

## Awareness and knowledge of erythropoiesis stimulating agents among chronic haemodialysis patients at a tertiary hospital in south west Nigeria

Akinwumi Ayodeji Akinbodewa \* and Oluseyi Ademola Adejumo

*Kidney Care Centre, Department of Medicine, University of Medical Sciences Teaching Hospital, Ondo State, Nigeria.*

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### Abstract

**Introduction:** Erythropoiesis Stimulating Agents contribute significantly to reduction in mortality among chronic kidney disease patients. Paucity of studies exist on haemodialysis patients' knowledge of Erythropoiesis Stimulating Agents. We set out to assess awareness and knowledge of Erythropoiesis Stimulating Agents among haemodialysis patients.

**Methodology:** This was a questionnaire-based, descriptive, cross-sectional study conducted between November 2017 and March 2018.

**Results:** There were 38 (60.3%) males and 25 (39.7%) females with a mean age of 50.3 ( $\pm$  15.4) years. Twenty six (41.3%) were aware of Erythropoiesis Stimulating Agents. Twenty four (92.3%) and 2 (7.7%) participants became aware of Erythropoiesis Stimulating Agents through doctors and nurses respectively. None was presented with educational materials on Erythropoiesis Stimulating Agents. Twenty four (92.3%) knew that erythropoiesis Stimulating Agents are injections and 15 (57.7%) knew that their main function is blood formation. Eight (30.8%) knew the correct target haemoglobin concentration for patients on erythropoietin. Only 1 (3.8%) and 2 (7.7%) participants could identify hypertension and headache as side effects of erythropoietin. Higher level of educational qualification ( $p=0.003$ ) was significantly associated to awareness of Erythropoiesis Stimulating Agents.

**Conclusion:** Awareness and knowledge of Erythropoiesis Stimulating Agents among haemodialysis patients was poor. Educational qualification was positively associated to awareness. Counselling method was substandard.

**Keywords:** Erythropoietin; Erythropoiesis Stimulating Agents; Knowledge; Awareness; Chronic kidney disease

### 1. Introduction

Erythropoietin (aka EPO, haematopoietin, haemapoietin) is a glycoprotein hormone that exists in both the endogenous and exogenous forms. Endogenous erythropoietin is a one O-linked and three N-linked glycosylation, 165 amino acid chain glycoprotein that is sourced primarily by the interstitial renal cortical peritubular cells (principally those associated to the proximal convoluted tubules) in response to cellular hypoxia with the remaining portion produced in the liver [1]. Hepatic production of EPO by the perisinusoidal cells normally supersedes renal production in the foetus and vice versa in adulthood. Insignificant quantities are also produced in the lungs, bone marrow, brain and spleen [1, 2]. Some authors have also shown EPO production by independent islands of macrophages *in vitro* [3].

\* Corresponding author: Akinwumi Ayodeji Akinbodewa  
Kidney Care Centre, Department of Medicine, University of Medical Sciences Teaching Hospital, Ondo State, Nigeria.

Exogenous erythropoietin are commonly called erythropoiesis stimulating agents (ESAs). They are the synthetic, recombinant human versions of EPO (rhEPO) manufactured with the sole objective of replacing depleted endogenous EPO in chronic kidney disease (CKD) patients even though their usage extends to patients with prematurity, chronic inflammatory diseases, cancers and myelodysplasias as well as those in need of surgery, autologous blood donation, intensive care and haematopoietic stem cell transplantation [4, 5]. Depending on the formulation, ESAs may be used twice or thrice weekly (erythropoietin  $\alpha$  and  $\beta$ ), fortnightly or once per month (CERA, continuous erythropoietin receptor activator aka methoxy-polyethylene-glycol-epoetin beta) [1].

Alongside vaccines, calcium, alpha-calcitriol, antihypertensives and dialysis, ESAs are an integral part of the care of chronic kidney disease (CKD) patients as the kidneys of those living with CKD have lost their ability to produce endogenous EPO due to chronic renal interstitial fibrosis. ESAs contribute significantly to reduction in cardiac complications which rank as the foremost cause of mortality among pre-dialysis and dialysis patients [6]. It is therefore important that all CKD patients are well aware of ESAs and utilize them optimally in order to achieve the target haemoglobin concentration of 11-12g/dl and derive the desired maximum clinical benefits which also include improvement in sleep quality, sexual function, cognitive function and overall quality of life [7].

However, despite their benefits, many factors still militate against utilization of these treatment modalities. For example, awareness and utilization of vaccines against infectious diseases was found to be poor among a group of Nigerian CKD patients on dialysis [8]. Factors such as misconceptions about medication and lack of perceived self-efficacy in medication were found to affect medication adherence among CKD patients include [9]. Generally, knowledge and understanding, communication and quality patient-provider relationship have been linked with better compliance to medications and clinical outcomes [10, 11, 12].

