Chula Med J Vol. 53 No. 2 March-April 2009

Effects of dosage and duration of enalapril usage on hematocrit levels in hemodialysis patients

Dungchit Panomvana* Srisamorn Rattanajinda*
Boonthum Jirajan** Sookruetai Lekhyananda***

Panomvana D, Rattanajinda S, Jirajan B, Lekhyananda S. Effects of dosage and duration of enalapril usage on hematocrit levels in hemodialysis patients. Chula Med J 2009 Mar – Apr; 53(2): 107 - 17

Objective : *To study the effect of enalapril on the hematocrit (Hct) levels of hemodialysis (HD) patients.*

Method : *A retrospective, before-after taking/stop taking enalapril crossover design was carried out in HD patients from the Kidney Foundation of Thailand, Bangkok. Hct levels were evaluated after the patients had taken enalapril for 4, 8 and 12 months.*

Result : *A total of 57 patients were recruited into the study. The administration of 10 mg/day dosage of enalapril showed higher effect on the decrement of Hct levels as compared to the 2.5 - 5.0 mg/day dosage of enalapril ($p = 0.023$). The decrements in Hct level at 8 and 12 months were not significantly higher than that of the first four months.*

Conclusion : *Enalapril significantly caused decrement in Hct level of HD patient especially at the first four months after taking. Duration of enalapril usage showed no effect.*

Keywords : *Enalapril, Dosage and duration, Hematocrit levels, Hemodialysis.*

Reprint request: Panomvana D, Department of Pharmacy (Clinical), Faculty of Pharmaceutical Sciences, Chulalongkorn University, Phayathai Road, Pathumwan, Bangkok 10330, Thailand E-mail address: duangchit.p@chula.ac.th

Received for publication. December 15, 2008.

* Department of Pharmacy (Clinical), Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok 10330, Thailand

** Rajavithi Hospital, Bangkok, Thailand

***Kidney Foundation of Thailand, Galyanivadhana Building, Priests' Hospital, Bangkok, Thailand

ดวงจิตต์ พนมวัน ณ อยุธยา, ศรีสมร รัตนจินดา, บุญธรรม จิระจันทร์, สุขฤทัย เลขยานนท์. ผลของขนาดยาและระยะเวลาที่ได้รับยาอีนาลาพริลต่อระดับฮีมาโตคริท ในผู้ป่วยที่ได้รับการฟอกเลือดด้วยเครื่องไตเทียม. จุฬาลงกรณ์เวชสาร 2552 มี.ค. – เม.ย.; 53(2): 107 – 17

วัตถุประสงค์ : *เพื่อศึกษาผลของยาอีนาลาปริลต่อระดับฮีมาโตคริตในผู้ป่วยฟอกไต*

วิธีการศึกษา : *รูปแบบการศึกษาเป็นแบบย้อนหลัง โดยเก็บข้อมูลเปรียบเทียบผลก่อนและหลังรับประทานยาอีนาลาปริลในผู้ป่วยฟอกไต โดยเก็บข้อมูลฮีมาโตคริต ณ เดือนที่ 4, 8 และ 12 หลังเริ่มรับประทานยาอีนาลาปริลเปรียบเทียบกับก่อนรับประทานยา โดยเก็บข้อมูลจากผู้ป่วย ณ สมาคมโรคไตแห่งประเทศไทย กรุงเทพ ฯ*

ผลการศึกษา : *รวมข้อมูลผู้ป่วยทั้งสิ้น 57 รายที่ถูกเก็บข้อมูลและนำมาวิเคราะห์ในการศึกษานี้ พบผลของยาอีนาลาปริลขนาด 10 มิลลิกรัมต่อวันส่งผลลดระดับฮีมาโตคริตมากกว่าขนาดยา 2.5 - 5.0 มิลลิกรัมต่อวัน ในผู้ป่วยฟอกเลือดอย่างมีนัยสำคัญทางสถิติ ณ เดือนที่ 4 หลังจากเริ่มรับประทานยา และไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติเมื่อติดตาม ระดับฮีมาโตคริตไป ณ เดือนที่ 8 และ 12*

