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Effectiveness Of Erythropoietin Therary In The Treatment Of The Anemia In Clients With End-Stage Renal Disease In Mississippi

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EFFECTIVENESS OF ERYTHROPOIETIN THERAPY IN THE TREATMENT OF THE ANEMIA IN CLIENTS WITH END-STAGE RENAL DISEASE IN MISSISSIPPI

by

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Effectiveness of Erythropoietin Therapy in the Treatment of the Anemia in Clients with End-Stage Renal Disease in Mississippi

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Dedication

I dedicate this endeavor to all the special people in my life who have had a part in this success.

My husband, Robert Duncan, who has supported me emotionally and physically throughout this past year.

My son, Brandon Beene, who has shown his excitement and encouragement to me through nursing school four times.

My mother-in-law and father-in-law, Mr. and Mrs. Robert Duncan, who have given their support and encouragement.

A special dedication to my very wonderful mother, Lamoys DuVall, though deceased, she continues to be a source of inspiration and strength for me.

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Abstract

Clients with end-stage renal disease (ESRD) often experience an associated anemia which has been attributed to an endocrine deficiency of erythropoietin. The purpose of this descriptive, retrospective study was to describe the characteristics of the effectiveness of erythropoietin (EPO) therapy on the anemia associated with ESRD. The research question generated was how effective is EPO therapy in the treatment of the anemia in clients with ESRD in Mississippi? Orem's Self-Care Model was the theoretical framework used for this study. The sample (N = 100) consisted of 55 males clients and 45 female clients from an ambulatory dialysis unit in Northeast Mississippi. The clients were receiving dialysis and EPO therapy. The researcher designed an instrument for data collection. Demographic findings, blood pressure, and blood transfusions were analyzed using descriptive statistics, including means, percentages, and frequencies. A paired t test was utilized to analyze the statistical significance between pretherapy and posttherapy hematocrit data. Findings indicated a significant increase in hematocrits at one month posttherapy, $t = -4.12$, $p < .05$; 3 months, $t = -7.45$ $p < .05$; and current levels, $t = -8.58$, $p < .05$. The mean baseline hematocrit was 24.56, and the

mean current hematocrit was 29.79. Blood pressures did not increase, t = 21.25, p > .05. The mean pretherapy systolic blood pressure was 169.57, and the mean posttherapy systolic pressure was 153.63. The mean diastolic blood pressure was 101.33, and the posttherapy mean diastolic pressure was 86.86. This study did not show a significant decrease in blood transfusion requirements. Eighty-eight percent of the clients did not receive transfusions pretherapy, and 79% did not receive transfusions posttherapy. The researcher concluded that EPO is effective in increasing hematocrit levels in the client with ESRD. Similar studies are needed to further document the effectiveness of EPO on the anemia of ESRD in clients in Mississippi. Implications for nursing include the importance of education, documentation, and continuity of care in health promotion and rehabilitation of the client with ESRD.

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Chapter I

The Research Problem

Introduction to the Problem

End-stage renal disease (ESRD) is a serious health problem in the United States. As of 1991, there were 142,488 people in the United States on some form of dialysis for the treatment of ESRD (Health Care Financing Administration, 1992). Mississippi statistics show a total of 2,236 ESRD clients in the state (ESRD Network, 1991). The number of people with ESRD is increasing yearly due to medical technology, such as dialysis which is extending the life of these clients. The focus of health care providers has been on increasing life expectancy. In doing so, health care providers have overlooked the quality of life.

The impact of ESRD on the client's life is extensive. The disease is characterized by symptoms related to the retention of uremic toxins (uremia) which results from loss of renal function (Luckmann & Sorenson, 1987). Early manifestations of uremia are fatigue and decreased mental acuity. As renal function declines, other symptoms appear which may include the following: nausea, vomiting, anorexia, cramps and muscular twitching, cold sensitivity,

and decreased exercise tolerance. In addition, some clients may experience angina and cardiac failure.

The symptoms of uremia can have a profound effect on clients. Lowered energy levels may result in decreased participation in vocational roles, household chores, and community and social activities. Also, cognitive function may decline, self-esteem may lessen, mood changes may occur, and the general sense of well-being may diminish (Nissenson, 1989).

The symptomatology presented by ESRD was once primarily attributed to uremia. However, it is now apparent that many of these symptoms are those related to the associated anemia. The symptoms of the anemia include fatigue, angina, exertional dyspnea, palpitations, cold sensitivity, anorexia, decreased or loss of sexual functioning, pallor, menstrual irregularities, and tachycardia. Cardiac failure, with reversible cardiac enlargement, cardiac bruits, and pulmonary and peripheral edema may develop if the anemia is severe (Stevens, Kurtz, Eckardt, & Winearls, 1992).