Our literature search showed paucity of data on patients' knowledge and usage of ESAs. We therefore set out to assess awareness and knowledge of ESAs among dialysis patients at the Kidney Care Centre, University of Medical Sciences Teaching Hospital, Ondo State, Nigeria.

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## 2. Material and methods

### 2.1. Study location

Kidney Care Centre is a 30-bedded multi-professional renal outfit with in-patient nursing, medical, dietetics and psychosocial support and capacity to accommodate 10 haemodialysis patients simultaneously. The Centre records 100-200 sessions of dialysis per month. There were 2 consultants, 4 medical officers, 2 house officers and 28 nursing staff in direct care of in-patients and the haemodialysis unit. The Kidney Care Centre is located within the University of Medical Sciences Teaching Hospital, Ondo State, and South Western part of Nigeria.

### 2.2. Study population

Study participants included chronic kidney disease patients receiving haemodialysis between November 2017 and March 2018.

### 2.3. Study design

This was a multi-stage, descriptive, cross-sectional study.

### 2.4. Study material

Interviewer-administered questionnaires were used to obtain their socio-demographic and clinical parameters and assess awareness and level of knowledge. The first stage of the study was to stratify the participants into two; those who were aware of ESAs and those who were unaware. This was determined by a requisite "Yes" or "No" response to the question, "Have you heard of Erythropoietin Stimulating Agents?" All subjects who responded "No" were documented as being unaware of ESAs and were thus excluded from stage two of the study which comprised of determination of the level of knowledge of ESAs among those who were aware. The questions assessed the following domains: formulation of ESAs, functions and routes of administration of ESAs, expected rise in packed cell volume in response to ESAs, target range of packed cell volume desirable for CKD patients on erythropoietin, side effects of ESAs and factors that could reduce their efficacy. Their sources of awareness and knowledge of ESAs were determined as well as the nature of counselling and education they received on ESAs. We also conducted a literature search on knowledge of ESAs via various search engines such as Pubmed, Google scholar, Researchgate, Medscape etc. using keywords that include

erythropoietin, erythropoiesis, Erythropoiesis Stimulating Agents, awareness, knowledge, usage, chronic kidney disease, dialysis and haemodialysis.

### 2.5. Inclusion criteria

All consecutive CKD patients undergoing chronic haemodialysis were recruited into the study.

### 2.6. Exclusion criteria

Non-consenting patients, pre-dialysis CKD patients, patients with acute kidney injury or those on short time dialysis for acute poisoning (or any other indications) were excluded from the study.

### 2.7. Sample size

Sixty three participants were recruited for the study.

### 2.8. Ethical approval

Informed consent was obtained from all individual participants included in the study.

### 2.9. Data analysis

Data was analysed using SPSS software (version 20.0; IBM SPSS Inc, Chicago, III). The results obtained were presented as percentages, frequencies and means ( $\pm$ Standard Deviation). Chi square ( $\chi^2$ ) test of association was used to identify the factors that determined level of knowledge among participants. Likelihood ratio was employed where the number of subjects in a column was less than 5. A  $p$  value of  $\leq 0.05$  was accepted as statistically significant.

## 3. Results

There were more males in the study (60.3%) with a mean age ( $\pm$ Standard deviation) of 50.3 ( $\pm$  15.4) years. The age range of the subjects was (range 19-83 years). The main aetiologies of CKD were chronic glomerulonephritis (CGN) (41.2%), diabetes mellitus (19.0%), CKD of unknown aetiology (16%) and hypertension (12.7%). Majority (96.8%) had received at least primary education (table 1).

Out of 63 subjects, 26 (41.3%) had heard about ESAs. Out of these 26 subjects, 18 (69.2%) had tertiary education while an equal fraction (15.4%) had primary and secondary education. Twenty four (92.3%) subjects became aware of erythropoietin through doctors while 2 (7.7%) became aware through nurses. Other avenues like friends, fellow patients, newsprint or social media were zero (table 1). Majority of the subjects heard of ESAs during consultation with medical doctors, some heard from nurses on the wards. None of the subjects was presented with a written document on ESAs during counselling (table 1).

