Unity in Diversity and the Standardisation of Clinical Pharmacy Services

Editors: Elida Zairina, Junaidi Khotib, Chrismawan Ardianto, Syed Azhar Syed Sulaiman, Charles D. Sands III and Timothy E. Welty

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Robert K. Chalmers Distinguished Educator Award. He has also received the Russell R. Miller Literature Award and the Education Award from ACCP. In 2013 he was the national Rho Chi Distinguished Lecturer. Dr. DiPiro was elected a Fellow in the American Association for the Advancement of Science. Dr. DiPiro Is a past Editor of The American Journal of Pharmaceutical Education. He is an editor for Pharmacotherapy: A Pathophysiologic Approach, now in its 10th edition. He is also the author of Concepts in Clinical Pharmacokinetics and Editor of the Encyclopedia of Clinical Pharmacy. He has published over 200 journal papers, books, book chapters, and editorials in academic and professional journals.

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Plenary speakers

Prof. Michael D. Katz—*Professor at Department of Pharmacy Practice & Science, The University of Arizona College of Pharmacy, USA*

Prof. Michael D. Katz is Professor at the University of Arizona College of Pharmacy Department of Pharmacy Practice & Science. He practices at the University of Arizona Medical Center within the Department of Internal Medicine, His practice interests include general internal medicine, endocrinology, HIV/AIDS, infectious diseases, and evidence-based practice. Dr. Katz teaches pharmacy and medical students in both the classroom and experiential settings. He was selected in 2001 as a Dean's Teaching Scholar by the Arizona Health Sciences Center and has received numerous teaching awards. He is a Past-Chair of the American Society of Health-System Pharmacists (ASHP) Commission on Therapeutics. Dr. Katz has numerous publications and including Pharmacotherapy Principles and Practices Study Guide: A Case-Based Care Plan Approach, now in its fourth edition. Dr. Katz is the Internal Medicine PGY2 Residency Program Director and directs all residency-related activities for the College of Pharmacy. He has been involved in international education and practice for even 15 years and he serves as the College of Pharmacy's Director of International Programs. In 2010 he received the University of Arizona's prestigious Excellence in International Education Award. He has consulted and lectured extensively in Japan and many other countries regarding pharmacy education and clinical pharmacy practice and he serves as the Co-Chair of the Board of Directors of the U.S—Thai Pharmacy Consortium. Dr. Katz directs the largest program of its kind to train clinical pharmacy faculty members from Saudi Arabia.

Dr. Umi Athiyah—*A/Prof of Department of Pharmacy Practice and Dean of Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia*

Dr. Umi Athiyah is the current dean of Faculty of Pharmacy at University of Airlangga, Indonesia. Dr. Athiyah teaches various subjects including Pharmaceutical Philosophy, Community Pharmacy, Law and Ethics in Pharmacy, Management of Pharmacy Services and Logistics, Professional Communication, Pharmacoeconomics, Information Technology and Pharmaceutical Marketing. She has a research interest in Pharmacy Practice and Health Care System. She has been involved in many community based services. She has been invited as a speaker both in national and international conferences. She is one of the co-authors of a Pharmacy Management handbook.

Prof. Alan Lau—*Professor of Pharmacy Practice and Director of International Clinical Pharmacy Education at the University of Illinois at Chicago (UIC) College of Pharmacy, USA*

