Impact of a Pharmacist-Implemented Anemia Management in Outpatients with End-Stage Renal Disease in Japan

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Given the absence of standard guidelines for use of recombinant human erythropoietin in patients with end-stage renal disease in Japan, in the present study, pharmacists actively managed the erythropoietin therapy, and the therapeutic and pharmacoeconomic outcome was evaluated. We compiled in-hospital guidelines for proper use of erythropoietin for outpatients with renal anemia under hemodialysis, and made recommendations, particularly about changes in the doses of erythropoietin and administration of iron preparations, to physicians. The clinical test values and the dosages of erythropoietin were monitored for 9 months and analyzed. As results of our participation, the number of renal anemia patients with over 30% of the hematocrit value as a therapeutic target increased from 7 to 32 among 41 patients. Twenty-three of the 41 patients could decrease the dose of erythropoietin, and 5 patients could cease receiving the drug. Monthly total units of erythropoietin used for the 41 patients could also be decreased from 915000 units to 642000 units, resulting in considerable improvement of cost performance. Thus, active participation of pharmacists in management of renal anemia had great therapeutic and pharmacoeconomic impact in Japan, as in North America.

Key words medication-use evaluation; erythropoietin; renal anemia; hemodialysis

In Japan, patient-oriented clinical pharmacy services, modeled after North American clinical pharmacy, have been developing in a decade, although roles of pharmacists in clinical activities vary with distinct countries. Pharmacists’ clinical activities do not only enhance the quality of drug therapy, but also contribute to improvement of pharmacists’ job satisfaction in both Japan and North America. Medication-use evaluation (MUE) is an important pharmacists’ clinical activity in Japan, as in North America, which would provide therapeutic and pharmacoeconomic benefits, particularly for the care of patients with certain complicated diseases such as end-stage renal disease. Although renal anemia is one of the leading complications in haemodialysis patients, Japanese physicians, in general, do not currently pay adequate attention for proper use of recombinant human erythropoietin. This may be due to low self-recognition of patients concerning anemia because of few subjective anemia-related symptoms and the absence of standard guidelines for proper use of erythropoietin preparations in Japan. According to our survey on patients in Tokushukai Nozaki Hospital (Daito city, Osaka, Japan) conducted in February, 2002, 41 patients (91.1%) among 45 haemodialysis patients received erythropoietin for renal anemia, and, in 34 patients (82.9%) of the 41 erythropoietin-treated patients, the hematocrit value was less than 30%, a therapeutic target value. At that time, only physicians were responsible for checking the blood parameters, deciding the dosage of erythropoietin and managing low responders to erythropoietin. In addition, each doctor had to make therapeutic decisions for the dialysis patients without any hospital guideline for the use of erythropoietin.

The U.S. NKF-K/DOQI guidelines and European best practice guidelines (EBPG) recommend administration of i.v. iron preparations as the first choice drug for treatment of anemia in low responders to erythropoietin, whereas the criteria, routes and doses of administration of iron preparations for such patients have neither been fully discussed nor standardized in Japan. In this context, we compiled in-hospital guidelines for proper use of erythropoietin and actively managed anemia in hemodialysis patients in Tokushukai Nozaki Hospital. Of note is that only 2 patients among 41 erythropoietin-treated patients received iron preparation at our hospital in February, 2002. Here, we describe that a pharmacist-implemented anemia management in patients with end-stage renal disease, in terms of MUE, has a great therapeutic and pharmacoeconomic impact in our hospital, as in North America.

METHODS

Outline of Outpatient Haemodialysis Unit in Tokushukai Nozaki Hospital Three physicians and 2 pharmacists were regularly working at the outpatient hemodialysis unit (9 beds with the hemodialysis apparatus) in Tokushukai Nozaki hospital (201 beds). There were 45 hemodialysis patients (22 males and 23 females; average age of 66.1 years; average hemodialysis duration of 7.6 years) in February, 2002. Seven patients came to the hemodialysis unit twice a week, while 38 patients received hemodialysis 3 times a week. Pharmaceutical care service including patient education and MUE by pharmacists started for all outpatients at the hemodialysis unit from May, 1996.

Fourteen pharmacists were regularly working in our hospital, and all of them participated in pharmaceutical care including patient education, which covered 82% of all inpatients. The two pharmacists were responsible for pharmaceutical care of hemodialysis outpatients, and delivered patient education and related pharmaceutical services to each patient at least once every two weeks. The work conditions for pharmacists were well organized, and did not necessarily appear to force them to perform excessive tasks.

Pharmacists’ Clinical Activities for Hemodialysis Outpatients Pharmacists performed clinical activities including four main activities as follows: 1) compiling guidelines for proper use of recombinant human erythropoietin in col-
laboration with physicians; 2) Providing drug information on renal anemia to physicians; 3) MUE based on laboratory test data; 4) Proposing plans to change prescriptions based on MUE.

Monitoring of Therapeutic and Pharmacoeconomic Effects of Pharmacists’ Activities The present pharmacist-implemented anemia management in outpatients with end-stage renal disease at our hospital started in February 2002, and the therapeutic and pharmacoeconomic outcome till November 2002 was monitored, analyzed and evaluated.