Anemia is an almost universal complication of ESRD. Approximately three fourths of the patients on dialysis in the United States have symptoms of anemia. Many more predialysis clients also suffer from this complication. The severity of the anemia varies, depending on the underlying renal disease. Higher hematocrits are observed in clients with polycystic kidney disease and lower hematocrits in

those with interstitial disease. The hematocrit starts decreasing when the glomerular filtration rate (GFR) falls below 50 ml per minute. Dialysis therapy is usually initiated when GFR is below 10 ml per minute. Dialysis can result in improvement of many of the symptoms of uremia; however, it does not completely reverse the uremic milieu. Therefore, the client is left in a chronic state of uremia and vulnerable to the many complications of uremia, including anemia. The average hematocrit for the ESRD client (prior to erythropoietin therapy) is 21% to 23%. Therefore, the anemia of chronic renal failure contributes significant morbidity to the clients on dialysis because of the associated symptoms (Rosenberg, 1992).

The anemia associated with ESRD has been recognized since 1836. However, very little was understood about this anemia. The etiology of the anemia has been attributed to many factors, but only in recent years has its pathogenesis emerged (Eschbach, Haley, & Adamson, 1990).

The etiology of the anemia associated with ESRD is multifactorial, but the primary cause is thought to be an endocrine deficiency of erythropoietin. Although shortened survival of red blood cells, blood loss through dialysis, and uremic toxins that inhibit marrow erythropoiesis may contribute to the anemia, studies indicate that inadequate erythropoietin production is the single most important cause (Duff, 1989).

The process of erythropoiesis is complex and not fully understood. The normal kidneys produce 90% of the erythropoietin, and the liver produces 10%. When anemia develops, the resulting hypoxia stimulates the release of erythropoietin hormone which increases plasma erythropoietin. Erythropoiesis occurs until the anemia is corrected, and the plasma erythropoietin returns to normal ranges. In this process there is a feedback relationship between the hematocrit and the plasma erythropoietin. The damaged kidneys in progressive renal failure cannot maintain a balance of homeostasis. Anemia develops and worsens with increasing tissue destruction (Eschbach et al., 1990).

In the past, anemia associated with ESRD has been treated with limited success. According to Stevens et al., (1992), treatments have included dialysis, androgen therapy, and red blood cell transfusions. With dialysis, improvement in the anemia is often seen within a few months. Improvement is dependent on the intensity of the dialysis. Androgen therapy has shown improvement when given parentally and in association with adequate dialysis. However, not all clients respond to androgen therapy, and there have been incidences of side effects in up to 25% of the clients. Blood transfusions given as a treatment for the anemia results in suppression of erythron activity and increases the requirement for subsequent transfusions. Frequent transfusions increase the client's risk of iron overload,

blood-borne viral infections, and risk of exposure of antibody production to HLA antigens which reduces the chance of receiving a successful transplant (Stevens et al., 1992).

Despite advances in understanding the physiology of the anemia associated with ESRD, naturally occurring erythropoietin cannot be obtained in sufficient quantities to treat the anemia. However, erythropoietin has been cloned through genetic coding. Recombinant human erythropoietin (r-HuEPO or EP0) has been developed, and it has a similar structure to the native human erythropoietin. This erythropoietin clone has been studied in world-wide clinical trials and is now being used in the treatment of the anemia associated with ESRD (Duff, 1989). Since approval for use in 1989 by the Food and Drug Administration, EPO has become a mainstay of therapy in the clients with ESRD (Rosenberg, 1992).

Significance to Nursing

Anemia is a major predictable complication of ESRD. It is often severe and hinders rehabilitation even though the client receives adequate dialysis. Anemia also affects the client's physiological and psychological functioning and social and vocational participation. Therefore, this study will enhance the nurse clinician's understanding of the impact of ESRD associated anemia on the client's life, as well as the pathogenesis of the anemia.

In addition, this study will increase the availability of current nursing research on ESRD, as well as increasing nursing awareness of the effectiveness of EPO on the anemia as indicated by improvement in symptomatology. The decreased requirement for blood transfusions will also benefit nursing by decreasing the possibility of contracting infection from blood-borne pathogens through handling of blood products. Also, by understanding the anemic state and the improvement in the anemic state by EPO, the nursing agent will be better prepared for appropriate history and physical assessment, teaching, and establishing intervention modalities directed toward rehabilitation of the client to a more productive lifestyle.

Theoretical Framework

Orem's Self-Care Model was the theoretical framework selected for this study. Within this model there are three related theories: the Theory of Self-Care, the Theory of Self-Care Deficit, and the Theory of Nursing Systems (Marriner-Tomey, 1989). These theories contain propositions vital to health promotion, such as health maintenance, prevention, care, rehabilitation, and functional living with a disease or disability (Riehl-Sisca, 1989). The Theory of Self-Care describes self-care as the ability to provide for oneself. The Theory of Self-Care Deficit identifies limitations the client has in meeting self-care and how nursing could intervene. The Theory of Nursing Systems

gives knowledge of a client's self-care demands and provides assistance in meeting these demands (Orem, 1985). Within the nursing systems, the client's self-care demands are met through one of the three systems (wholly compensatory, partly compensatory, and supportive-educative) depending on the ability of the client to meet the demands and the degree of nursing intervention needed (Marriner-Tomey, 1989).

