ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN – POLONIA
VOL. XLVIII, 1 SECTIO D 1993

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Erythropoietin Treatment in Patients on Maintenance Haemodialysis in Dialysis Centers of South-East Region of Poland – Present State

Leczenie rekombinowaną erytropoetyną chorych przewlekle hemodializowanych w Ośrodkach Dializ Regionu Południowo-Wschodniego – stan obecny

South-East region of Poland includes six voivodeships, with about 3.6 mln of inhabitants. Nine dialysis centers work in this region with 273 places to perform maintenance haemodialysis outside Lublin, and 53 places in Lublin Clinic Center.

The aim of this paper was to analyse the state of r-Hu EPO treatment in chronic dialysis patients. We would like to compare the treatment possibilities in the clinic unit with other haemodialysis units of our region and with data from Western Europe that we know from EDTA report (4).

Simultaneously we decided to estimate real possibilities of iron treatment monitoring. As it is well known (1, 6) correct management of iron suplementation treatment, allows for the significant reduction of r-Hu EPO administration.

MATERIAL AND METHODS

Questionnaires with questions about the r-Hu EPO treatment and iron balance monitoring were sent to all regional dialysis centeres. On the ground of the obtained data we made the comprehensive list of the results we have got and we compared it with the results from our Clinic and EDTA data from 1991 (4).

RESULTS

On the ground of the information from questionnaires we have got the results of the r-Hu EPO treatment estimation (Table 1). There are 273 patients on maintenance haemodialysis in regional centers, in the clinic center the number of patients is 53 – altogether 326 patients. In regional haemodialysis units 34% patients are treated with r-Hu Epo constantly, 16.8% periodically. Constantly treated patients, that is patients, who according to attending physicians absolutely require r-Hu EPO treatment, are dependent on blood transfusions. Periodically treated patients are the patients in whom r-Hu EPO treatment is administered according to its accessibility to obtain the value of hematocrite up to 30% and hemoglobin level about 9 g%.

In the clinic dialysis unit during the last year we had the possibilities to administer r-Hu EPO to all the patients who need that treatment. According to indications of many authors (3, 5) it means – hematocrite below 30% and hemoglobin concentration below 9 g%. Using these criteria 50,9% out of 53 patients needed the therapy. Two patients could not get treatment because of contraindications (malignant hypertension, difficulties with the access to the blood vessels). In general 47% of patients were treated constantly.

r-Hu EPO dosage, route of its administration, kind of pharmaceutical preparation used in treatment.:

In the questionnaire there were questions about the range of r-Hu EPO dosage in the treated patients weekly. Average highest and lowest dosages are given in Table 2. It results from the table that weekly r-Hu EPO dosage fluctuates among patients from 1000 units up to 15000 units. In the clinical center weekly dosages oscillate from 2000 units to 18000 units, the average weekly dosage is 6103 units. In two dialysis units r-Hu EPO was administered only subcutaneously, though in patients with high r-Hu EPO dosages or poorly developed subcutaneously tissue it was also administered intravenously. It was the same in the clinic center. During the last year in all dialysis units r-Hu EPO Eprex produced by Cilag was chiefly used. Recormon produced by Boehringer Mannheim was administered in 4 units but in small amounts only.

The main contraindication to the r-Hu EPO treatment taken into account by physicians and observed r-Hu EPO treatment side effects or complications:

The physicians from all the 8 centers claim that they take into consideration as contraindication to r-Hu EPO treatment difficulties in regulating high blood pressure and problems with access to blood vessels. However, in answer to the question about the observed difficulites, the increase of blood pressure was noticed only in 10% of patients in 6 centers, and then in 30% of patients in the remaining two centers. An increased readiness to A–V fistula thrombosis was observed in 7 centers though the frequency of this complication is mentioned as existing in less than 10% of patients. Local reactions during subcutaneous r-Hu EPO administration were seen three times. Seizures that could take place in connection with r-Hu EPO treatment were observed only once.

In the clinical center we take malignant hypertension and serious problems with the access to the blood vessels into consideration as contraindications to

Table 1. Analysis of the state of rHu Epo treatment in South-East region of Poland

	Number of patients	Age range mean	Sex		Time of r-Hu EPO treatment years	HD patients using r-Hu EPO (%)		Total
			F	M		permanently	periodically	
Regional dialysis centers	273	15–75 43	113	160	a few months to 4 years	92 34%	46 16.8%	138 50.8%
Clinical center	53	24–68 44.3	21	32	4 years	25 47%	–	25 47%
EDTA dates 1991	–	–	–	–	–	Belgium 77.9% Norway 71.3% UK 29.8%		

Table 2. Weekly dosages of r-Hu EPO (IU)

Center	From	To	
1	2000	6000	
2	2000	15000	
3	4000	12000	
4	2000	5000	Clinical center range: 2000–18000
5	1000	9000	mean 6103 ±3829
6	1000	6000	
7	1000	6000	
8	1000	12000	
$\bar{x}$ ±SD	1750 ±1035	8865 ±3685	

Table 3. Routine prescription of iron in r-Hu EPO treated HD patients

Center	Iron orally	Iron iv	Total
1	–	87.5%	87.5%
2	12%	65%	77%
3	15%	61%	76%
4	25%	63%	88%
5	36%	33%	69%
6	–	31%	31%
7	100%	–	100%
8	13%	87%	100%
Clinical center			
Patients treated with r-Hu EPO	13.7%	41%	54.7%
Pts not requiring r-Hu EPO	–	53.8%	53.8%

r-Hu EPO treatment. As a result one patient with very serious problems with the access to the blood vessels and one malignant hypertensive patient have not been r-Hu EPO treated. We don't observe local reactions at all, patients do not complain of muscle pain during r-Hu EPO treatment either.