Prof. Alan Lau is Professor of Pharmacy Practice and Director of International Clinical Pharmacy Education at the University of Illinois at Chicago (UIC) College of Pharmacy. He obtained his Bachelor of Science in Pharmacy and Doctor of Pharmacy degrees at the State University of New York at Buffalo and then completed a clinical pharmacy residency at UIC. He pioneered the development of clinical pharmacy services for renal failure patients on dialysis. Dr. Lau had obtained many research grants for clinical and laboratory research in renal pharmacotherapeutics and clinical pharmacology, with a recent focus on mineral and bone disorder in chronic kidney disease. He has published many research papers and book chapters, including chapters in the textbooks Pharmacotherapy, Applied Therapeutics—The Clinical Use of Drugs and Basic Skills in Interpreting Laboratory Data. Dr. Lau was one of the founding members of the Nephrology Practice and Research Network of the American College of Clinical Pharmacy. In addition, he had served on the Board of Director and as Chairman of the Renal Scientific Section in the American Society for Clinical Pharmacology and Therapeutics. Dr. Lau was elected to be vice-chairman of the Nephrology/Urology Expert Committee of United States Pharmacopeia (USP) in 2007. In 2010, he was elected as a Distinguished Practitioner to the National Academies of Practice in Pharmacy. Since 2011, Dr. Lau has been working with the American College of Clinical Pharmacy on international program development and is now the International Program Director. He also has been appointed guest professor/faculty at the National Taiwan University, University of Hong Kong, University of Malta and also the Central South University in Changsha, China. Dr. Lau has been invited to give lectures on pharmacotherapy and clinical pharmacy service development in many countries, including Japan, South Korea, China, Hong Kong, Taiwan, Thailand, Vietnam, Malaysia, Singapore, Philippines, Indonesia, Saudi Arabia, Turkey and Malta.

Prof. Roger Lander—*Professor of Pharmacy Practice at Samford University, in Birmingham, Alabama, USA*

Prof. Roger Lander currently serves as Professor of Pharmacy Practice at Samford University, in Birmingham, Alabama, USA. He received his B.S.in Pharmacy and Pharm.D. from the University of Missouri-Kansas City and completed a clinical pharmacy residency program at Truman Medical Center. He then served as a faculty member at UMKC's Schools of Medicine and Pharmacy. Moving to Samford in 1986, he has developed practices in adult medicine, nutrition, ambulatory care, and pharmacokinetics. He previously served as Vice-Chair, Chair and Assistant Dean for Practice Programs. In 1994, Professor Lander helped develop a clerkship for Samford students at Guy's and St. Thomas' Hospitals in London and assisted the pharmacy there in the development of their ambulatory anticoagulation services. Professor Lander helped establish Samford's faculty/student exchange program with Meijo University in Nagoya, Japan and has traveled widely throughout Asia for information exchange and to assist colleges and hospitals in their clinical teaching and practice. He helped develop study opportunities at Samford for pharmacists from England, Japan, Korea, China, Malaysia, Indonesia, and Vietnam. Dr. Lander is one of the founders of the Asian Conference on Clinical Pharmacy. He has traveled to Indonesia at least a dozen times to assist pharmacists in their practice development.

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SYMPOSIUM 1: DEVELOPING CLINICAL PHARMACY

Prof. Charles D. Sands—*Former Dean and Professor (retired), McWhorter School of Pharmacy, College of Health Sciences, Samford University, Birmingham, Alabama, USA*
Dr. Surakit Nathisuwan—*Associate Professor in Clinical Pharmacy in Clinical Pharmacy Division, Department of Pharmacy, Faculty of Pharmacy, Mahidol University, Bangkok, Thailand*
Ms. Nor Hasni Bt Haron—*Senior Principal Assistant Director Pharmaceutical Services Division, Ministry of Health of Malaysia*
Dr. Budi Suprapti—*A/Prof at Department of Clinical Pharmacy, Faculty of Pharmacy, Universitas Airlangga. Head of Pharmacy Department at Universitas Airlangga Teaching Hospital, Surabaya, Indonesia*
Dr. Margaret Choye—*Clinical Assistant Professor at College of Pharmacy, the University of Illinois at Chicago, USA. Clinical Pharmacist in Internal Medicine at the University of Illinois at Chicago Hospital and Health System, USA*