**Table 1** Socio-demographic and clinical parameters of participants

Clinical parameters	Overall subject population (N=63) Frequency (%)	Subjects aware of ESAs (N=26) Frequency (%)
<b>Gender</b>		
Male	38 (60.3%)	15 (57.7%)
Female	25 (39.7%)	11 (42.3%)
<b>Age range (years)</b>		
19-44	19 (30.2%)	3 (11.5%)
45-64	32 (50.8%)	19 (73.1%)
$\geq 65$	12 (19.0%)	4 (15.4%)
<b>Marital status</b>		
Married	54 (85.7%)	24 (92.4%)
Single	6 (9.5%)	1 (3.8%)

Widowed	3 (4.8%)	1 (3.8%)
<b>Religion</b>		
Christianity	55 (87.3%)	24 (92.4%)
Islam	8 (12.7%)	2 (7.6%)
Others	0	0
<b>Educational qualification</b>		
Tertiary	28 (44.4%)	18 (69.2%)
Secondary	20 (31.7%)	4 (15.4%)
Primary	13 (20.6%)	4 (15.4%)
None	2 (3.2%)	0
<b>Diagnosis</b>		
Hypertensive kidney disease	8 (12.7%)	1 (3.8%)
Diabetic kidney disease	12 (19.0%)	9 (34.6%)
Chronic glomerulonephritis	26 (41.2%)	11 (42.3%)
HIV nephropathy	5 (7.9%)	1 (3.8%)
Obstructive nephropathy	1 (1.6%)	0
ADPKD	1 (1.6%)	1 (3.9%)
CKD unknown aetiology	10 (16.0%)	3 (11.5)
<b>Sources of awareness</b>		
Doctors	-	24 (92.3%)
Nurses	-	2 (7.7%)
Fellow patients	-	0
Friends	-	0
Social media	-	0
Mass media	-	0

ADPKD, Autosomal Dominant Polycystic Kidney Disease; CKD, chronic kidney disease; ESAs, Erythropoiesis Stimulating Agents

Twenty four (92.3%) were aware that ESAs come as injections and 15 (57.7%) were aware that their main function is blood formation while 13 (50%) of subjects were aware that iron sucrose would be needed for ESAs to give maximum haematopoietic benefit. Twelve (46.2%) subjects knew that erythropoietin Beta should be taken thrice weekly. Five (19.2%) subjects knew that monthly haemoglobin concentration of subjects on ESAs should increase by an estimated 1-2g/dl. Eight (30.8%) knew the correct recommended target haemoglobin concentration range for CKD patients on ESAs. Only 1 (3.8%) and 2 (7.7%) of participants could identify hypertension and headache as side effects of ESAs. As for reducing efficacy of ESAs, twelve (46.2%) and 9 (34.6%) of participants knew that malnutrition and inadequate dialysis could play a role. Patients with tertiary education contributed to at least 50% of all correct responses in all domains (table 2).

**Table 2** Frequency of correct responses by subjects on Erythrocyte Stimulating Agents

Question domain*	Frequency (percent) of correct responses (N= 26)	Contribution of correct responses by subjects with tertiary education N=18 (Percent)†
In what form is Erythrocyte Stimulating Agents? (a) Supplement (b) tablet (c) <i>injection</i> (d) vegetable (e) blood tonic.	24 (92.3%)	17 (70.8%)
Which of these are the types of Erythrocyte Stimulating Agents you know?		
Erythropoietin Alpha	11 (42.3%)	9 (81.8%)
Erythropoietin Beta	8 (30.8%)	7 (87.5%)
Darbopoietin		
CERA	4 (15.4%)	3 (75%)
How regularly should Erythropoietin Beta be taken? (a) daily (b) once every week (c) <i>3 times a week</i> (d) once a month.	12 (46.2%)	9 (75%)
By what estimated margin should Erythropoietin increase the haemoglobin concentration on monthly interval? (a) <i>1-2g/dl</i> (b) 3-4g/dl (c) 5-6g/dl (d) 7-8g/dl (e) 10-12g/dl	5 (19.2%)	4 (80%)
What other drugs are needed for Erythrocyte Stimulating Agents to work well?		
(a) Iron Sucrose	13 (50%)	11 (84.6%)
(b) Vitamin C	2 (7.7%)	1 (50%)
(c) Folate	2 (7.7%)	2 (100%)
What is the target haemoglobin concentration for CKD patients on Erythrocyte Stimulating Agents? (a) 14-16g/dl (b) 18-20g/dl (c) <i>11-12g/dl</i> (d) 6-8g/dl (e) 3-5g/dl	8 (30.8%)	7 (87.5%)
The main function of Erythrocyte Stimulating Agents is (a) blood cleansing (b) sleeping well (c) urine formation (d) improve sexual performance (e) <i>blood formation</i> (f) better mental activity (g) weight gain	15 (57.7%)	11 (73.3%)
The side effect of Erythrocyte Stimulating Agents includes		
(a) hypertension	1 (3.8%)	1 (100%)
(b) headache	2 (7.7%)	1 (50%)
(c) stroke	0	0
Which of these can prevent Erythrocyte Stimulating Agents from working effectively?		
(a) malnutrition	12 (46.2%)	9 (75%)
(b) inadequate dialysis	9 (34.6%)	9 (100%)
(d) infection	4 (15.4%)	4 (100%)
(e) active blood loss	2 (7.7%)	2 (100%)

CKD, chronic kidney disease; CERA; Continuous Erythropoietin Receptor Activator; \*Correct responses italicized where applicable; †The percentages calculated are calculated using the formula:  $n/N \times 100$ . This was done to show the contribution of subjects with tertiary education to correct responses given by N = 26 group

Higher level of educational qualification ( $p=0.003$ ,  $LR=13.894$ ) was significantly associated to awareness of ESAs. Gender ( $p=0.461$ ,  $LR=0.127$ ) and religion ( $p=0.274$ ,  $LR=1.056$ ) were not significantly associated to awareness of ESAs (table 3).