สรุปผลการศึกษา : *ยาอีนาลาปริลขนาด 10 มิลลิกรัมต่อวันส่งผลลดระดับฮีมาโตคริตในผู้ป่วยฟอกไตทางหลอดเลือด อย่างมีนัยสำคัญทางสถิติ ณ เดือนที่ 4 หลังเริ่มรับ*

คำสำคัญ : *อีนาลาปริล, ขนาดยาและระยะเวลาการได้รับยา, การฟอกเลือดด้วยเครื่องไตเทียม.*

Anemia is a common problem in patients with kidney diseases. Introduction of recombinant human erythropoietin (rHuEpo) into the clinical practice has been a very important development in the management of anemia, a consistent clinical feature of end-stage renal disease (ESRD).[1] However, the required dose of erythropoietin (Epo) to correct anemia does vary among patients. Some can be unresponsive in spite of very high dose received. The common causes for inadequate response to Epo are iron deficiency, infection and inflammation, osteitis fibrosa, aluminium toxicity, folate or vitamin B_{12} deficiency, inadequate dialysis and malnutrition. Nevertheless, the reason for incomplete response to Epo is not completely clear, as some patients lacking these factors can also be unresponsive to Epo.[2]

Several studies had investigated the effects of angiotensin - converting enzyme inhibitors (ACE inhibitors) on Epo responsiveness, controversial results have been reported. Some studies reported that ACE inhibitors increased Epo maintenance doses in hemodialysis (HD) patients;[1,3-9] on the contrary, other studies showed that ACE inhibitors therapy did not appear to affect the response to Epo in chronic HD patients.[10 - 14] Different doses of ACE inhibitors and Epo were used in different studies. Some administered high dose of ACE inhibitors while some used low dose of ACE inhibitors. Besides, most of the studies, the comparisons were performed between patients of different groups (patients with Epo alone in one group and patients with Epo plus ACE inhibitors in another group) which had different baseline conditions. Furthermore, no study that concentrated on the effects of dosage and duration of using ACE inhibitors on hematocrit (Hct) levels and/or on the erythropoietin dosage requirements has been reported.

This retrospective study was therefore designed to evaluate the effect of enalapril, its dosage and duration of its use on the Hct levels of HD patients using a when not taking/ when taking crossover design. The Hct levels of patients between when they were on enalapril and when they were not on enalpril for 4, 8 and 12 months were compared based on the conditions of receiving stable dosages of erythropoietin and enalapril with no supplement of iron or packed red cells throughout the observation period.

Patients and Methods

Patients with chronic kidney disease from the Hemodialysis Unit, the Kidney Foundation of Thailand at Galyanivadhana Building, the Priests' Hospital who were at least 20 years old, had been on maintenance hemodialysis for at least one year, had been treated with enalapril for at least four months, during July 1997 to June 2005, were recruited into this study. The period of four months was set in order to account for the life cycle of red blood cells and to ensure the steady state conditions. The dosage of enalapril was determined by the primary nephrologist based on the condition of the patient, optimum dosage of 5, 10, 20 or 40 mg/ day were given in order to achieve the optimal blood pressure control. The subject were recruited into the study to find out whether or not Epo was administered as long as the same dosage regimen was maintained throughout the observation period which required at least eight months (four months when not taking enalapril and four months while taking enalapril). The sequence of comparison at first period, there were 48 patients who were in a group of not taking enalapri and 9 patients who were in a group of taking enalaprit. Moreover,

there was no evidence shown in the patient's profiles of why they stopped using enalapril in 9 patients after continue receiving for 4 months. Patients who were intolerant to enalapril and required to be treated with packed red cells or parenteral iron supplement dosage adjustment of erythropoietin and/or enalapril had to be continued within the 4 months period, were excluded.

The Hct levels of the patients when not taking enalapril and after using enalapril for 4 months, 8 months and 12 months periods were observed continuously as long as their Epo and/or enalapril dosages were not changed and packed red cells or iron supplement was not administered.

Study design

The protocol of this study was approved by Rajavithi hospital ethical committee.

A retrospective crossover design was used. The observation period could either be started at the time when the patient was or was not treated with enalapril. If the observation time was started at the point while the patient was administered with enalapril, s/he should remain on the same dosage regimen of enalapril for at least four months before stopped taking enalapril or switched to another group of antihypertensive agent and should remain without ACE inhibitors for at least four months. Patient whose starting point was at the time while s/he was not consuming enalapril should be without enalapril for at least four months before started taking enalapril and remained on the same dosage regimen of enalapril for 4, 8 or 12 months. Therefore, the patients hereby serve as their own controls.

