 m^2 (p = 0.002) and -20.693 mL/minute/1.73 m^2 (p = 0.001) (Table 3). From observation result of all patients (n = 21) obtained 8 patients (39%) experienced acute renal disorder consisting of 7 patients experienced acute renal impairment level 1 criteria (KDIGO) and one patient experienced acute renal impairment level 2 KDIGO criteria (Figure 1, Table 4).

Prevalence of Urine Production with Increased Serum Creatinine in 6th day

Giving pre-chemotherapy and post-chemotherapy hydration is expected to prevent and minimize nephrotoxic effects of cisplatin by decreasing contact time of platinum with tubular cells nephron. Urine production target was 100 mL/hour before and after chemotherapy. Urine production can be used as a reference for nephrotoxicity degree (KDIGO 2012), but is not used as an absolute data. As an example (table 2) 2 patients who prekemoterapi urine output < 100 mL/hour after getting second post-chemotherapy hydration both of them can achieve a urine production target ≥ 100 mL/hour. Prevalence studies calculate prevalence ratios (relative risk) by using a 2 x 2 table, prevalence comparison of AKI in the group who have risk factors (urine output < 100 mL/hour) with the prevalence of AKI in patients who have not risk factors (production urine ≥ 100 mL/hour).

In the pre-chemotherapy urine produce group, prevalence ratio = 1.35 with confidence interval 0.47 to 2.87, while ratio of prevalence urine post chemotherapy in 12nd hour = 0.83 with confidence interval of 0.38 to 2.22. Confidence interval values prevalence ratio exceed 1, so the factor were tested on sample population represented can be concluded as risk factor and/or protective factor.

Renal Function Recovery After Chemotherapy in 3rd week. In this research, there was an additional monitoring measurement of renal function after three weeks of chemotherapy to see recovery by comparing serum creatinine examination, eClCr Cockroft Gault and eClCr MDRD in the sixth day post-chemotherapy with 3rd week post chemotherapy (Table 5). Creatinine serum decreased by 0.13 ± 0.37 mg/dL (p = 0.151), eClCr Cockroft Gault has increased 5.62 ± 23.66 mg/dL (p = 0.328), eClCr MDRD 9.54 ± 22.69 mg/dL (p = 0.092). From the statistical analysis different test of t-test there was no significant difference between kidney function post-chemotherapy, and day-to-six weeks to three. Distribution Cockroft Gault and MDRD eClCr Pre and post-chemotherapy presented in figure 2 and 3.

Table. 4 Patients with Acute Nephrotoxicity Post Chemotherapy Cisplatin 75 mg/m^2 in 6th day

Patients	Cycle	Rising Creatinine Serum in 6th day to *Baseline* (x times *baseline*)	Level of Effect Acute Renal Disorder	
			Level	Range
A	2	1.80	1	1.5 – 1.9
B	3	1.50	1	1.5 – 1.9
C	2	1.56	1	1.5 – 1.9
D	3	1.57	1	1.5 – 1.9
E	2	1.83	1	1.5 – 1.9
F	2	1.50	1	1.5 – 1.9
G	5	1.50	1	1.5 – 1.9
H	4	2.41	2	2.0 – 2.9

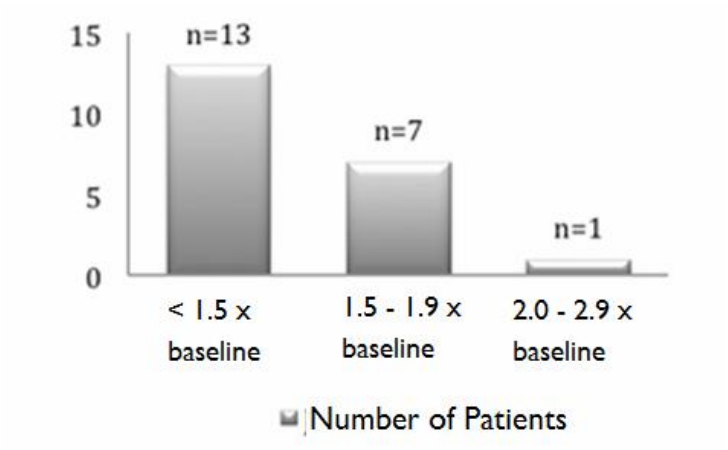

Figure 1. Distribution of patients have with increased creatinine serum post chemotherapy Cisplatin 75 mg/m^2 in 6th day

