

Utilization and Outcomes of Erythropoietin Among Patients with Different Health Insurance Schemes at the University Hospital

ผลลัพธ์ของการใช้ยาอีริโทรพัวิตินในผู้ป่วยที่มีระบบประกันสุขภาพที่แตกต่างกัน ณ โรงพยาบาลมหาวิทยาลัย

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The purpose of the study was to compare the difference of health schemes for hemoglobin level, dose of erythropoietin, and the percentage of hemodialysis patients who achieved hemoglobin goal according to NKF-DOQI guidelines. The cross-sectional study was conducted during January 2009 to January 2010 with 152 hemodialysis patients at Siriraj Hospital. Differences between parametric data were examined for statistical significance by using ANOVA while categorical data were analyzed by using chi-square test. The p-value <0.05 was accepted as statistically significance. A total of 47.4 percent of patients were men, with a mean age 57.32±14.52 years; 60.5 percent were Civil Service Medical Benefit Scheme (CSMBS), 17.1 percent were Social Service Scheme (SS), 8.6 percent were Universal Coverage Scheme (UC), and 13.8 percent were others. Comparisons between health schemes showed the following significant differences: erythropoietin dose, 3-month average of hemoglobin, and percentage patients achieved the goals of CSMBS patient is higher than SSS, UC, and other health scheme patients (p<0.05). However, more CSMBS patients have the hemoglobin greater than 13 g/dL which is the level that NKF-DOQI guidelines concerned. The results may indicate the overuse and underuse of erythropoietin between the health schemes. The important criteria for erythropoietin use is the target hemoglobin level. Thus further studies should be focused on this topic of the cost effectiveness analysis of erythropoietin use, and effective interventions in this collective, enhance surveillance and adapt health services to balance equity of erythropoietin or high cost drugs access among health insurance.

Keywords: Civil Servant Medical Benefit Scheme (CSMBS), Social Security Scheme (SSS), Universal Health Coverage (UC), erythropoietin, cost effectiveness, hemoglobin

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วัตถุประสงค์ของการศึกษานี้เพื่อเปรียบเทียบความแตกต่างระดับฮีโมโกลบิน ขนาดยาอีริโทรพัวิติน และจำนวนร้อยละของผู้ป่วยในระบบสุขภาพที่แตกต่างกันที่ได้รับการฟอกเลือดด้วยเครื่องไตเทียมที่มีระดับฮีโมโกลบินอยู่ในเกณฑ์มาตรฐานของ NKF-DOQI guidelines การศึกษาแบบภาคตัดขวางระหว่างเดือนมกราคม พ.ศ. 2552 ถึงเดือนมกราคม พ.ศ. 2553 ในผู้ป่วยที่ฟอกเลือดด้วยเครื่องไตเทียมจำนวน 152 ราย ของโรงพยาบาลศิริราช วิเคราะห์ความแตกต่างของตัวแปรแบบพาราเมตริกด้วยสถิติ ANOVA และวิเคราะห์ข้อมูลแบบจำแนกด้วยสถิติ chi-square โดยกำหนดระดับนัยสำคัญที่ 0.05 กลุ่มผู้ป่วยร้อยละ 47.4 เป็นเพศชาย มีอายุเฉลี่ย (\pm ค่าเบี่ยงเบนมาตรฐาน) 57.32 (\pm 14.52) ปี สำหรับสิทธิการรักษาของผู้ป่วยเป็นแบบระบบสวัสดิการข้าราชการ ร้อยละ 60.5 ระบบกองทุนประกันสังคม ร้อยละ 17.1 ระบบหลักประกันสุขภาพถ้วนหน้า ร้อยละ 8.6 และอื่นๆ ร้อยละ 13.8 เมื่อเปรียบเทียบระหว่างสิทธิการรักษา พบว่า ผู้ป่วยในระบบสวัสดิการข้าราชการมีค่าเฉลี่ยของการใช้ยาอีริโทรพัวิติน ค่าเฉลี่ย 3 เดือนของระดับฮีโมโกลบิน และมีจำนวนร้อยละของผู้ป่วยที่มีระดับฮีโมโกลบินอยู่ในเกณฑ์มาตรฐานของ NKF-DOQI guidelines สูงกว่าผู้ป่วยในระบบกองทุนประกันสังคม ระบบหลักประกันสุขภาพถ้วนหน้า และอื่นๆ อย่างมีนัยสำคัญ ($p < 0.05$) อย่างไรก็ตาม พบว่า ผู้ป่วยในระบบสวัสดิการข้าราชการมีระดับฮีโมโกลบินสูงกว่า 13 กรัม/เดซิลิตร ซึ่งเป็นระดับที่สูงกว่าที่ NKF-DOQI guidelines แนะนำ นอกจากนี้ ผลการศึกษานี้ แสดงให้เห็นถึงการใช้อีริโทรพัวิตินที่มากเกินไป ความจำเป็นและที่น้อยกว่าความจำเป็นในผู้ป่วยที่มีระบบสุขภาพที่แตกต่างกัน ประเด็นที่สำคัญอย่างหนึ่งของการใช้อีริโทรพัวิติน คือ เป้าหมายของระดับฮีโมโกลบิน ดังนั้น การศึกษาต่อไปควรมีการวิเคราะห์ต้นทุนประสิทธิผลของการใช้อีริโทรพัวิตินในประเด็นดังกล่าว และมีมาตรการวัดที่มีประสิทธิภาพเพื่อควบคุมการใช้อีริโทรพัวิตินและปรับการบริการทางสุขภาพเพื่อให้เกิดการเข้าถึงยาอีริโทรพัวิตินหรือกลุ่มยาที่มีราคาแพงอื่นๆ ระหว่างระบบสุขภาพต่างๆ