**Table 3** Association between awareness of Erythrocyte Stimulating Agents and determinants

Determinants	Awareness		Chi square (p value)
	Aware	Not aware	
Gender			
Male	15 (57.7%)	23 (62.2%)	0.127 (0.461)
Female	11 (42.3%)	14 (37.8%)	
Religion			Likelihood ratio (p value)
Christianity	24 (92.3%)	31 (83.8%)	1.056 (0.274)
Islam	2 (7.7%)	6 (16.2%)	
Educational qualification			Likelihood ratio (p value)
Tertiary	18 (69.2%)	10 (27%)	13.894 (0.003)
Secondary	4 (15.4%)	16 (43.2%)	
Primary	4 (15.4%)	9 (24.3%)	
None	0	2 (5.4%)	

#### 4. Discussion

A high proportion of our haemodialysis patients (58.7%) had not heard about ESAs. This is an important information as it implies a high probability of non-usage by such patients. It also may be a reflection of a bigger picture; that is unavailability of standard structure, guidelines and protocol for counselling of CKD patients by medical and nursing personnel (which naturally would have included erythropoietin and its importance in CKD care) [13].

Patients with chronic diseases have been shown to do better when they are fully aware of their disease and the need to adhere to their medications for optimal therapeutic benefits. For instance, patients were found to be 30% less likely to be re-admitted when they are well instructed on how to take their medications and when to make appointments for follow up in the out-patient clinic [14, 15].

The level of knowledge of ESAs among our haemodialysis subjects who were aware of ESAs was suboptimal in most domains that were tested. Aside three domains where a high number of participants (92.3%) knew that ESAs come as injections, 57.7% recognized blood formation as the main function of ESAs and 50% of the subjects knew that iron sucrose would be needed to achieve best marrow response, the study participants performed below par in the rest of the domains. This finding may be adduced to poor depth of counselling delivered by the medical staff. For example, our study showed that medical staff only offered informal counselling sessions on ESAs as majority of our subjects only heard about ESAs during clinic consultation and by the bed side. One study already demonstrated that insufficient patient education which is often fragmented with no obvious goal setting could result in poor awareness of disease and consequent inadequate self-care among patients [16].

Another indicator to the unstructured approach by our medical staff was the lack of educational resources (either soft or hard copy formats) for the patients during counselling. The standard patient education process has been known globally to consist of the following steps; documented needs assessment, planning, implementation and evaluation in order to achieve an efficient and effective patient-centered care [17, 18].

The deficient knowledge base among our study participants may not be unconnected to the disproportionate doctor/nurse-to-patient ratio that is common place in many hospitals in Nigeria. At the study centre, the number of medical staff was small compared to the patient load. Ideally, nurse educators ought to have dedicated time for counselling of individual patients but that is not usually the case in our setting. This problem is equally documented by Marcum and Bergh where inadequate time and poor staffing were found to militate against patient education [19, 20].

The educational qualification of our study participants was found to be an important patient-related factor that influenced knowledge of ESAs in our study. This is in conformity to the finding by Mezza et al where prior knowledge of treatment with an ESA correlated positively with educational level [21].

The study was limited by its single centre design which accounts for the low number of study participants and less reliability of inferences from the study.

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## 5. Conclusion

Awareness and knowledge of ESAs among our haemodialysis patients was poor. Higher educational qualification influenced knowledge of ESAs positively and counselling on ESAs was mostly unstructured and fragmented due to poor staff strength.

### *Recommendations*

We hereby recommend a more elaborate, multi-centre study involving a higher number of participants. Medical staff strength in the renal units require beefing up in order to have more dedicated health educators among them. Where this cannot be immediately achieved, their efforts should be fortified with leaflets, booklets, audio or audio-visuals (sometimes, it could be a combination of some or all).

Group counselling for dialysis patients may also be a short-term, time-saving measure in settings where there is a high patient-staff ratio. Through this method, knowledge sharing may be enhanced through a strong patient-to-patient communication and support. It is also important to ensure that medical personnel are well trained on ESAs to ensure adequate knowledge of ESAs among would-be educators [22].

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## Compliance with ethical standards

### *Disclosure of conflict of interest*

The authors declare that they have no competing interests.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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