Orem defined four metaparadigm concepts including person, nursing, environment, and health. The person is a whole of inseparable physical, psychological, interpersonal, and social factors. Nursing is an active process to overcome or prevent the development of self-care deficits or provide therapeutic care for an individual who is unable to perform self-care. The environment consists of elements external to the individual. Health is the stability of internal and external conditions which permits the individual to perform self-care (Leddy & Pepper, 1989). Within the framework of this study, the person was identified as the client with ESRD receiving EPO therapy for the treatment of associated anemia. Nursing represents the process of identifying the effectiveness of EPO therapy. The environment was the ambulatory dialysis unit with which the client was associated. Health was reflected by the therapeutic response to EPO therapy. Orem's Self-care Model provided structure and organization to this study through clear, identifiable definitions. Also, the propositions

vital to health promotion were applicable to the client with ESRD since care is directed toward maintenance, prevention, and rehabilitation.

Assumptions

The assumptions on which this study was based were

1. Persons require continuous deliberate inputs to themselves and their environment to remain alive and functioning.

2. Mature persons experience privations in the form of limitations for self-care actions and care of others involving making life-sustaining and function-regulating inputs.

3. Human agency is experienced in identifying, developing, and transmitting to others the ways and means to identify requisites for and make inputs to self and others (Marriner-Tomey, 1989).

Purpose of the Study

The purpose of this study was to evaluate the effectiveness of recombinant human erythropoietin therapy in the treatment of the anemia in clients with ESRD in Mississippi.

Statement of the Problem

The problem evaluated was the degree of improvement in the anemia associated with ESRD following initiation of

recombinant human erythropoietin therapy as part of the therapeutic medical regimen.

Research Question

The research question generated was this: How effective is recombinant human erythropoietin therapy in the treatment of the anemia in clients with ESRD in Mississippi?

Definition of Terms

For the purpose of this study, the following terms were identified:

Client: A person who is receiving recombinant human erythropoietin therapy (r-HuEPO, EPO) for the treatment of the anemia associated with ESRD, on some form of dialysis, and living in Mississippi.

End-Stage Renal Disease (ESRD): An irreversible progressive reduction of functioning renal tissue which can no longer maintain the body's internal environment and necessitates treatment with dialysis or kidney transplant for survival (Luckmann & Sorenson, 1987).

Anemia: A decrease in oxygen-carrying capability of the blood with a hematocrit value less than 37% in females and 42% in males and associated with ESRD.

Effective erythropoietin therapy: Recombinant human erythropoietin is a clone of the naturally occurring erythropoietin hormone which stimulates the process of erythropoiesis and is used in the treatment of the anemia

associated with ESRD. In the therapeutic response, the hematocrit level will be 33% or greater, and the client will be independent of blood transfusions except for the replacement of blood loss.

Chapter II

Review of the Literature

Review of the literature revealed an active interest by physicians and researchers in the treatment of the anemia associated with ESRD. The available literature is from current clinical trials. Some of the clinical trials are ongoing, and the data are not yet available. However, one available study by Eschbach, Egrie, Downing, Browne, and Adamson (1987) evaluated the effects of intravenous EPO given three times a week to 25 hemodialysis clients. Prior to initiating the study, the participants underwent extensive medical evaluation. Criteria for client participation was met and included the following: hematocrit $\leq$ 25, on hemodialysis for at least 3 months, medically stable, controlled hypertension or no hypertension, not pregnant, no evidence of hemolysis or blood loss, no evidence of toxic effects of aluminum, not receiving androgen or immunosuppressive therapy, serum aspartate aminotransferase stable or no more than twice normal, and no evidence of other systemic illness that may mask the effectiveness of EPO therapy.

Recombinant human erythropoietin was given intravenously three times a week after dialysis. Response

to the therapy was evaluated by the effect on blood transfusion requirements, hematocrit, ferrokinetics, and reticulocyte response.

Dose dependent increases in effective erythropoiesis were observed. Dosages ranged between 15 and 500 units per kilogram of body weight (u/kg). At the maximum dose, changes of at least 10 percentage points were observed in the hematocrit within 3 weeks. The ferrokinetics increased three to four times basal values. Twelve clients out of 18 no longer required blood transfusions, and 11 had hematocrit increases of 35% or more. Four of the clients with hematocrit increases experienced an increase in blood pressure and one had a grand mal seizure. However, this client had had a similar type seizure 3 years prior to the study but was not receiving anticonvulsant therapy. The majority of the clients had increased serum creatinine and potassium levels. Functional iron deficiency developed at doses of 15 u/kg or more. Twelve of the 18 clients received intravenous iron dextran and one (allergic to iron dextran) was administered oral iron therapy. Iron excess decreased in all clients who responded to EPO therapy. No antibodies developed in response to EPO, no organ dysfunction occurred, nor were other toxic effects observed.

Another study by Watson, Gimenez, Cotton, Walser, and Spivak (1990) evaluated the efficacy of subcutaneous EPO therapy in clients with chronic renal failure and anemia

(predialysis). Eleven clients participated in the double-blind, placebo controlled study. The EPO group received subcutaneous 100 u/kg body weight three times per week, and the other group received a placebo injection. After 12 weeks the placebo group received EPO 150 u/kg three times a week until a target hematocrit was achieved. During the study, blood pressure was monitored, and blood work was obtained regularly for hematocrit, hemoglobin, reticulocyte count, and iron profile determinations.