Hct level at the starting point was recorded and continually observed and recorded every week throughout the 4 or 8 or 12 months periods. Patients who had too many missing data were excluded from the study.

Several laboratory blood values when the patients were not on enalapril and when they were on enalapril for four months were recorded and compared: blood urea nitrogen (BUN), creatinine, uric acid, sodium, potassium, chloride, bicarbonate, calcium, phosphate, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), intact parathyroid hormone (iPTH), ferritin, total iron-binding capacity (TIBC) and iron.

Statistical methods

The demographic data of all patients were presented as descriptive statistics, such as percentage, mean $\pm$ SD. Laboratory data of all patients when not taking enalapril and when taking enalapril for four months were compared using the paired t-test. The percentages of change in Hct levels between patients who were taking different doses ($\leq$5, 10, 20 and 40 mg/day) of enalapril were compared using the independent t-test and ANOVA analysis. Hct levels when the patients were not on enalapril and when they were on enalapril for 4, 8 and 12 months were compared using the paired t-test.

Results

A total of 57 patients, who met the criteria and all the required data could be observed and recorded for at least four months after enalapril had been administered, were recruited into the study. Their demographic data are shown in table 1.

Table 1. Demographic data of the patients.

Demographic data		**Number of patients N = 57(%)**
Total patients		57
Sex		(100%)
Male		35 (61.4%)
Female		22 (38.6%)
Mean age (yrs)	41.36 ± 11.28 (range; 22 - 63)	
Mean dry weight (kg)	52.48 ± 11.04 (range; 33.50 - 95.00)	
Mean height (cm) =	159.71 ± 8.38 (range; 145 - 195)	
Duration of hemodialysis (yrs)	4.91 ± 3.35 (range; 1-15)	
Frequency of dialysis (times/wk)	2.53 ± 0.50 (range; 2 - 3)	
Causes of chronic kidney disease		
Glomerulonephritis : Biopsy-proven		
- Focal Segmental Glomerulonephritis		1 (1.8%)
- IgA Nephropathy		1 (1.8%)
- Mesangial proliferative IgM Nephropathy		2 (3.5%)
- Crecentric Glomerulonephritis (RPGN)		1 (1.8%)
Glomerulonephritis : Presumed (no biopsy)		20 (35.1%)
Diabetic Nephropathy		5 (8.8%)
Hypertension		9 (15.8%)
Cystic Kidney Disease		1 (1.8%)
Obstructive Nephropathy, CTIN		4 (7.0%)
Lupus Nephritis		1 (1.8%)
Allograft Dysfunction		1 (1.8%)
Unknown		10 (17.5%)
No data		1 (1.8%)
Comorbid condition		
Chronic Heart Failure (CHF)		1 (1.8%)
Hypertension (HTN)		33 (57.9%)
Acute Myocardial Infarction (AMI) or Unstable Angina (UA) and HTN		3 (5.3%)
CHF and HTN		7 (12.3%)
HTN and DM		1 (1.8%)
AMI or UA and CHF and HTN		1 (1.8%)
AMI or UA and HTN and DM		2 (3.5%)
AMI or UA and CHF and HTN and DM		2 (3.5%)
None		2 (3.5%)
No data		5 (8.8%)

There were no significant changes with regard to the laboratory data except for serum potassium ($p = 0.037$) as shown in table 2. The serum potassium increased after the patients had taken enalapril for four months.

The results indicate that Hct levels were significantly lower when taking enalapril ($p < 0.001$), as shown in table 3. The decrement in Hct levels was more prominent among the patients who were not treated with Epo ($p = 0.064$).

The dosage of enalapril was categorized into 4 groups, i.e., 2.5 - 5 mg/day, 10 mg/day, 20 mg/day and 40 mg/day. Only the dosage of 10 mg/day showed significantly higher effect on the decrement in Hct levels when compared to the dosage of 2.5 - 5 mg/day ($p = 0.023$). However, no other dosages showed any significant difference in the effect on the percentage of decrement in Hct levels from one another. The results are shown in table 4.