คำสำคัญ: ระบบสวัสดิการข้าราชการ ระบบกองทุนประกันสังคม ระบบหลักประกันสุขภาพถ้วนหน้า อีริโทรพัวิติน ต้นทุนประสิทธิผล ระดับฮีโมโกลบิน

Introduction

Main medical benefit schemes in Thailand consist of Civil Servant Medical Benefit Scheme (CSMBS), Social Security Scheme (SSS), and Universal Health Coverage (UC). The achievement of UC scheme which was built between the previous currency crisis in 1997 and current financial crisis in 2008 in Thailand as a safety net to protect lower income groups.

The Civil Servant Medical Benefit Scheme (CSMBS) is the only health scheme providing full coverage for erythropoietin (EPO). While patients under CSMBS are provided under minimal cost containment policy, those under UC and SSS have no or inadequate access and if needed, they have to pay out of pocket. Since the health care spending is spiraling, economic evaluation could be a useful tool to assist

policy makers in making their decision on alternatives. Drug system analysis is important for understanding the situation of our standing both the country and the community levels. Hospital is the place that related to all level of people especially the hospital where including all health schemes such as Siriraj Hospital. In the limited budget, the allocation of budget for all people is essential doing but difficult to practice. The health resource allocation policy could then be more efficient and the inequity dilemmatic problem could, to a certain scope, be answered.

Nowadays many chronic kidney disease (CKD) patients receive recombinant human EPO for their anemia as a part of routine therapy.^{1,2} Since erythropoietin is an expensive therapy, it has created economic burden onto the health care system of every country. In 2006, EPO has generated US\$10 billion in sales worldwide and \$2 billion in the USA from the Medicare program alone.^{3,4} This was increased from \$1 billion in 2002.⁵ In Thailand, trend of erythropoietin expenditure is increasing. Only the largest university hospital, overall of EPO expenditure was 119,597,547.00 Thai Baht in 2007 and increased to 171,666,386.00 Baht in 2009. These strongly impacted the hospital expenditures and a capped budget can not solve this problem, and the important factor that influenced this problem was the different of health schemes. EPO is listed in the National List of Essential Drugs (NLED) in Subclass

5.2 which could be covered by every health benefit scheme but in the different criteria. For example in the real practice, UC patients can reimburse EPO when the hospital join with the National Health Security Office (NHSO) and established the criteria of using and sending the reason of prescribing to the NHSO while CSMBS patients can reimburse EPO without the criteria for reimbursement [at Siriraj Hospital, UC patients can not reimburse the cost of EPO because Siriraj Hospital does not join with NHSO for hemodialysis (HD)]. About SSS patients, the cost of EPO can be reimbursed when their hemoglobin (Hb) level is lower than 11 or 10 g/dL, SSS patients can reimburse EPO 2,000 or 4,000 IU per week, respectively. Finally, the UC and SSS patients have to receive the burden of expenditure while CSMBS patients have free for service payment mechanism.