SYMPOSIUM 2: ADVANCED PRACTICE 1

Dr. Hiroyuki Kamei—*Office of Clinical Pharmacy Practice and Health Care Management, Faculty of Pharmacy, Meijo University, Nagoya, Japan*
Dr. Hanna Sung—*University of the Pacific, Thomas J. Long, School of Pharmacy and Health Sciences in California, USA*
Dr. Alexandre Chan—*Deputy Head and a tenured Associate Professor at the Department of Pharmacy, Faculty of Science at National University of Singapore (NUS) and the Duke-NUS Medical School, Singapore*
Prof. Jae Wook Yang—*Professor and Director of the Institute of Clinical Research and Practice, College of Pharmacy, Sahhmyook University & Vice President of Korean College of Clinical Pharmacy*
Prof. Dr. Syed Azhar Syed Sulaiman—*Professor at School of Pharmaceutical Sciences at University Sains Malaysia, Penang, Malaysia*

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Dr. Mehdi Rajabi—*Clinical Pharmacy and Pharmacy Practice, Islamic Azad University, Pharmaceutical Sciences Branch, Tehran, Iran. Clinical Pharmacist, Member of General Pharmaceutical Council of Great Britain*
Mrs. Fan Zhang—*Lanzhou University, a Pharmacist-in-Charge at Pharmacy Department of the First Hospital of Lanzhou University in China*
Dr. Lunawati Bennet—*Assoc. Professor of Pharmaceutical Sciences at Union University School of Pharmacy in Jackson, Tennesse, USA*
Prof. Robert D. Sindelar—*Professor and former Dean of Faculty of Pharmaceutical Sciences, University of British Columbia; and Advisor, External relations, Centre for Health Evaluation & Outcomes Sciences (CHEOS), Providence Health Care research Institute and University of British Columbia, Canada*
Dr. Baharudin Ibrahim—*School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia*

SYMPOSIUM 4: INTERPROFESSIONAL EDUCATION

Dr. Christine B. Teng—*Assoc. Professor of Department of Pharmacy, National University of Singapore Principal Pharmacist (Clinical), Dept of Pharmacy, Tan Tock Seng Hospital, Singapore*
Mr. Tan Wee Jin—*Principle Pharmacist at Guardian Health & Beauty, Singapore*
Dr. Ching Jou Lim—*Senior lecturer in the Discipline of Social and Administrative Pharmacy, University Sains Malaysia, Malaysia*
Mr. Mac Ardy J. Gloria—*University of the Philippines, The Philippines*
Dr. Vivian Lee Wing Yan—*Assoc. Professor of the School of Pharmacy and the Assistant Dean (Student Development) of the Faculty of Medicine, Chinese University of Hong Kong*

SYMPOSIUM 5: ADVANCED PRACTICE 2

Prof. Timothy E. Welty—*Professor and Chair of Clinical Science in the College of Pharmacy and Health Sciences at Drake University, Iowa, USA*
Dr. Takao Shimazoe—*Department of Clinical Pharmacy and Pharmaceutical Care, Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan*
Prof. Zhou Quan—*Professor and Vice Dean of Department of Pharmacy, The Second Affiliated Hospital of Zhejiang University, China*
Prof. Sukhyang Lee—*Professor of Clinical Pharmacy at College of Pharmacy, Ajou University, Korea*
Prof. Kheirollah Gholami—*Professor and Chairman at the Department of Clinical Pharmacy, College of Pharmacy, Iran*

SYMPOSIUM 6: HEALTH CARE DELIVERY IN COMMUNITY PHARMACY

Prof. Michael D. Hogue—*Assoc. Dean for the Center for faith and Health at Samford University's College of Health Sciences, Birmingham, Alabama, USA*
Dr. Elida Zairina—*Senior lecturer of Department of Pharmacy Practice, Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia*
Ms. Leonila M. Ocampo—*Chairman of the Hygieian Insitute for Education, research and Training Inc, The Philippines*
Ms. Yong Pei Chean—*Senior Manager, Khoon Teck Puat Hospital and Council Member, Pharmaceutical Society of Singapore*
Drs. Saleh Rustandi—*Chairman of Himpunan Seminat Farmasi Masyarakat (HISFARMA) of Indonesia*