Table 2. Laboratory data of the patients.

Serum chemistry	N	Without enalapril		N	After taking enalapril for 4 months		P-value*
		Mean ± SD	range		Mean ± SD	range	
BUN	55	63.19 ± 20.22	30 - 127	48	63.86 ± 16.79	38 - 107	0.398
Creatinine	57	11.61 ± 3.60	5.50 - 24.20	55	10.84 ± 2.58	5.4 - 18.58	0.107
Uric acid	50	7.32 ± 2.04	2.90 - 11.70	49	7.44 ± 1.79	4.3 - 11.4	0.890
Sodium	57	140.71 ± 2.99	132 - 148	57	139.96 ± 3.24	132 - 148	0.113
Potassium	57	4.56 ± 0.65	3.2 - 6.2	57	4.80 ± 0.74	3.28 - 6.7	0.037
Chloride	57	100.89 ± 3.57	91.80 - 109	56	101.22 ± 4.62	93 - 119	0.507
Bicarbonate	57	23.87 ± 4.98	2.5 - 31	57	24.09 ± 3.43	15 - 33	0.781
Calcium	56	9.55 ± 1.43	2.64 - 13.30	55	9.45 ± 1.86	2.4 - 14.4	0.750
Phosphate	57	4.91 ± 1.78	1.43 - 11	55	4.92 ± 1.93	0.66 - 9.2	0.961
Albumin	50	4.19 ± 0.39	3.3 - 5.4	52	4.10 ± 0.37	2.8 - 4.7	0.078
SGOT (AST)	16	19.63 ± 12.01	9 - 45	21	18.95 ± 12.59	4 - 58	**
SGPT (ALT)	16	18.44 ± 14.44	6 - 50	21	20.09 ± 24.90	5 - 125	**
Parathyroid hormone	26	304.39 ± 317.41	5.58 - 1361	26	475.61 ± 397.08	30.7 - 1305	0.660
Serum Ferritin	9	634.80 ± 329.44	140.5 - 1058	12	640.92 ± 549.10	82.1 - 1610	**
TIBC	7	169.75 ± 106.46	25.08 - 271	9	255.01 ± 97.54	39 - 346	**
Serum Iron	6	68.67 ± 16.97	49 - 92	8	86.63 ± 37.96	13 - 130	**

* Comparison of laboratory data before and after taking enalapril.

** Number of subjects whose data could be recorded (N) was too small for valid statistical calculation.

Table 3. Effects of enalapril on Hct levels.

Total patients	N	Hct levels % (mean ± SD)		Percentage of changes (mean ± SD)	P-value
		Not taking enalapril	Take enalapril		
Total	57	30.11 ± 5.96	27.16 ± 5.88	-9.67 ± 9.61	< 0.001
Patients without erythropoietin	30	29.33 ± 7.23	25.77 ± 6.86	-11.90 ± 10.87	< 0.001
Patients with Erythropoietin	27	30.96 ± 4.10	28.70 ± 4.17	-7.19 ± 7.43	< 0.001
P - value		0.307	0.059	P = 0.064	

Table 4. Effects of different dosages of enalapril on Hct levels.

Dose of enalapril	N (57)	Hct levels % (mean±SD) Not taking enalapril	take enalapril	Percentage of change (mean ±SD)	p-value
2.5-5 mg/day	25	29.96 ± 5.54	27.72 ± 5.09	-7.22 ± 7.30	< 0.001
10 mg/day	13	28.54 ± 5.24	24.31 ± 5.92	-14.87 ± 12.63	0.002
20 mg/day	12	31.33 ± 6.77	28.08 ± 6.26	-9.85 ± 10.73	0.008
40 mg/day	7	31.43 ± 7.70	28.86 ± 7.31	-8.41 ± 5.86	0.007
		ANOVA analysis		0.229	
		2.5 - 5 mg/day	10 mg/day	20 mg/day	40 mg/day
2.5 - 5 mg/day		-	P = 0.023	P = 0.387	P = 0.697
10 mg/day		-	-	P = 0.298	P = 0.221
20 mg/day		-	-	-	P = 0.749
40 mg/day		-	-	-	-