Table 5. Monitoring of BUN, Creatinine Serum, eClCr Post Chemotherapy Cisplatin 75 mg/m^2 in 6th day and 3rd week

Patients (Total N = 21)	6th day Post Chemotherapy				3rd week Post Chemotherapy			
	BUN (mg/dL)	SK (mg/dL)	eClCr CG (mL/minute)	eClCr MDRD (mL/minute)	BUN (mg/dL)	SK (mg/dL)	eClCr CG (mL/minute)	eClCr MDRD (mL/minute)
Average	21,16 ± 16,9	1,12 ± 0,34	60,28 ± 23,64	65,01 ± 21,91	11,44 ± 3,74	0,99 ± 0,22	65,90 ± 17,83	74,56 ± 21,66
Range	6 – 65	0,6 – 2,4	23,5 – 134,1	20,71 – 120,36	6 – 19	0,5 – 1,4	44,3 – 106,82	45,4 – 145,13

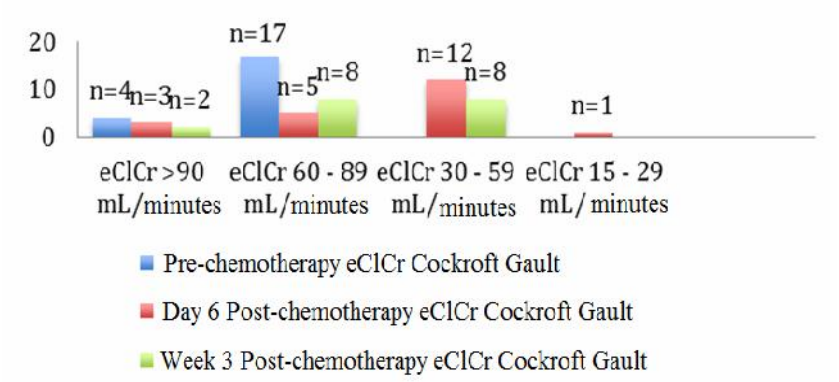

Figure 2. Patients Distribution based on eClCr Cockroft Gault Pre Post Chemotherapy Cisplatin 75 mg/m^2

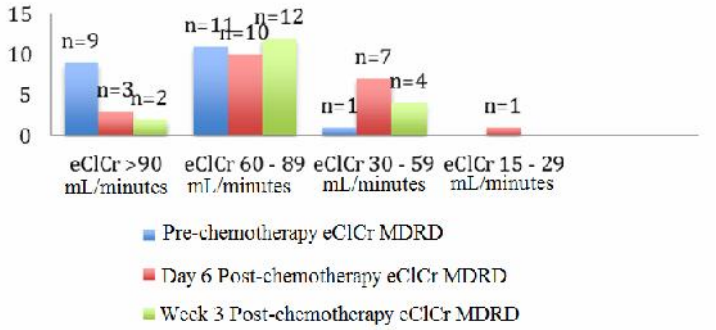

Figure 3. Patients Distribution based on eClCr MDRD Pre Post Chemotherapy Cisplatin 75 mg/m^2

DISCUSSION

The observations in emphasized evaluation of renal function in cervical cancer patients who received cisplatin 75 mg/m^2 by administering saline hydration NaCl1L pre chemotherapy and NaCl 1 L post-chemotherapy hydration with addition of 30 g mannitol in SMF Obstetrics Gynecology.

Monitoring of measurement of urine volume during hydration pre and post chemotherapy (at begun pre-hydration up to 12 hours later). There were 2 patients (9.5%) were measured before chemotherapy their urine production < 100 mL/hour , both of patients with stage IIIa and IIIb. According FIGO criteria stage IIIa yet happen cancer expansion to the pelvic wall while on stage IIIb happened cancer expansion to pelvic wall, hydronephrosis and renal function impaired. After the second hydration, 1 L of NaCl with addition of 30 g of mannitol as much as 100% of patients achieving urine production target > 100 mL/hour which measured at 3rd hour post chemotherapy hydration, while at the 12th hour post chemotherapy hydration contained 71.5% patients achieving urine production target > 100 mL/hour (6 patients did not achieve the target). From examination history of intravenous pyelogram (IVP) and abdominal ultrasound, urine output of eight patients pre/post chemotherapy did not achieve the target > 100 mL/hour was not obtained renal dysfunction and hydronephrosis, however to check final condition of patient if there was or was not an obstruction/ hydronephrosis, it IVP examination/abdominal ultra-sound should be repeated.

