The estimation of erythropoietin levels in the blood serum and cystic fluid in patients with solitary renal cysts

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Abstract

Introduction: The role of erythropoietin (EPO) in patients with renal cysts remains unclear. Some authors suggest that EPO may be produced in renal cysts (RC). The aim of the study was to answer the question why concentration of EPO in the cystic fluid (fEPO) is higher than the serum level of EPO.
Material and methods: Serum levels of EPO (sEPO) and cystic fluid levels of EPO (fEPO) were determined in a group of 33 patients (age ranging from 24 to 56 years) with renal cysts and no symptoms of either renal insufficiency or anaemia. Similar tests (excluding fEPO) were performed in the healthy controls – K (33 adults, age ranging from 26 to 53 years). Haematological parameters and serum urea (UREA) and creatinine (CREA) concentration were also determined.
Results: Levels of EPO in the cystic fluid were, on the average 35 times higher than serum levels of EPO. Levels of sEPO in patients with RC were comparable to the control group C. Significantly higher urea levels, lower reticulocyte count, lower haemoglobin concentration and increased anisocytosis of the red cells were found in the study group compared to the control group.
Conclusions: The study suggests that in patients with solitary renal cysts there is no erythropoietin penetration from the cyst fluid into the blood serum. The role of high erythropoietin concentration in renal cyst fluid requires further study.

Key words: kidney, renal cysts, erythropoietin.

Introduction

Renal cysts occur in one third of people older than 50 years. Persons with renal failure who are on long-term dialysis may also develop cystic changes in the kidneys.

A hypothesis that erythropoietin (EPO) may be produced in renal cysts (RC) was put forward during an observation of patients with renal cysts coexisting with renal failure [1-3].

In patients with RC who had elevated serum levels of creatinine (CREA), there were higher serum levels of EPO observed than in patients with RC

who had normal creatinine levels. This phenomenon may contribute to the „defense mechanism" aiming at reducing anaemia resulting from renal insufficiency [4, 5].

If that is true, concentration of EPO in the cystic fluid (fEPO) should be higher than the serum level of EPO. Studies were done to explain this phenomenon.

Material and methods

Serum levels of EPO (sEPO) and cystic fluid levels of EPO (fEPO) were determined in a group of 33 patients (age ranging from 24 to 56 years) with renal cysts and no symptoms of either renal insufficiency or anaemia, treated in the Department of Urology. The assays were performed using Anthos Labtec ht II microtitracic platelets counter and reagents from Boehringer Mannheim (immunoenzymatic method, ELISA technique). The following laboratory tests were performed using haematology analyzer H-1 Technicon: blood cell count, haemoglobin (HGB), haematocrit (HCT), red cell count (RBC), mean cell volume (MCV), mean cell haemoglobin (MCH), MCH concentration (MCHC); reticulocyte count (BLR) was determined applying the microscopic method.

The serum urea concentration (UREA) and creatinine serum concentration (CREA) were also determined (biochemical analyzer RA-XT Technicon, reagents from Technicon).

On the basis of EPO levels the proportion of serum EPO concentration to cystic fluid EPO concentration (sEPO/fEPO) was calculated. Similar tests (excluding fEPO) were performed in the healthy controls – K (33 adults, age ranging from 26 to 53 years). The following values were calculated for the purpose of statistical analysis: mean value (X), standard deviation (SD), minimal value (MIN), maximum value (MAX). The statistical significance of differences was determined according to the Wilcoxon's test.

Results

Results of the study are presented in Tables I-III. Levels of EPO in the cystic fluid were, on the average 35 times higher than serum levels of EPO. Only in 4 study patients the proportion was reverse, i.e. the concentration of EPO in the serum was higher than in the cystic fluid (Table I). Levels of sEPO in patients with RC were comparable to the control group K (Table II). Only in few isolated cases levels of sEPO were higher than the maximum level observed in the healthy controls.

Although neither renal insufficiency nor anaemia were diagnosed in the study patients with RC, we found higher urea levels, lower reticulocyte count, lower haemoglobin concentration and increased anisocytosis of the red cells in the study group compared to the control group (Tables II, III).