Statistical analysis was done using the Student's t test for unpaired data. Values were expressed as mean $\pm$ SE. The mean baseline hematocrit of both groups was similar: EPO, 29% $\pm$ 2% and placebo, 28% $\pm$ 2%. After 12 weeks, the hematocrit of the treated group had increased to 35% $\pm$ 2% ($p < 0.001$). The placebo group was 26% $\pm$ 2%. After 12 weeks of EPO therapy, the placebo group had a significant increase in hematocrit to 32% $\pm$ 2% ($p < 0.001$ versus baseline). Baseline blood pressures in the EPO group were 169/83, after 12 weeks 136/76, and 144/78 at 52 weeks. The placebo group's baseline mean blood pressures were 135/75, 149/83 at 12 weeks, and 139/81 at 52 weeks.

One placebo-treated client had a seizure related to hyponatremia after ingestion of water load in preparation for glomerular filtration rate estimate. One EPO client experienced numbness of fingers of the right hand during the maintenance phase when the hematocrit was stable. This was

thought to be related to a transient ischemic attack. The significance of the two studies is that they indicate that EPO therapy is effective in treatment of anemia of chronic renal failure in both hemodialysis and predialysis clients. However, clients receiving continuous ambulatory peritoneal dialysis (CAPD) also benefit from EPO therapy.

The recommended route of administration for the predialysis and CAPD clients is subcutaneous, since self administration can be easily taught. Subcutaneous administration is also feasible in the hemodialysis client. However, intravenous administration is recommended only for the hemodialysis patient.

The recommended dose range to maintain a stable hematocrit (35 $\pm$ 3) varies between 15 and > 300 u/kg, intravenously three times a week, with a median of 75 u/kg. The frequency of dosing is dependent upon the route. Because of pharmacokinetics, the intravenous dose must be given two to three times per week. However, weekly subcutaneous administrations of EPO are as effective as the same total dose divided into three 15 u/kg doses/week (Eschbach et el., 1990).

The recommended target range for the hematocrit level is 33% to 40% in order to achieve maximum benefits from oxygen delivery and to reduce side effects. Therefore, the dosage is dependent on the client's response to EPO. The best starting dose is in the lowest range which produces

gradual but consistent increases in the hematocrit (Duff, 1989).

Treatment with EPO stimulates erythropoiesis, increases hematocrit levels, and eliminates blood transfusion requirements in virtually all hemodialysis clients with uncomplicated anemia (no iron deficiency, inflammation, or other signs of aluminum toxicity) (Nissenson, 1989). However, there have been other positive effects from EPO therapy demonstrated in clients.

Positive effects on the hematocrit from treatment with EPO therapy extends to other subjective and objective improvements. The subjective benefits include improvement in sexual functioning, increased energy levels, and better sleep patterns. The objective improvements include an increase in brain and cognitive function and exercise tolerance.

A study cited by Nissenson (1989) measured brain event-related potentials in 13 clients receiving hemodialysis, before and after 12 weeks of EPO therapy. The mean hematocrit level increased from 22.7% at initiation of the study to 36.6% after treatment. Nine of 13 clients demonstrated improvement in P3 latencies with tone and vowel stimuli, indicating fast and more efficient information processing by the brain. This study was extended to 17 clients receiving hemodialysis and EPO for at least one year. Mean hematocrit levels increased from 23% prior to

EPO to 37% in a year. Improvement in P3 latencies was observed in only 9 clients which indicated a lack of improvement in the speed of processing information in the other clients. However, the amplitude of the P3 waves increased significantly for the entire group ($p < .03$). The findings indicated a 19% improvement in parietal function, 63% improvement in vertex function, and 160% improvement in frontal brain area function.

The improvements in cognitive functioning were related to the corrected anemic state with EPO. These findings also suggested that part of the uremic syndrome of ESRD clients receiving hemodialysis is attributed to the effects of the anemia on the central nervous system and can be reversed with correction of the anemia.

Improvement in exercise tolerance has also been observed. A Canadian Erythropoietin Study Group (cited in Nissenson, 1989) conducted a randomized double-blind study in 118 clients receiving hemodialysis and had hemoglobin levels below 9 gm/dl, including a placebo group. Clients treated with EPO exhibited significant improvements in physical and fatigue dimensions of the kidney disease specific questionnaire ($p < .002$) and in a 6-minute walk test ($p = .002$). Another study cited by Nissenson (1989) indicated that partial correction of the anemia of ESRD significantly increased oxygen uptake at the anaerobic threshold ($p < .01$) and peak peripheral oxygen uptake

($p < .002$). Treatment with EPO revealed an increase in hemoglobin from 5.9 ± 0.61 g/dl to 10.9 ± 0.59 g/dl ($p < .001$) and improvement of exercise tolerance from partial correction of the anemia.

The studies cited by Nissenson (1989) indicated a relationship between exercise tolerance and treatment with EPO. However, although there was an increase in exercise tolerance in clients, the level did not return to normal. This indicated that retained uremic toxins may play a role, as well as a lack of conditioning in many ESRD clients.