Patients who received hydration fluid should be euvolemi in state. Addition of fluid on hypovolemia

state for rehydration, fluids will fill intravascular space first. In this study, no plasma BJ examination to assess whether the patient was in a euvolemi state in pre and post-chemotherapy. Urine production can be used as a reference for nephrotoxicity level (KDIGO 2012), but is not used as an absolute data. As an example from table 5.3, there were two patients who prekemoterapi urine output < 100 mL/hour, but after getting post chemotherapy hydration urine measurements of in 3rd hour these patients can achieve urine production target ≥ 100 mL/hour. In the physiology of urine production and elimination is affected by (1) blood flow towards glomerulus, (2) formation and ultrafiltration process by glomerulus and tubules, (3) urine excretion through ureters, bladder and urethra (Munar 2013). Urine production influenced by many factor including dehydration, fever, diarrhea and amount of water intake, but in this study these effects were not measured. Ideal infusion in this study was through infusion pump. By infusion pump speed of addition can be set accurately so condition of each subject was homogeneous. Limitations of this study, hydration fluid administration using conventional infusion, so speed of giving each patient can be vary.

Mannitol is a diuretic osomotik which works by increase in osmolarity of glomerular filtration, it caused the fluid excretion and inhibit electrolytes reabsorption in renal tubules. The occurrence of diuresis decrease platinum contact time with renal tubular cells. The half-life of mannitol ranged between 15-100 minutes, with onset of diuretic for 1-3 hours (Anderson et al 2002). In this study, diuretic effect of mannitol is proven by increased urine produce 3 hours post chemotherapy with an average value of 275 mL/hour. The addition of mannitol on post-chemotherapy hydration in this study support achievement urine production target ≥ 100 mL/hour in the 3rd hour post chemotherapy for all patients (N = 21).

Rising urine produce 3 hours after addition of mannitol cause overshoot condition urine production at beginning of period leads to dehydration if not offset by additional fluid balance. This was followed by decline in average of urine ouput at 12 hours post-chemotherapy. Renal function monitoring in 6th day post chemotherapy was obtained increase of creatinine serum 0.272 mg/dL (p = 0.003), which was followed by a decrease eClCr Cockroft Gault and MDRD with an average decrease value -16.127 mL/minute/1.73 m^2 (p = 0.002) and -20.693 mL/menit/1,73 m^2 (p = 0.001) (Table 3). The results of this study were not much different from research Santoso et al research there was an increase of creatinine serum in 6th day post-chemotherapy with an increased value 0.18 mg/dL and decrease of creatinine clearance for 24 hour 13.42 mL/minute (Santoso et al 2003). In the calculation eClCr formula there were some differences results eClCr Cockroft Gaul and MDRD (Fig. 2 and 3). It was due to variables differences in both of formula. EClCr Cockroft gault formula influenced by variables of age, weight and creatinine serum. eClCr MDRD-6 formula influenced by variables of age, BUN, creatinine serum, albumin and correction factor for dark skin race. Limitations of Cockroft Gault formula is patients with muscle disorders, malnutrition, advanced kidney disorders, liver disease, obesity, critically-ill condition and unstable renal function. MDRD formula calculation is intended for patients with PGK who have stable conditions (GFR < 90 mL/minute), non-diabetic patients and Caucasian race. The accuracy of this formula is not used in pediatric patients, geriatric, hospitalized patients, and patients with other ethnicities.

The information obtained from the pharmacy most of the patients who returned to post chemotherapy in 6th day had side effects severe nausea and vomiting. Cisplatin is high emetogenic. The risk of severe side effects of vomiting that increased in female patients, young age, high dose cisplatin administration, and rapid infusion. Severe vomiting condition is dehydration that aggravated the condition of acute renal impairment. In this study difficult to do an assessment how severe vomiting side effects experienced by patients during 6 days post chemotherapy because the patient does not exactly remember how much the frequency of vomiting experienced so no definitive data obtained. On 6th day post chemotherapy was not examined BJ plasm and so cannot know level of dehydration that may be experienceed by the patient. Condition of nausea and vomiting affects on nutritional intake of patient. There were 21 patients admitted loss of appetite for 3-7 days post chemotherapy. This condition will cause body break down non- carbohydrate sources (protein and or fat) as an energy source, so it will affect to patient's body mass.