Dosage, kind of pharmaceutical preparation and the route of iron administration:

Percentage of iron treated patients during r-Hu EPO treatment in each centre and routes of iron administration are given in Table 3. There are haemodialysis units where 100% of r-Hu EPO treated patients take iron supplementation and there is one unit where only 31% r-Hu EPO treated patients take iron. On average about 76% patients during r-Hu EPO treatment take iron suplementation. Intravenously Ferrum-lek is administered in all the centers, whereas orally Hemofer-Polfa, Ascofer-Polon and Resoferon-Geigy.

Iron metabolism monitoring:

In the questionnaire there were questions about assays routinely carried out: blood count, reticulocytosis, thrombocytosis, blood iron transferrin, ferritin concentrations and TIBC. Blood cell count was carried out once a week in three

centers, every 2 weeks in four centers and once a month in one center. In the clinical center blood cell count is performed once a month. Thrombocytes and reticulocytes are routinely determined every 2 weeks in two HD units, once a month in three and every 3 months in three centers. In the clinical HD unit these assays are carried out once every 2 months. Iron blood concentration is analysed every 2 weeks in one, once a month in six, once every 3 months in one center. In the clinical center iron blood concentration is estimated every 3 months. Only in one center there are possibilities for transferrin blood level monitoring once a month. None of seven other centers has the possibilities to monitor transferrin and ferritin blood level or TIBC. In the clinical center transferrin blood level and TIBC is evaluated every 3 months and ferritine is assayed every 6 months.

DISCUSSION

During the last year in our clinical haemodialysis unit we had the possibilities to treat with r-Hu EPO all haemodialysis patients that require the treatment. After half a year of observation under very careful iron status monitoring (iron, transferrin, ferritin blood concentration, TIBC) we could divide the dialysis patients population into two subgroups: one of these who demand r-Hu EPO treatment and one of these who do not need it (2). As diagnostic criteria of beginning r-Hu EPO treatment we accepted the criteria commonly published by other authors, i.e. the decrease of hematocrite under the level of 30% and hemoglobin level below 9g% (3, 5). It turned out after taking into consideration these criteria that 50.9% of haemodialysis patients require constant treatment. Epo treatment data from EDTA 1991 differ a lot between various West European countries (4). The number of r-Hu EPO treated patients in Belgium and Norway is higher than 70% (Table 1) in contrast to the number of r-Hu EPO treated patients in Great Britain which was estimated as about 30% of dialysis patients population. From the questionnaire that we got from south-east regions it seems that about 34% of patients were constantly r-Hu EPO treated during the last year, periodically about 16.8%. Periodically treated patients are the patients who in spite of indications for r-Hu EPO treatment (3, 5) take this medicine only periodically due to insufficient funds in hospitals. Summing up, 50.8% of patients would be constantly treated if r-Hu EPO were available to all the patients that need such therapy. Therefore it seems that requirement for r-Hu EPO treatment in our population of patients minus patients with clear contraindications in the clinical center (4%) should be estimated as about 50% patients on maintenance haemodialysis. Administered average weekly maintenance r-Hu EPO dosages were very similar in the clinical center and regional centers. The situation relating to the iron status monitoring is alarming. In all except one haemodialysis unit the only iron store index is iron blood level. As it is well known (1, 6) that index does not give full information about iron store in haemodialysis patients.

Taking into consideration that in seven centers more that 70% of patients are constantly iron treated and most of them take it parenterally, it should be

supposed that these patients have considerably increased iron store that cannot be estimated using iron blood level monitoring as the only index. It seems that such behaviour of attending physicians is connected with the will of improving hematocrite and hemoglobin level in haemodialysis patients using all possible methods, especially in the situation of money shortages in hospitals that influence the access to r-Hu EPO. Therefore, the urgent postulate is to enable periodically (once in 3 months) TIBC and transferrin evaluation and at least once a year ferritin estimation in all haemodialysis patients. In the clinical center where we have possibilities of monitoring such markers and where the iron store is equalized according to its state and iron metabolism indexes actually much smaller group of patients requires constant parenteral iron supplementation. On the other hand, more attention should be paid to the iron supplementation in patients who are not r-Hu EPO treated – maybe after the iron deficiency supplementation it would be possible to obtain better control of anaemia.

Regarding the observed complications, generally they are reduced to the high blood pressure and the increase of thrombosis readiness. These two are the main initial fears before starting r-Hu EPO treatment by attending physicians. Questions from the questionnaires do not allow for direct definition how often hypertension and increased request for hypotensive medication in r-Hu EPO treated patients are observed. These observations differ from center to center: some doctors say, that 1/3 of patients have increased blood pressure after being treated with r-Hu EPO others, that only 10% of patients have such symptoms. It seems that also the ability of adequate estimation of the „dry weight" of patients and dialysis center possiblities (bicarbonate dialysis for instance) may bring about such differences in the physicians subjective opinion on the problem of haemodialysis patients' exposure to hypertension during r-Hu EPO treatment.

CONCLUSIONS

1. It seems that 50% of patients in regional centers and in the clinical center demand permanent r-Hu EPO treatment.
2. There is an urgent need of improving the ability to monitor iron status in patients treated with r-Hu EPO and iron in regional centers.

STRESZCZENIE

Na podstawie danych z ankiet otrzymanych z ośrodków dializ regionu Południowo-Wschodniego przeanalizowano stan leczenia r-Hu EPO i monitorowania gospodarki żelazowej. Stałego leczenia r-Hu EPO wymaga około 50% hemodializowanych chorych.

Istnieje pilna potrzeba rozszerzenia możliwości monitorowania parametrów gospodarki żelazowej u chorych hemodializowanych i leczonych r-Hu EPO w regionalnych ośrodkach dializacyjnych.

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