To study the effect of duration of enalapril usage on Hct levels, the Hct levels of the same patient at 4 months, 8 months and 12 months after taking enalapril were observed and compared. Of the 57 patients recruited into the study, there were only 23 patients who were continually receiving constant dose of enalapril, constant dose of Epo (including those who did not take any Epo) without requirement for any packed red cells or iron supplement throughout 8 months after enalapril had been given. Among these, only 13 patients who continued on the aforementioned conditions throughout 12 months after enalapril were taken. The Hct levels of these patients were therefore continually observed and recorded for 8 months and 12 months after taking enalapril, respectively. The results showed that Hct levels were significantly decreasing at the first four months after taking enalapril, the decrement in Hct level was slightly further but not

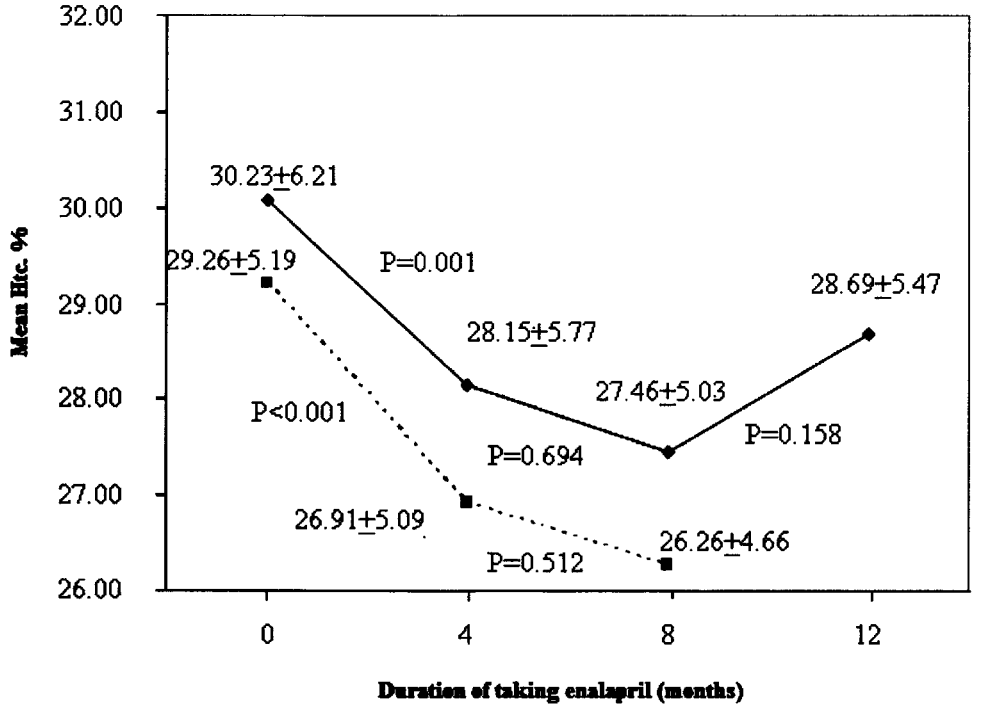

Figure 1. The effect of duration of taking enalapril on Hct levels.

statistically significant at the second four months (eight months) after taking enalapril. Then, the Hct levels seem to be stable or even slightly adjusting up at the third four months (12 months) after taking enalapril, as shown in figure 1.

The influence of sex, age, duration of hemodialysis, frequency of hemodialysis and baseline Hct levels on the effect of enalapril on Hct levels were also evaluated. No significant influence of any of these factors could be observed.

Discussion

The results from this retrospective crossover design study indicate that the use of enalapril, an angiotensin-converting enzyme inhibitor (ACEI), in hemodialysis patients significantly decreased Hct levels as compared to the time when they did not use enalapril. ACEI is a strong inhibitor of angiotensin II production while angiotensin II is needed for erythropoietin formulation, then, in turn decreasing red cells production. [1,3] The Hct levels decreased significantly after consuming enalapril for four months as compared to the level observed during the four months before enalapril was started. As for those who were taking enalapril for at least four months at the beginning of the observation point; then, enalapril was stopped. After enalapril was withdrawn for four months, the Hct levels increased significantly. There results imply that the inhibition of angiotensin II production caused by enalapril was reversible and

temporary. Once the drug was been removed, the effect discontinued. These results are similar to those reported by Erturk *et al.* who found that withdrawal of ACEI from hypertensive chronic hemodialysis patients who were also receiving erythropoietin resulted in increasing in Hct levels. [2]