Observations obtained from 8 patients (39% of study sample) had acute renal disorders based on criteria of rising creatinine serum KDIGO consisting of 7 patients experiencing acute renal impairment stage 1 and one patient experienced acute renal impairment stage 2 (Table 4). There were 2 of 8 patients in stage 3B accompanied by hydronephrosis, but there was no urine production problem in both. Based on abstracts of American Society of Clinical Oncology (ASCO), 118 patients who received cisplatin 85 mg/m^2 with hydration > 2L, 43 patients (36.4%) experienced nephrotoxicity of cisplatin is characterized by decrease in eClCr ≥ 30%. Acute renal impairment (decrease eClCr ≥ 50%) occurred in 18 patients (15.3%) (Marceau et al 1999).

Acute renal impairment in this study due to several things including cisplatin therapy itself that affect on renal tubular function, development process of metastasis diseases such as hydronephrosis and dehydration. Cisplatin has severe nausea and vomiting side effects (> 90 %) which was immediate or delayed. Excessive vomiting can lead to dehydration, causing intravascular volume depletion triggers prerenal disorder (BCCA 2008, Munar 2013). Giving intravenous or oral rehydration fluids can overcome dehydration due to nausea and vomiting. After patient was hospital oral rehydration can be continued at home for 3-5 days with urine target 3-4 L/day for 2-3 days (Vacher et al 2008). Researchers have suggested that every patient did not have fluid restriction for consuming water as much as 6-8 glasses of water/day for 3-5 days post chemotherapy, but in practice there were not all patients able to comply severe nausea vomiting occurs. To ensure renal function 6th day post chemotherapy influenced by dehydration additional checks that can be done is BJ plasma .

This study was to calculate the prevalence ratio (relative risk) using a 2 x 2 table as the comparison prevalence of AKI in group who have risk factors (urine output < 100 mL/hour) with prevalence of AKI in patients without risk factors (urine production ≥ 100 mL/hour). In the result, prevalence ratio of urine production pre chemotherapy 1.35 with confidence interval from 0.47 to 2.87, prevalence ratio of urine production post chemotherapy in 12th hour 0.83 with confidence interval from 0.38 to 2.22. The prevalence ratio of confidence interval values exceeded 1, it cannot be concluded that factor being tested in a population sample represented risk factor and or protective factor of cisplatin nephrotoxicity. Other factor may affect is exposure of platinum from previous cycle, effects of dehydration due to nausea, vomiting, age and others that need for further research.

According to medical record that there was renal function data in 3rd week post chemotherapy (BUN, creatinine serum, albumin, eClCr Cockroft Gault and MDRD) and performed different T-test compared by examination of renal function in the sixth day. 18 patients were evaluated to see post chemotherapy recovery in the third week. Result of different t-test was not found statistically significant difference between creatinine serum, eClCr (according to Cockroft Gault and MDRD) in post chemotherapy evaluation in the 6th day compare by post chemotherapy in 3rd week with p value > 0.05 (Table 5.11, 5.12). Periode of renal function recovery takes 2-4 weeks (Vacher et al 2008). Limitations in this study, patients on inclusion criteria were in diverse cycle, so platinum exposure will be different from another patients. From the Hayes study in 20 patients who received multiple doses of cisplatin, 11 patients were observed to see trend of creatinine serum during the 21 days were found that creatinine serum increased on 5th to 7th day post chemotherapy. Creatinine serum will be decrease after 7th day and last for 3 weeks (Hayes et al 1977) .

Besides blood creatinine serum and BUN chemistry laboratory tests there are other laboratory examinations support etiology/cause of acute renal impairment, including urinalysis examinations and markers. Urinalysis examination is look at proteinuria level, hematuria, leukosituria or urinary sediment examination. Tubular renal function impairment markers can be detected by examination of β_2 -Microglobulin (Dager and Halilovic 2011).

CONCLUSION

Renal function evaluation studies of cervical cancer patients who received cisplatin chemotherapy 75 mg/m^2 with NaCl Mannitol hydration in 21 patients included inclusion criteria revealed that urine production has reached target in the third hour post-chemotherapy, but acute nephrotoxicity degrees 1 and 2 still occurs in 39% of patients.

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