RESULTS

In-Hospital Guidelines for Proper Use of Erythropoietin in Tokushukai Nozaki Hospital As a result of discussion with physicians, two therapeutic targets, 30% hematocrit and 100 ng/ml ferritin, were employed. Currently, no standard guideline for the target value of hematocrit is available in Japan. NKF-K/DOQI recommends the target hematocrit value of 33—36%, while EBPG indicates 33% as a target value and expects 36—37.5% as a median among patients after the treatment. On the other hand, the manufacturer’s manual for the erythropoietin preparation that we used indicates 30% or more of hematocrit as the therapeutic target in treatment of anemia. Taken together with the fact that only about 20% of erythropoietin-treated patients at our hospital showed hematocrit values above 30% in February, 2002 (a starting point of the present trial), we employed a target hematocrit value of 30% for the present trial. In contrast, the target value of ferritin, 100 ng/ml, was used in accordance with NKF-K/DOQI and EBPG.

Recombinant human erythropoietin (epoetin beta) at 1500 IU, a starting dose, was administered 3 times weekly to patients with a hematocrit value less than 30%. By checking the hematocrit value, pharmacists made recommendations to physicians to change the dose of erythropoietin. For low responders to erythropoietin administration, pharmacists checked the ferritin value, and made recommendations to physicians to give iron preparation (ferric oxide, saccharated for i.v. administration; sodium ferrous citrate for oral administration) when iron deficiency was present. The iron preparation at 40 mg, a starting dose, was administered i.v. once a week to patients with a ferritin value less than 100 ng/ml. In an exceptional case, a patient who had an allergic history to i.v. iron preparations received oral iron preparation at 50 mg/kg once a day. Detailed guidelines are shown in Fig. 1. The original proposal for the guideline was made by pharmacists, and then improved by discussion with doctors.

The Therapeutic and Pharmacoeconomic Outcome of a Pharmacist-Implemented Anemia Management In February 2002, 41 out of 45 hemodialysis patients were given erythropoietin, and 34 out of 41 erythropoietin-treated patients had less than 30% hematocrit. Among the 34 low hematocrit patients, 23 patients showed a ferritin value less than 100 ng/ml, indicating iron deficiency. According to the In-Hospital Guidelines for Proper Use of Erythropoietin, the 23 iron-deficient patients were administered iron preparations. Twenty two patients were given i.v. and one patient was given oral medication due to an allergic history to i.v. iron preparations as described above. Among 41 patients given erythropoietin, the number of patients reaching the therapeutic target of over 30% hematocrit increased from 7 (17.1%) in February 2002 to 32 (78.0%) in November 2002, indicating improvement of anemia symptoms (Fig. 2). The average hematocrit value in 41 erythropoietin-treated patients was 28.5% in February 2002, and became over 30% from June to November 2002. Twenty three (56%) out of the 41 patients were able to decrease the dose of erythropoietin. The percentage of patients who could discontinue erythropoietin gradually increased from February 2002, reaching 12.2% (five patients) (Fig. 3) in November 2002. Monthly total units of erythropoietin used at our hemodialysis unit decreased from 915000 IU in February 2002 to 546000 and 624000 IU in September and November 2002, respectively (Fig. 4). The monthly costs of erythropoietin at our unit gradually decreased from 1.86 million yen in February 2002, and reached 1.12 and 1.37 million yen in September and November 2002, respectively (Fig. 4).

We confirmed no significant seasonal influence on the conditions of hemodialysis patients treated with erythropoietin throughout 6 months before and 10 months (the monitoring
period) after February, 2002, and even after November, 2002 (after the monitoring). In addition, there was no change in medical staffs including doctors and pharmacists at our hospital and in therapeutic policies other than treatment of anemia during the present trial.

DISCUSSION

In Japan, erythropoietin has often been administered without sufficient MUE to hemodialysis patients with end-stage renal disease. The erythropoietin therapy for low responders to erythropoietin have not been well controlled, and various factors underlying the poor therapeutic outcome, such as iron deficiency, have been rarely investigated or considered, which might lead to financial wasting. Several attempts to maintain the hematocrit value by administering iron preparations and to decrease the consumption volume of erythropoietin preparations have been made from the pharmacoeconomic viewpoint in U.S.A. and Europe.8—10) Most recently, even in Japan, a physicians’ research group has reported that a small dose of iron preparations resulted in a 30% reduction of erythropoietin consumption for one year in Japan.11) Nevertheless, Japanese physicians, in general, still do not pay sufficient attention for proper management of erythropoietin therapy for patients with end-stage renal disease. Therefore, a pharmacist-implemented management of renal anemia would have a great impact in a multidisciplinary team approach to improve the care of hemodialysis patients in Japan.

In our present attempts, the hematocrit value was greatly improved in erythropoietin-treated patients and the monthly total doses of erythropoietin at our hemodialysis unit were dramatically decreased, resulting in approximately 26% decrease in the monthly cost of erythropoietin consumption. As the cost of iron preparations used was relatively negligible, pharmacists’ activities had not only therapeutic but also pharmacoeconomic beneficial effects.

All doctors accepted pharmacists’ recommendation for management of hemodialysis patients, except for a few patients who had serious systemic conditions or suffered from side effects of drugs. This could be a result of adequate discussion with doctors for decision of therapeutic strategy and criteria before starting the present trial. Of importance is to understand and respect roles of each healthcare personnel in discussion. Pharmacists’ active participation in MUE, as shown in the present study, would be beneficial even for pharmaceutical care of patients with other chronic diseases, e.g., bisphosphonates for osteoporosis, statins for hyperlipidemia, donepezil hydrochloride for dementia, etc.

We propose that Japanese pharmacists should actively participate in management of anemia in hemodialysis patients with end-stage renal disease.

REFERENCES