Higher dosage of enalapril showed significantly higher effect on the decrement in Hct levels only when compared between the groups of patients who consumed 2.5 - 5 mg/day to those who consumed 10 mg/day. As for the group who consumed 20 mg/day or 40 mg/day of enalapril, although the percentages of decrement were slightly higher than those obtained from patients who consumed 2.5 - 5 mg/day, these differences were not statistically significant at a = 0.05 and the mean percentages of decrement in Hct levels were not higher than those caused by 10 mg/day of enalapril. This might imply that the effect caused by enalapril had some limitation or could become saturated.

On the other hand, several confounding factors might involve since the values compared in this part of the study were from patients of different groups; their conditions could be different. For example, the baseline Hct levels of the patients who received 40 mg/day of enalapril were higher than those of the patients who received lower doses of enalapril. Although the dosage of Epo in the same patient was kept constant throughout the study period, but the dosage of Epo in different groups of patients could be different. Several factors[15] that might influence the results such as serum parathyroid hormone and serum ferritin were not monitored and recorded. As this is a retrospective study, these recommended data were missing. Besides, the number of patients recruited in each dosage group, especially the higher dosages, i.e., 20 mg/day and 40 mg/day, were too small to ensure a definitive conclusion. These might not cause much influence if the study was a crossover design as in the other parts of this study. However, for a parallel design, these factors might be relevant.

The results the from 13 patients, who continued on the same dose of enalapril and erythropoietin throughout the 12 - month period with no supplement of packed red cells or iron, indicated that enalapril caused significant decrement in Hct level during the first four months after starting enalapril. But it did not significantly decrease the Hct level was observed in the second four months (eight months) after taking enalapril. However, at the 12^{th} month, the effect of enalapril on erythropoietin formation might reach its maximum or become saturated, biological substances of the patients might be able to regulate or compensate the erythropoietin formation process might thus slightly reverse back. This might be one of the reasons for controversial results reported by several previous studies. There were only 13 patients out of the 57 patients enrolled in the study who could continue on the same dosage of enalapril and Epo (including those who were not treated with Epo) throughout 12 months without any requirement for packed red cells or iron supplement. This was not surprising since enalapril caused decrement in Hct levels, increased the condition of anemia which is the common problem in chronic hemodialysis patients. The main reasons for dropped out in the later months were requirement for increment in the dosage of Epo, required treatment with packed red cells or iron in some patients, the dosage of enalapril was required to be changed or stopped taking enalapril (changed to other

hypertensive drug). Patients, who were also taking Epo, dropped out at the later months mainly due to change in the dosage of enalapril while patients, who were not taking Epo dropped out at the later months mainly due to requirement for Epo or packed red cells.

This study, nevertheless, has several favorable points. For instance, the number of subjects recruited into this study was higher than most previous ones; the monitoring time was longer; the study design was mostly a crossover pattern; the patients could then become their own controlled which could eliminate several confounding factors. This study compared the effects of enalapril in patients who were and were not treated with erythropoietin. Since erythropoietin is a strong confounding factor of Hct level, the effect of enalapril could then be clearly concluded especially in patients who were not treated with erythropoietin. In addition, this study also categorized patients according to enalapril dosages and monitored them on the constant conditions for a 12-month period. These parts of information had never been reported.

The present study had also several limitations. First, this study was a retrospective study, some required data were not recorded or were missing. Second, enalapril might not be the only factor that caused decreasing in Hct levels since several other confounding factors, such as, the process of hemodialysis itself, serum parathyroid hormone, serum ferritin that often were monitored and controlled in most studies had not been recorded and controlled in our study. Third, the effect of erythropoietin and packed red cells might be prolonged for more than 4 months and thus could interfere the results. Fourth, the numbers of patients recruited were too small especially for the parallel design part of the study which categorized into different subgroups with different dosages of enalapril and/or erythropoietin.