The current study contrasts to the cited studies in several major areas. The cited studies were clinical trials utilizing controlled experimental populations. The researchers administered EPO therapy and evaluated its effect and efficacy on the anemia associated with ESRD by monitoring hematologic values, as well as other laboratory values. These studies also evaluated cognitive and exercise tolerance following EPO therapy. In the current study, the researcher made no attempt to control the variables. The effectiveness of EPO on the anemia associated with ESRD as indicated by an increased hematocrit and an independence from blood transfusions was reported from data collected.

Similarities to the researcher's study included the use of hemodialysis and CAPD clients as sample populations, including clients receiving intravenous or subcutaneous administrations of EPO. The studies were also similar in

reporting the effect of EPO on hematocrit levels and blood transfusion requirements. All the studies were concerned with the long-term effects of EPO therapy on potential rehabilitation.

If EPO therapy is initiated early, clients with ESRD may remain more actively involved in home, community, and vocational activities for a longer period of time. All of the reported improvements in exercise tolerance, sexual potency, cognitive function, and quality of life should have a major impact on the general well-being of the clients.

By remaining more actively involved in activities of daily living, it may be possible that fewer clients would assume the debilitating passivity of the "sick role." The locus of control could be shifted from the individual to other family members or the community, and there would be less possibility of the individual experiencing decline in feelings of self-worth, competency, and autonomy.

Chapter III

The Method

Research Design

A descriptive, retrospective investigation was chosen for this study in order to describe the characteristics of the effectiveness of recombinant human erythropoietin therapy on the anemia associated with ESRD as indicated by an increased hematocrit and an independence from blood transfusions except for the replacement of blood loss. The descriptive, retrospective study design was applicable to the current research, because the investigator engaging in a descriptive, retrospective study makes no attempt to control the variables, but summarizes the status of phenomena of interest as they exist, and reports the findings as they have occurred from some cause in the past (Polit & Hungler, 1991).

Variables

Variables of interest. Variables of interest in this study were the changes in hematocrit levels, blood transfusion requirements, the effect of EPO on the blood pressure and other laboratory values, side effects from EPO, other forms of therapy (i.e., iron or androgen), factors

affecting efficacy (e.g., inflammation, aluminum toxicity, and surgery), and EPO dose.

Setting, Population, and Sample

The setting for this study was an ambulatory dialysis unit in North Mississippi. The unit has a total of 242 clients. Services provided include in-center hemodialysis and home training for hemodialysis or peritoneal dialysis. There are 196 in-center hemodialysis clients, 7 home hemodialysis clients, and 39 clients who receive continuous ambulatory peritoneal dialysis (CAPD). From the total population, 204 receive EPO therapy. The sample consisted of the clients who were receiving EPO therapy and consented to participate in the study (N = 100).

Instrumentation

The instrument for data collection was designed by the researcher. The instrument included the following demographic data: age, ethnicity, and sex. Other data consisted of the underlying renal disease, EPO dose, laboratory values (ferritin, hematocrit, reticulocyte, and other values that may have been affected by the EPO therapy). The instrument also included side effects and other forms of therapy. To protect anonymity and confidentiality of the client, no names were used on the instrument (see Appendix A).

Data Collection Procedure

Following approval of the Committee on Use of Human Subjects in Experimentation of Mississippi University for Women (see Appendix B), permission to conduct this study was obtained by written consent from the medical director and the administrator of the dialysis center (see Appendix C). Client permission for use of medical records was obtained by written consent. The consent explained the purpose and procedure for data collection, as well as the ability of the client to withdraw from the study at anytime up to data analysis (see Appendix D).

Data Analysis

For the purpose of this study, descriptive statistics including use of means, frequency, and percentages were utilized. A paired *t* test was utilized to analyze the statistical significance between the pretherapy and posttherapy data collected with the alpha level set at the .05 level of significance. The paired *t* test was appropriate for this study because two measures can be obtained from the same client to determine the average difference in values before and after a treatment (Polit & Hungler, 1991).

Limitations

The following limitations were identified:

1. Collection of data was hindered because laboratory tests identified to determine efficacy of EPO were not performed as part of the clinical protocol.

2. Laboratory tests were not performed at consistent intervals identified by the researcher.

3. Collection of data was hindered due to inconsistent record keeping and availability of records within the clinical setting.

4. Sample size and data collection were affected because of the practice of withholding EPO dosage once the hematocrit reached therapeutic range.

Chapter IV

The Findings

The purpose of this descriptive, retrospective study was to describe the characteristics of the effectiveness of EPO therapy on the anemia associated with ESRD. Increased posttherapy hematocrit levels and an independence from blood transfusions, except for the purpose of blood replacement, were the criteria selected to indicate effectiveness. A paired *t* test was utilized to analyze the statistical significance between the pretherapy and posttherapy hematocrit data. Demographic findings, blood pressures, and blood transfusions were analyzed using descriptive statistics, including means, percentages, and frequencies.