SYMPOSIUM 7: PHARMACY EDUCATION

Dr. Takashi Egawa—*Clinical Pharmaceutics and Health Sciences, Department of Pharmaceutical and Health Care Management, Faculty of Pharmaceutical Sciences, Fukuoka University, Fukuoka, Japan*
Prof. Yolanda R. Robles—*Professor and former Dean College of Pharmacy, University of the Philippines*
Prof. Rong-sheng Zhao—*Professor in Peking University Third Hospital, China. Assistant to President, Deputy-Director in Pharmacy Department of Peking University Third Hospital, China*
Dr. Manit Saetewa—*Staff of Faculty of Pharmaceutical Sciences, Ubon Ratchathani University, Thailand*
Drs. Nurul Falah Eddy Pariang—*President of Indonesian Pharmacist Association, Indonesia*
Prof. Josepp T. Dipiro—*Dean, Professor and Archie O. McCalley Chair at the Virginia Commonwealth University, School of Pharmacy, Richmond, Virginia, USA*

SYMPOSIUM 8: ADVANCED PRACTICE 3

Dr. Daraporn Rungprai—*Academic Staff of Faculty of Pharmacy, Silpakorn University, Thailand*
Ms. Hong Yen NG—*President, 110th Council, Pharmaceutical Society of Singapore Specialist Pharmacist (Oncology), Singapore General Hospital*
Prof. Agung Endro Nugroho—*Professor of Department of Pharmacology and Dean of Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia*

Dr. Farshad Hashemian—*Assoc. Professor at Islamic Azad University, Pharmaceutical Sciences Branch, Tehran, Iran*
Dr. Junaidi Khotib—*Assoc. Professor of Department of Clinical Pharmacy at Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia*

SYMPOSIUM 9: IMPROVING PATIENT MEDICATION SAFETY

Dr. Wimon Anansakunwatt—*Siriraj Hospital, Thailand*
Mr. Mohammed Nazri Abdul Ghani—*Principal Pharmacist and Medication Safety Officer (MSO) of KK Women's & Children Hospital, Singapore*
Ms. Yoon Sook Cho—*Director of Pharmacy Department, Seoul National University Hospital, Korea*
Dr. Sutthiporn Pattharachayakul—*Assistant Professor at the Department of Clinical Pharmacy, Prince of Songkla University, Thailand*
Dra Mariyatul Qibtiyah—*Head of Paediatric Pharmacy Services at Dr Soetomo Hospital, Surabaya, Indonesia*
Prof. Charles F. Lacy—*Professor of Pharmacy Practice and Vice President of Roseman University of Health Sciences, Henderson, Nevada, USA*

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Continuous infusion versus intermittent bolus furosemide in heart failure NYHA III-IV

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ABSTRACT: The study was designed to investigate the therapeutic effect of Continuous Infusion (CI) and Intermittent Bolus (IB) administration of furosemide on patients with NYHA class III-IV heart failure hospitalized in Dr. Soetomo Hospital Surabaya. Thirteen patients received CI of furosemide and 10 patients received IB furosemide. Total urine output, net urine output (nUO/24 h) and urinary sodium excretion were monitored over 24 h. nUO/24 h of IB and CI were 1292 ± 299 mL and 2081 ± 637 mL, respectively. CI group showed significantly higher total urinary output than IB group (3399 ± 793 mL/24 h vs. 2556 ± 343 mL/24 h). The urinary sodium excretion of CI and IB were 302 ± 73 mmol/24 h and 228 ± 58 mmol/24 h, respectively. CI of furosemide resulted in higher total urinary output, net urinary output and urinary sodium excretion than IB furosemide in patients with NYHA class III and IV heart failure.