Conclusion

In conclusion, enalapril caused significantly decrement in the hematocrit levels of hemodialysis patient especially during the first four months after starting the drug. This result could be more apparent among the patients who were not treated with erythropoietin. Higher dosage of enalapril or longer duration of enalapril usage did not show any further extent of this effect significantly. Further studies using prospective design in higher number of patients and better controls of all the confounding factors are hereby suggested before any definite conclusion could be made.

Acknowledgements

The authors are grateful to the every staff member of the Hemodialysis Unit, the Kidney Foundation of Thailand at Galyanivadhana Building, the Priests' Hospital. This study was supported by the Graduate School, Chulalongkorn University, Bangkok.

References

1. Albitar S, Genin R, Fen-Chong M, Serveaux MO, Bourgeon B. High dose enalapril impairs the response to erythropoietin treatment in haemodialysis patients. Nephrol Dial Transplant 1998 May; 13 (5): 1206 - 10
2. Erturk S, Nergizoglu G, Ates K, Duman N, Erbay B, Karatan O, Ertug AE. The impact of

withdrawing ACE inhibitors on erythropoietin responsiveness and left ventricular hypertrophy in haemodialysis patients. Nephrol Dial Transplant 1999 Aug; 14(8): 1912 - 6

3. Macdougall IC. The role of ACE inhibitors and angiotensin II receptor blockers in the response to epoetin. Nephrol Dial Transplant 1999 Aug; 14 (8): 1836 - 41
4. Hirakata H, Onoyama K, Hori K, Fujishima M. Participation of the renin-angiotensin system in the captopril-induced worsening of anemia in chronic hemodialysis patients. Clin Nephrol 1986 Jul; 26 (1): 27 - 32
5. Dhondt AW, Vanholder RC, Ringoir SM. Angiotensin-converting enzyme inhibitors and higher erythropoietin requirement in chronic haemodialysis patients. Nephrol Dial Transplant 1995 Nov; 10 (11): 2107 - 9
6. Matsumura M, Nomura H, Koni I, Mabuchi H. Angiotensin-converting enzyme inhibitors are associated with the need for increased recombinant human erythropoietin maintenance doses in hemodialysis patients. Risks of Cardiac Disease in Dialysis Patients Study Group. Nephron 1997; 77 (2): 164 - 8
7. Hess E, Sperschneider H, Stein G. Do ACE inhibitors influence the dose of human recombinant erythropoietin in dialysis patients? Nephrol Dial Transplant 1996 Apr; 11 (4): 749-51
8. Erturk S, Ates K, Duman N, Karatan O, Erbay B, Ertug E. Unresponsiveness to recombinant human erythropoietin in haemodialysis patients: possible implications of angiotensin-converting enzyme inhibitors. Nephrol Dial Transplant 1996 Feb; 11(2): 396 - 7
9. Walter J. Does captopril decrease the effect of human recombinant erythropoietin in haemodialysis patients? Nephrol Dial Transplant 1993; 8(12): 1428
10. Charytan C, Goldfarb-Rumyantzev A, Wang YF, Schwenk MH, Spinowitz BS. Effect of angiotensin-converting enzyme inhibitors on response to erythropoietin therapy in chronic dialysis patients. Am J Nephrol 1998; 18(6): 498 - 503
11. Abu-Alfa AK, Cruz D, Perazella MA, Mahnensmith RL, Simon D, Bia MJ. ACE inhibitors do not induce recombinant human erythropoietin resistance in hemodialysis patients. Am J Kidney Dis 2000 Jun; 35 (6): 1076 - 82
12. Hayashi K, Hasegawa K, Kobayashi S. Effects of angiotensin-converting enzyme inhibitors on the treatment of anemia with erythropoietin. Kidney Int 2001 Nov; 60 (5): 1910 - 6
13. Cruz DN, Perazella MA, Abu-Alfa AK, Mahnensmith RL. Angiotensin-converting enzyme inhibitor therapy in chronic hemodialysis patients: any evidence of erythropoietin resistance? Am J Kidney Dis 1996 Oct; 28(4): 535 - 40
14. Sanchez JA. ACE inhibitors do not decrease rHuEpo response in patients with end-stage renal failure. Nephrol Dial Transplant 1995; 10(8):1476-7
15. National Kidney Foundation. IV. NKF-K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease: update 2000. Am J Kidney Dis 2001 Jan; 37(1 Suppl 1): S182 – 238