The data collected and analyzed for this study are presented in this chapter. Characteristics of the clients are described first, followed by a description of the statistical analysis related to pretherapy and posttherapy data. Some data were excluded from collection and analysis due to inconsistencies in monitoring and documentation.

Description of the Sample

The sample (*N* = 100) consisted of clients from an ambulatory dialysis unit in North Mississippi. All clients were receiving EPO therapy and some form of dialysis. There

were 55 male clients (32% white, 23% black) and 45 female clients (17% white, 28% black). Thirty percent of the clients were between the ages of 23 and 40 years, 51% were between the ages of 50 and 60 years, and 19% were between the ages of 70 and 88 years. The mean age of the clients was 53.5 years. All clients had received EPO therapy which was administered intravenously and/or subcutaneously. Dosages ranged from 5,000 units to 27,000 units per week.

Analysis of Data

The research question generated was how effective is EPO therapy in the treatment of the anemia in clients with ESRD in Mississippi? A paired t test was utilized to compare pretherapy hematocrit levels to posttherapy levels at 1 month, 3 months, and current intervals. Also, 1-month posttherapy hematocrits levels were compared to the 3-month and current hematocrit levels.

There was a significant increase from hematocrits 1 month after receiving EPO therapy, $t = -4.12$, $p < .05$. Hematocrits after 3 months of EPO therapy also increased, $t = -7.45$, $p < .05$. Significant increases in current hematocrit levels were also analyzed, $t = -8.58$, $p < .05$. The mean baseline hematocrit was 24.56, and the mean current hematocrit level was 29.79. These data are presented in Table 1.

Table 1

Comparison of Hematocrit Levels Using the t Test

	N	M	SD	t
Base	100	24.56	4.49	-4.12*
1 month	100	26.47	4.78	
Base	100	24.56	4.45	-7.45*
3 months	100	28.96	4.43	
Base	100	24.56	4.45	-8.58*
Current	100	29.79	4.18	

*$p < .05$.

There were also significant increases in 3-month hematocrits when compared to the 1-month hematocrits, $t = -5.39$, $p < .05$. Current hematocrits compared to the 1-month hematocrits increased significantly as well, $t = -5.34$, $p < .05$.

There was a total of 59 units of packed red blood cells (PRBC) transfused prior to receiving EPO therapy. Four units were given in preparation for surgery or after surgery, 10 units for gastrointestinal (GI) bleeding, and 45 units in relationship to low hematocrit levels or an unknown cause. Sixty-three units of PRBCs were transfused posttherapy. Twelve units were given in preparation for

surgery or after surgery, 12 units for GI bleeding, and 39 units because of low hematocrits or an unknown cause. Eighty-eight percent of the clients did not receive blood transfusions prior to EPO therapy, and 79% of clients did not receive transfusions posttherapy. These data are presented in Table 2.

Table 2

Distribution of Transfusions Pre-EPO and Post-EPO

	Units transferred prior to EPO	Units transferred after EPO
Total	59	63
Surgical/postsurgical	4	12
GI bleeding	10	12
Low hematocrits/unknown cause	45	39

Therefore, concluding from the statistical analysis of data, EPO was related to a significant increase in posttherapy hematocrit levels. However, no significant decrease or independence from blood transfusions occurred posttherapy.

Additional Information

There was no significant increase on posttherapy blood pressures when compared to pretherapy blood pressures. The mean pretherapy systolic blood pressure was 169.57, and the mean posttherapy systolic blood pressure was 153.63, $t = 21.25$, $p > .05$. The mean diastolic blood pressure pretherapy was 101.33, and the posttherapy mean diastolic pressure was 86.86, $t = 21.19$, $p > .05$. Therefore, EPO therapy did not cause an increase in systolic or diastolic pressures posttherapy.

Chapter V

The Outcomes

The anemia associated with ESRD has been recognized since 1836. The etiology of the anemia has been attributed to many factors, but only in recent years has its pathogenesis emerged (Eschbach et al., 1990). However, the primary cause is thought to be an endocrine deficiency of erythropoietin (Duff, 1989).

Despite advances in understanding the anemia associated with ESRD, naturally occurring erythropoietin cannot be obtained in sufficient quantities for treatment. However, a synthetic clone has been developed through genetic coding (Duff, 1989). In 1989 the erythropoietin clone, recombinant human erythropoietin (r-HuEPO, EPO), was approved for use by the Food and Drug Administration, and EPO has become a mainstay of therapy (Rosenberg, 1992).

Clinical trials studying the efficacy of EPO have been conducted and some are ongoing. However, the purpose of this study was to evaluate the effectiveness of EPO therapy in the treatment of the anemia in clients with ESRD in Mississippi. Orem's Self-Care Model was used to guide this descriptive, retrospective study. The conclusions,

implications, and recommendations which evolved from these findings are presented.