1 INTRODUCTION

Heart failure is a leading cause for hospitalization of patients older than 65 years. Patients are mostly admitted with dyspnea caused by volume overload. Intravenous loop diuretics are the main treatment for such patients (Palazzuoli et al. 2014). Intermittent bolus (IB) diuretics may cause rapid loss of intravascular volume. This can cause abnormality of electrolyte, renal dysfunction, activation of sympathetic nervous system (SNS) and renin angiotensin aldosterone system (RAAS). This stimulation increases renal sodium level, water resorption and plasma volume. Sympathetic excitation leads to peripheral vasoconstriction, arrhythmia, apoptosis and cardiac remodeling. On the other hand, continuous infusion (CI) can produce sustained and greater diuresis. Thus, intravascular volume fluctuation is minimum, avoiding wide swings in neurohormonal activation and electrolyte imbalance (Amer et al. 2012).

There have been several studies comparing loop diuretic intermitten bolus and continous infusion; however the results are contradictory. A randomized, double-blind study of 308 subjects with ADHF, DOSE, compared high-dose versus low-dose and continous versus intermittent infusion of furosemide. This study did not show positive outcome in either primary and secondary endpoints from regimen comparison. However, there was higher rate of acute kidney injury in the high-dose group (Felker et al. 2011). This result is in line with a randomized study of 41 patients which concluded that there were no considerable differences (Allen et al. 2010). Another randomized, parallel-group study of 56 ADHF patients receiving furosemide compared continuous and intermittent administration. The study concluded that intermittent infusion of furosemide was well tolerated and significantly more effective than intermittent (Thompson et al. 2010). Despite wide use of furosemide in clinical practice, there is as yet no certain guideline to administer furosemide effectively (Salvador et al. 2005). Thus, this study is conducted to evaluate the efficacy and safety of intermittent bolus versus continuous infusion furosemide in a clinical setting.

2 MATERIAL AND METHOD

2.1 *Study design*

This was a single-center, prospective, consecutive study comparing continuous infusion (CI) versus intermittent bolus (IB) of furosemide in patients admitted to Dr. Soetomo Hospital, older than 30 years with clinical diagnosis of NYHA class III and IV heart failure. Ethical clearance was obtained from the ethical committee of Dr. Soetomo hospital. Patients were excluded if creatinine

serum levels were more than 2 mg/dL and if they received non-steroidal anti-inflammatory drugs, with exception of low dose aspirin (<325 mg). Patients were randomized into CI or IB group.

Total daily fluid balance was assessed for 24 h using flow sheets for each subject. Urinary sodium excretion was measured. Blood pressure was assessed three times daily. Electrolyte status and renal function were determined over 24 h. Doses of furosemide used were 60–120 mg.

2.2 *Outcome measurement*

The parameters of efficacy end point were net urine output, total urine output and urinary sodium excretion over 24 h. Net urine output is defined as urine output subtracted by oral plus intravenous (IV) fluid intake. Safety end point parameters were creatinine serum level to monitor the decrease in renal function. Sodium and potassium serum concentrations were assessed. Blood pressure was also monitored for hypotension observation.

2.3 *Data analysis*

All data were analyzed using independent t-test. Variables were presented as mean ± standard deviation and p value < 0,05 was considered significant.

3 RESULT AND DISCUSSION

A total of 23 patients were randomized. There were 10 patients receiving IB and 13 patients receiving CI of furosemide. Baseline characteristics of IB and CI group were not significantly different (Table 1).

Table 1. Baseline characteristics.