Although, it is widely accepted that the renal anemia patients should receive EPO therapy.⁶ The United States National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF-DOQI) working group reformulated its recommendations by stating that the hemoglobin target in patients receiving EPO should generally be 11-12 g/dL.⁷ Lower erythropoietin responsiveness is a strong, independent predictor of mortality risk. Both the inability to achieve a target hemoglobin and administration of high dose EPO were each significantly associated with increased risk of

death, myocardial infarction, and congestive heart failure or stroke.⁸⁻¹¹ However, randomized trials have suggested that targeting greater hematocrits/hemoglobin levels and exposure to high doses of EPO is associated with a greater risk of cardiovascular complications and mortality. A major critical point in thinking about higher Hb targets was the publication of two large studies in nondialysis CKD in 2006: Cardio-vascular Risk Reduction by Early Anemia Treatment with Epoetin (CREATE)¹² and Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHOIR).¹³ Both studies found trends toward increased mortality risk and for other adverse outcomes as well as a recent meta-analysis in 2007 found that treatment to higher Hb targets resulted in an increasing of risk for mortality. There is controversy regarding the appropriate target hemoglobin level.^{14,15} The problem between containing drug expenditure and managing the anemia in chronic kidney disease is the major issue that many studies cannot agree upon the appropriate target Hb level. Thus, the decision to treat anemic chronic kidney disease patients depends on the practice guidelines that physicians rely on. Nevertheless, the important factors that influence the patient treatment in the real world are the limited of economic factor and their health schemes. Although, we have the foundation to help the patients especially the patients of SSS or UC scheme who cannot pay the excess reimbursed drug but the budget

to support is limited and cannot help all of them, thus this study was conducted for evaluate the difference of health schemes for the case study of the high-cost drugs such as EPO use in hemodialysis patient at Siriraj Hospital. The findings of the study represented the situation of drug use at the university hospital in the real world and imply to the policy for handle the situation in the future.

Materials and Methods

The study was a cross-sectional descriptive design during January 2009-January 2010 with 152 hemodialysis patients at Siriraj Hospital. Study population was hemodialysis patients who use EPO at least 6 months with titration of EPO therapy was permitted but excluded the patients who under 18 years old, change the modality of dialysis, switch to other anemia treatment methods between the study. The study was approved by the Institutional Review Board Ethics Committee. Data regarding quantity, date of received drugs obtained from pharmacy dispensing database, clinical profile of patient at HD unit was used to assess the duration of HD, frequency of EPO use, gender, age of patients, health schemes, underlying diseases such as diabetes mellitus, hypertension, and myocardial infarction, combined with the data of medical record database by using the Tenth Revision of the International Classification of Diseases and Related Health Problems (ICD-10) codes and the average for 3 months of Hb level from clinical

profile and clinical laboratory database was analyzed.

Analysis. Demographic data were obtained included age, gender, marital status, underlying diseases (diabetes, hypertension, myocardial infarction, and others), frequency of hemodialysis, length of hemodialysis, the average of 3 months of Hb level, and the proportion of patients who achieved Hb goal (11-12 g/dL, should not be >13 g/dL) among health schemes. Differences between parametric data were examined for statistical significance by using ANOVA while categorical data were analyzed by using chi-square test. The p-value

<0.05 was accepted as statistically significance.

Results

A total of 47.4 percent of HD patients were men, with a mean age 57.32 ± 14.52 years. Duration of hemodialysis was 7.66 ± 4.87 years, 60.5 percent were Civil Service Medical Benefit Scheme, 17.1 percent were Social Service Scheme, 8.6 percent were Universal Coverage Scheme, and 13.8 percent were others. Characteristics and clinical characteristics of the patient samples were classified by medical benefit schemes such as CSMBS, SS, UC, and others (Table 1).