Summary of Significant Findings

The sample consisted of 100 clients from an ambulatory dialysis unit in Northeast Mississippi. The mean age for the group was 53.5 years. There were 55 male clients (32% white, 23% black) and 45 females (17% white, 28% black). EPO dosages ranged from 5,000 units to 27,000 units per week. Analysis of hematocrits for the group was compared. There was a significant increase for hematocrits: 1 month after receiving EPO therapy, $t = -4.12$, $p < .05$; 3 months after EPO, $t = -7.45$, $p < .05$; and current, $t = -8.58$, $p < .05$. Significant increases in hematocrits occurred from 1 month to 3 months after therapy, $t = -5.39$, $p < .05$, and in hematocrits from 1 month to current, $t = -5.35$, $p < .05$.

With respect to blood transfusions, there was no significant decrease in the posttherapy analysis. Eighty-eight percent of the clients did not receive blood transfusions prior to EPO, as compared to 79% after EPO.

Blood pressures did not increase posttherapy. The mean pretherapy systolic blood pressure was 169.57, and the mean posttherapy systolic pressure was 153.63, $t = 21.25$, $p > .05$. The mean diastolic blood pressure pretherapy was 101.33, and the posttherapy mean diastolic pressure was 86.86, $t = 21.19$, $p > .05$.

Discussion of Significant Findings

Statistical significance was shown in hematocrit increases at intervals of 1 month, 3 months, and current time. Systolic and diastolic blood pressures were also shown to have statistical significance. These findings were congruent with the studies by Eschbach et al. (1987) and Watson et al. (1990) which found that therapeutic doses of EPO have a positive effect on hematocrit levels. The study by Watson et al. (1990) also demonstrated stable blood pressures. The researcher postulates that clients receiving therapeutic doses of EPO will experience an increased level of well-being, potential for rehabilitation to activities of daily living, and independence from blood transfusions. The study by Nissenson (1989) supports this postulation.

This study did not show a significant decrease in blood transfusion requirements. However, the researcher concludes that intervening variables, such as insufficient documentation by the dialysis unit relating to the need for transfusions and by the classification of the transfusions by the researcher, may have altered the findings. For instance, if no documentation was available to support the proper classification for a blood transfusion, the transfusion was classified under low hematocrits/unknown cause. During the chart review, physician orders for stool specimens for occult blood were observed. However, no documentation for collection nor laboratory results were

available. This data may have also been affected by factors that may affect erythropoietin effectiveness, such as inflammation, aluminum toxicity, surgical procedures, and iron deficiency. Four clients who received transfusions posttherapy were receiving Desferal, a chelating agent. Seventeen of the 21 clients who received blood transfusions posttherapy were also receiving or had received Dextran or another brand of intravenous iron replacement therapy. Another intervening variable affecting a significant decrease or independence from blood transfusions may be the practice of withholding EPO therapy once the hematocrit has reached therapeutic range. This practice is frequently performed for reimbursement purposes.

Orem's Self-Care Model provides three related theories which are applicable to the client with ESRD. These theories are the Theory of Self-Care, Theory of Self-Care Deficit, and the Theory of Nursing Systems. These theories contain propositions vital to health promotion, such as health maintenance, prevention, care, rehabilitation, and functional living with a disease or disability (Riehl-Sisca, 1989). By functioning within the framework of this theory, the care and intervention for the client with ESRD would be more focused and directed toward an optimal level of rehabilitation.

Conclusions

The following conclusions were derived from the findings of this study. The sample included both male and female clients, as well as both black and white races in near equal proportions. There were significant increases in the hematocrits after receiving EPO therapy, and the blood pressures were not increased. This conclusion is congruent with other research findings (Eschbach et al., 1987; Watson et al., 1990).

The researcher concluded that Orem's Model of Self-care is applicable to the client with ESRD. This model will assist the health provider by directing focused rehabilitative care.

Implications

A number of implications for nursing science were derived from this study. Implications were suggested for nursing theory, education, and practice.

Nursing theory is tested through research. Findings from previous studies did not use Orem's Self-Care Model. The results of this study indicate the need for continued use of Orem's Self-Care Model as a conceptual framework for assessing the effect of EPO therapy on the anemia associated with ESRD. The caregiver should not only provide diligent assessment and intervention, but also formulate functional documentation for assessment, intervention, and problems which is vital for continuity of care.

As the number of clients with ESRD increases due to improved medical technology, it is essential that nurse practitioners employed in all areas of health care be prepared to respond to the educational needs of the client with ESRD. With improved health, these clients will continue vocational and social interaction longer. The results of this research should be communicated to the client with ESRD as a positive result of therapeutic intervention. Also, this research indicates the importance of documentation, compliance, and organization.

Nurses must acknowledge the importance of education relating to the effects of illness and disease on the longevity of the client. Through knowledge, understanding and change occur. With continued, positive education, the nurse can affect the client's health and rehabilitation.

Recommendations

Based on the findings of this study, recommendations are as follows:

Research

1. Conduct a similar study to identify the effectiveness of EPO on the anemia associated with ESRD.

2. Conduct a similar study utilizing clients on dialysis and EPO for the same length of time.

3. Implement a similar study directed at functional improvements, such as exercise tolerance, sexual improvement, and feelings of well-being.

4. Conduct a study using Orem's Self-Care Model as a guide for a proposed intervention for education.

Nursing

1. Develop educational programs for the clients which promote understanding of ESRD and the therapeutic interventions used in management of the disease.