	Intermittent bolus (n = 10)	Continuous infusion (n = 13)
Age, mean ± SD (y)	51 ± 13	58 ± 9
Sex, n		
Female	4	4
Male	6	9
Other medication, n		
Spironolactone	9	6
ISDN	6	9
ACE Inhibitor	9	12
Digoxin	4	4
Coronary risk factor (%)		
DM	30	31
HT	60	54
CAD	10	15

Efficacy analysis was done by observing total urine output, net urine output and urinary sodium excretion for 24 h. The total urinary output/24 h in patients receiving IB and CI was 2,556 ± 344 mL and 3,399 ± 79 mL, respectively (p = 0.003; Fig. 1). Net urinary output/24 h of receiving IB and CI group was 1,292 ± 299 mL and 2,081 ± 637 mL, respectively (p = 0.0017; Fig. 1). The urinary sodium excretion/24 h in IB and CI group was 228 ± 58 mmol and 302 ± 73 mmol, respectively (p = 0.016; Fig. 2). Based on the result, there is significant difference in the total urinary output/24 h, the net urinary output/24 h and the urinary sodium excretion/24 h between CI and IB group.

Theoretically, CI of furosemide provides effective level of furosemide to inhibit Na/K/Cl transporter during infusion, resulting in increasing diuresis and natriuresis. Slow input of drug in CI increases secondary response produced by time-course drug delivery to the site of action. A low, but effective, concentration administered continuously increases diuretic effect of furosemide (Meyel 1992, Fergusson 1997, Wittstein 2006).

On the other hand, study by Aaser et al. (1997) found that there is no significant difference in 24 h

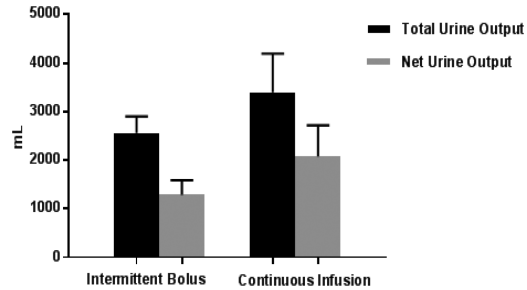

Figure 1. Efficacy end point showed by total urine output and net urine output after continuous infusion (CI) and intermittent bolus (IB) of furosemide.

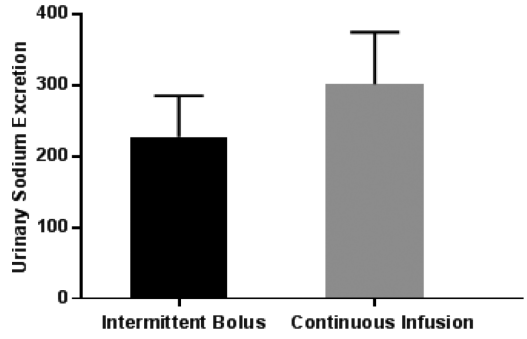

Figure 2. Urinary sodium excretion with intermittent bolus vs. continuous infusion of furosemide.

urine output of patients receiving furosemide CI and IB. However, crossover studies show a greater diuresis in CI as compared to IB administration. A prospective randomized crossover study compared CI and single IV administration of furosemide on nine patients with NYHA class III and IV heart failure. Single dose of 30–40 mg/8 h was used. CI of furosemide was started by loading dose of 30–40 mg, continued with 2.5–3.3 mg/h for 48 h. The 48 h urine output after CI and single IV administration of furosemide was 2,865–6,365 mL (mean value = 3,790 mL) and 3,125–7,365 mL (mean value = 4,490 mL), respectively. Moreover, 48 h urinary sodium excretion for CI and single IV administration were 135–677 mEq and 115–547 mEq, respectively, indicating that 48 h urine output and urinary sodium excretion of CI are higher than single IV dose (Lahav et al. 1992). Another randomized crossover study on 20 patients compared efficacy of IV administration and 8 h infusion of furosemide. Dose used was 250–5,000 mg/24 h. The results showed that there was significant difference in 24 h urine output (CI vs. IV: 2860 ± 240 mL vs. 2660 ± 150 ml). Urinary sodium excretions in CI group and IV group were 210 ± 40 mmol and 150 ± 20 mmol, respectively. Additionally, there were five patients with reversible hearing problems in single dose IV group. Thus, CI might be more effective than single IV, and generated less ototoxicity (Dorman et al. 1996). Study in 56 patients evaluated effectiveness of CI versus intermittent infusion of furosemide and showed that patients receiving CI furosemide exhibit a greater diuresis as compared to those who received intermittent infusion (3,726 ± 1,121 mL/24 h vs. 2,955 ± 1,267 mL/24 h), respectively. This indicates that CI is safer and more effective than intermittent infusion (Thompson et al. 2010). Moreover, the result of the present study supports the previous study, showing that CI of furosemide is more effective than IB administration in patients with heart failure.