Table I. Erythropoietin (EPO) concentration in patients with renal cysts

	EPO in blood serum (pg/ml)	EPO in renal cyst fluid (pg/ml)	Fluid/serum ratio
X	27.73	628.83*	34.89
SD	22.82	485.72	38.82
Min. value	2.56	2.56	0.14
Max. value	122.0	1395.0	135.32

*$p<0.001$

Table II. Haematological results in patients with renal cysts (RC) and the control group (C)

Group	RBC $x10^{12}/l$	HGB g/dl	HCT %	MCV fl	MCHC g/dl	RDW %	HDW g/dl	BLR $x10^{9}/l$
Patients with renal cysts (RC)	4.69±0.32	13.4±1.1*	42±3	90.3±4.4	32.1±1.2	13.9±1.7*	2.6±0.5	34±17*
Control group (C)	4.92±0.29	14.9±0.9	45±4	91.5±3.2	33.2±1.1	12.7±0.4	3.1±0.4	47±9

*$p<0.05$

Table III. Urea, creatinine and sEPO concentration in patients with renal cysts (RC) and the control group (C)

Group	UREA mmol/l	CREA mmol/l	sEPO pg/ml
Patients with renal cysts (RC)	6.4±1.5*	94±15	28±23
Control group (C)	4.7±1.2	87±13	36±13

*$p<0.05$

Discussion

Perhaps the most common cystic change of all is the appearance of one or more "simple renal cysts" in adults. These cysts may be only a few millimeters in size, or may reach 10 cm or more. They are rarely numerous enough so that intervening normal parenchyma is not recognizable, and they are very unlikely to be the cause for renal failure. These cysts are lined by a flattened cuboidal epithelium and filled with a clear fluid. On occasion, there may be hemorrhage into a larger cyst, and it may appear as a mass lesion that can be difficult to differentiate from a renal cell carcinoma.

Endocrine abnormalities in patients with chronic renal failure are well documented. In some articles acquired cystic kidney disease has been related to improvement of anemia in dialysis patients. It has been suggested that this could be due to erythropoietin production by the cysts [6].

Pavlovic-Kentera et al. measured serum erythropoietin levels by radioimmunoassay and compared to the severity of anemia in patients with end stage renal disease of different etiology, on chronic hemodialysis. It was demonstrated that the difference in severity of anemia in those patients is a consequence of a difference in erythropoietin production, rather than due to a difference in the level of erythropoiesis inhibitors. It was stressed that in patients with polycystic kidney disease the kidney tissue kept its endocrine function although it had no residual excretory renal function. The positive correlation between hematocrit values and erythropoietin levels indicates that in these patients the erythropoietin synthesis is not regulated by general hypoxia. It is suggested that control of erythropoietin production in the diseased kidney differs from normal physiological control [7].

The study conducted by Fernandez et al. showed that hemoglobin and erythropoietin were significantly higher in patients with polycystic kidney disease. Patients without cysts had the lowest levels of hemoglobin and erythropoietin, although no significant difference was found in those with multiple bilateral cysts or in those with 1-3 isolated cysts [6].

In another study [8] serum erythropoietin levels were randomly collected and measured by a sensitive radioimmunoassay in a hemodialysis population. For analysis, the patients were divided into two groups: those with polycystic kidney disease and those with other kidney diseases. It was demonstrated that polycystic kidney disease patients manifested higher hematocrit, reticulocyte counts, and serum erythropoietin levels when compared to other kidney disease patients. The data suggest an inappropriately low serum erythropoietin level for the severity of anemia in uremic hemodialysis patients and that greater availability of erythropoietin results in more effective erythropoiesis, even in the uremic environment [8].

Trials connected with the estimation of erythropoietin levels in patients with solitary renal cysts are few. On the basis of the obtained results, the role of EPO in the cystic fluid cannot be unambiguously explained. No evidence of fluid EPO penetration to the serum is provided.

A new question arises, whether fluid EPO could be a growth factor for renal cysts, similarly to inflammation mediators or the interleukins which are present in the cystic fluid [9, 10].

Conlusions

The study suggests that in patients with solitary renal cysts there is no erythropoietin penetration from the cyst fluid into the blood serum. The role of high erythropoietin concentration in renal cyst fluid requires further study.

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