2. Develop medical records which allow for adequate documentation of health status, laboratory results, and treatments.

3. Utilize Orem's Self-Care Model as the conceptual framework for assessment, intervention, rehabilitation, prevention, and health promotion.

4. Become active in health care reform issues which affect the clients and nurses as health providers.

The findings of this study contribute to the existing knowledge related to the efficacy of EPO therapy on the anemia associated with ESRD. This study adds new knowledge relating to the client with ESRD in Mississippi. This study suggests areas for future research which would impact client care and health care delivery which could impact all clinicians.

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APPENDIX A

DUNCAN'S DATA COLLECTION TOOL

DUNCAN'S DATA COLLECTION TOOL

NUMBER	AGE	ETHNICITY	SEX	NUMBER OF BLOOD TRANSFUSIONS BEFORE	AFTER	BASE HEMATOCRIT	ONE MONTH HEMATOCRIT	THREE MONTH HEMATOCRIT	CURRENT HEMATOCRIT	R–HUEPO DOSE
						Date: ____ Level:	Date: ____ Level:	Date: ____ Level:	Date: ____ Level:	
						Date: ____ Level:	Date: ____ Level:	Date: ____ Level:	Date: ____ Level:	
						Date: ____ Level:	Date: ____ Level:	Date: ____ Level:	Date: ____ Level:	
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						Date: ____ Level:	Date: ____ Level:	Date: ____ Level:	Date: ____ Level:	

COMMENTS: ______________________________

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DUNCAN'S DATA COLLECTION TOOL

NUMBER	TYPE OF RENAL DISEASE	OTHER THERAPY IRON	OTHER THERAPY ANDROGEN	OTHER THERAPY OTHER	FACTORS EFFECTING EFFICACY		RETICULOCYTE CT BASE	RETICULOCYTE CT 1 MONTH	RETICULOCYTE CT 3 MONTHS	RETICULOCYTE CT CURRENT	FERRITEN BASE	FERRITEN 1 MONTH	FERRITEN 3 MONTHS	FERRITEN CURRENT	SIDE EFFECTS

COMMENTS: _____

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APPENDIX B

APPROVAL OF MISSISSIPPI UNIVERSITY FOR WOMEN COMMITTEE ON USE OF HUMAN SUBJECTS IN EXPERIMENTATION

MISSISSIPPI UNIVERSITY FOR WOMEN
Columbus, MS 39701

Office of the Vice President for Academic Affairs
Eudora Welty Hall
P.O. Box W-1603
(601) 329-7142

March 17, 1993

Ms. Elizabeth J. DuVall Duncan
c/o Graduate Nursing Program
Campus

Dear Ms. Duncan:

I am pleased to inform you that the members of the Committee on Human Subjects in Experimentation have approved your proposed research.

I wish you much success in your research.

Sincerely,

Thomas C. Richardson
Vice President
for Academic Affairs

TR:wr

cc: Mr. Jim Davidson
Ms. Jeri England
Dr. Nancy Hill
Dr. Rent

APPENDIX C

AGENCY MEMORANDUM OF AGREEMENT

Agency Memorandum of Agreement

I am Elizabeth Duncan, a registered nurse and a graduate student at Mississippi University for Women, Columbus, Mississippi. As part of my studies, I am conducting a descriptive, retrospective study on the effectiveness of EPO therapy in the treatment of the anemia associated with end-stage renal disease. I will be comparing pretherapy laboratory values and blood transfusion requirements to posttherapy laboratory and transfusion requirements.

I am requesting your permission to obtain the laboratory and demographic data needed for this research from your client's medical records. A consent form for release of information will be provided to each client receiving EPO and dialysis for informed consent. Confidentiality and anonymity of the clients will be maintained. No names or identifying information will appear on any document or in the study.

I have read the above statement and understand the purpose of the study. I hereby give my approval for Elizabeth Duncan to review patient records to obtain the necessary data for this study.

_____	_____
Date	Administrator's Signature
_____	_____
Date	Medical Director's Signature

APPENDIX D

INFORMED SUBJECT CONSENT FORM

Informed Subject Consent Form

I am Elizabeth Duncan, a registered nurse and a graduate student at the Mississippi University for Women in Columbus, Mississippi. As part of my studies, I am conducting research on the effectiveness of EPO therapy on the anemia associated with end-stage renal disease. For this study, I will need to obtain the following information from your medical record: age, sex, race, laboratory values, EPO dose, blood transfusion and blood pressure data, other types of therapy, information pertaining to effectiveness and side effects, and type of underlying renal disease. I will be using this information to compare the pretherapy (EPO) data to the posttherapy data, which will indicate how effective EPO has been in the treatment of the anemia associated with end-stage renal disease (ESRD).

Participation in this study is voluntary. All information will be confidential and no names will appear on any form or in the study. You may withdraw from the study at anytime up to data analysis.

This study will provide current research information to the nurses caring for patients with ESRD. This information will benefit the patients through teaching by the nurses.

I understand the information given to me. I understand that I have the right to withdraw from this study up to data analysis and my name will not be used.

_____ _____

Date Client's Signature