CI of furosemide produces less hemostatic effect, and no stimulation to RAAS, SNS and arginine vasopressin, resulting in a better drug response. On the other hand, IB increases renin and sympathetic response, so that the decline in plasma concentration of furosemide decreases blood pressure. However, the present study showed that there is no significant difference between CI and IB in all parameters of safety endpoint, systolic and diastolic blood pressure and heart rate (Table 2).

Single IV administration of furosemide leads to fluctuation of furosemide plasma level (Fergusson 1997). Furosemide can induce diuresis and natriuretic response when the concentration in tubules is adequate to block $Na^+/K^+/ 2Cl^-$ transporter. There is post-diuretic sodium retention as a compensation mechanism when the urinary furosemide level decreases, usually around 6 h post administration (Bruyne 2003, Ross et al. 2006). In single IV, natriuretic response and sodium retention will reduce the efficacy of furosemide (Fergusson 1997). Post-diuretic sodium retention is an acute diuretic resistance mediated by the activation of RAAS and SNS (Shankar et al. 2003, Wittstein 2006). Single IV dose produces massive diuresis and greater urine volume in a shorter time, leading to sudden decrease in intravascular volume. On the other hand, CI produces smaller reduction in intravascular volume, leading to the consistent increase in urine volume (Fergusson 1997, Bristow 2005).

A study compared furosemide, a short-acting loop diuretic, and azosemide, a long acting loop diuretic, to examine whether CI of furosemide could mimic the effect of long-acting loop diuretic. The report shows that furosemide gives a better improvement on heart rate variability than azosemide. This is due to the fact that furosemide, but not azosemide, stimulates renin release and SNS activity. Furthermore, furosemide, but not azosemide, inhibits the decrease in parasympathetic activity, which is commonly found in heart failure. The inhibition on the decreasing parasympathetic activity during heart failure protects the patient from cardiac sudden death event due to ventricular arrhythmia (Tomiyama et al. 1998).

In the present study, there was no difference in serum sodium, potassium and creatinine level attributed to the side effect of CI and IB administration of furosemide. This finding is in line with the study by Lahav et al. (1992) showing that there is no difference in side effect event. The result of other study evaluating the use of furosemide in patients with severe heart failure and renal insufficiency suggests that CI of furosemide is more effective and gives fewer side effects (Gerlag & Van Meijel 1988).

Table 2. Secondary end point.

	Intermittent bolus (n = 10)	Continuous infusion (n = 13)	p
Δ Systolic blood pressure (mmHg)	12 ± 18	12 ± 20	0.99
Δ Diastolic blood pressure (mmHg)	8 ± 18	17 ± 15	0.377
Δ Heart rate (beats/min)	13 ± 14	10 ± 13	0.508
Δ Serum sodium (mg/dL)	–2.7 ± 7.4	–6.8 ± 11.4	0.333
Δ Serum potassium (mg/dL)	0.3 ± 0.8	0.61 ± 0.9	0.467
Δ Serum creatinine (mg/dL)	0.01 ± 0.26	0.09 ± 0.50	0.647

4 CONCLUSION

The result of the present study suggests that CI of furosemide is more effective than IB administration in patients with NYHA class III and IV heart failure, as shown by the higher total urinary output, net urinary output and urinary sodium excretion after CI of furosemide. It is also suggested that furosemide, either by CI or BI administration, may not affect serum sodium, potassium and creatinine levels.

ACKNOWLEDGEMENT

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