Table 1. Basic characteristics by medical benefit schemes

| Characteristics | UC (n = 13) | CSMBS (n = 92) | SSS (n = 26) | Others (n = 21) |
|--|----------------|-------------------|-----------------|--------------------|
| Age: ^a mean±SD (years) | 45.46±16.00 | 63.39±11.97 | 44.54±8.95 | 53.90±14.17 |
| Gender (% , n) | | | | |
| Male (n = 72) | 15.38 (2) | 50.00 (46) | 57.69 (15) | 42.86 (9) |
| Female (n = 80) | 84.62 (11) | 50.00 (46) | 42.31 (11) | 57.14 (12) |
| Marital status^a (% , n) | | | | |
| Single (n = 45) | 61.54 (8) | 17.39 (16) | 42.31 (11) | 47.62 (10) |
| Couple (n = 107) | 38.46 (5) | 82.61 (76) | 57.69 (15) | 52.38 (11) |
| Underlying diseases (% , n) | | | | |
| Diabetes ^a (27.63%, 42) | 7.69 (1) | 34.78 (32) | 3.85 (1) | 38.10 (8) |
| Hypertension (76.97%, 117) | 76.92 (10) | 78.26 (72) | 84.62 (22) | 61.90 (13) |
| Myocardial infarction (13.82%, 21) | 7.69 (1) | 21.90 (20) | 0.00 (0) | 0.00 (0) |
| Others (9.21%, 14) | 15.39 (2) | 9.78 (9) | 7.69 (2) | 4.76(1) |
| Frequency of hemodialysis (% , n) | | | | |
| 3 times per week ^a (58.55%, 89) | 7.69 (1) | 68.48 (63) | 53.85 (14) | 52.38 (11) |
| 2 times per week (41.45%, 63) | 92.31 (12) | 31.52 (29) | 46.15 (12) | 47.62 (10) |
| Length of HD:^a | | | | |
| Mean±SD (years) | 11.54±4.96 | 7.16±4.72 | 9.06±5.08 | 5.74±3.66 |

^ap<0.05

Notes: CSMBS = Civil Service Medical Benefit Scheme, SSS = Social Service Scheme, UC = Universal Coverage Scheme, HD = hemodialysis

Hemoglobin Level and EPO Dose Per Week. The average for 3 months of Hb level in CSMBS patients was higher than other health scheme groups as well as EPO doses (Table 2).

Achievement of Hb Goal as NKF-DOQI Guidelines. Comparisons of the percentage and number of patients achieving their Hb goal (11-12 g/dL, should not be >13 g/dL) according to NKF-DOQI guidelines among

health schemes. The results (Table 2) showed that CSMBS patients achieved the goals greater than SSS, UC, and other health scheme patients, and the differences were statistically significance ($p=0.035$). However, the result showed that 7 patients (CSMBS =6, others =1) had the Hb level greater than 13 g/dL which is the level that NKF-DOQI guidelines concerned whereas no patient in SSS and UC reached greater than 13 g/dL.

Table 2. Three months average of hemoglobin level, EPO dose per week, and percentage patients achieved

| Data | Hb Level (g/dL) Mean±SD | EPO Dose (Unit) Mean±SD | Patients Achieving NKF-DOQI Guidelines (n, %) |
|-----------------|----------------------------|----------------------------|---|
| UC (n = 13) | 9.90±1.73 | 5,358.97±2,518.31 | 4 (30.77) |
| CSMBS (n = 92) | 11.20±1.25 | 8,254.58±5,483.44 | 53 (57.61) |
| SSS (n = 26) | 9.98±1.36 | 4,666.67±2,524.55 | 9 (34.62) |
| Others (n = 21) | 10.49±1.51 | 6,283.33±2,573.54 | 7 (33.33) |
| Total = 152 | 10.78±1.45 | 7,071.27±4,760.28 | 73 (48.03) |
| p-value | 0.000 | 0.002 | 0.035 |

Discussions and Conclusions

The findings not only indicated that patients with CSMBS had the most achievement of Hb goal as NKF-DOQI guidelines but also have the hemoglobin level greater than 13 g/dL which is the level that NKF-DOQI guidelines concerned. Hb level greater than 13 g/dL may be related to the administration of high dose EPO were each significantly associated with increased risk of death, myocardial infarction, and congestive heart failure or stroke as the previous study concerned. According

to these results, it could be summarized that EPO using were dependent on EPO accessibility and the different reimbursement policy of the health schemes. These findings implied the inequitable access to and use EPO between the health schemes. High access to drugs is the advantage of CSMBS, but it may lead to economic loss because of overuse while underused may occurred in SSS and UC. Although EPO is on the reimbursement list of Essential Drugs in Subclass 5.2 but inequity still occurred. Because of the criteria of EPO

using under the NHSO is strongly impacted the hospital expenditures and the policy maker of the hospital can not agree to join with the system of the NHSO. This is the reason that UC patients at Siriraj Hospital can not reimburse EPO and some patients need to request donations from the Siriraj Foundation. Further studies should be focused on the evaluation of the cost effectiveness of EPO use, effective measures to control EPO use, and methods to balance equity of EPO or high cost drug access among health insurance schemes. The results should be proposed to the Pharmacy and Therapeutic Committee or the decision maker to improve the guidelines or criteria for appro-

priate and cost-effective use of drug in the hospital. The pattern of this study should be applied for evaluation of other drugs use in usual clinical practice. Cost containment and cost effective use of EPO or the high cost drug might be the advantage of the health system.

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