Dialyzing severely anemic patients who are objectors to blood transfusion due to conscience: a single-center experience

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Received 03 October 2019
Revised 19 October 2019
Accepted 28 January 2020
Published 30 December 2021

Journal of Current Medical Research and Practice
2021, 6:373–378

Background
Benchmark minimum packed cell volume (PCV) for blood transfusion in most dialysis centers is 20% (hemoglobin 6.7 g/dl). Below that level, the dialysis units in Benin City usually transfuse patients predialysis or intradialysis to make dialysis a safer procedure for the patient. However, some groups of patients like the Jehovah's witnesses refuse blood transfusion on grounds of conscience and have often times been refused dialysis on account of a PCV lower than 20% (hemoglobin 6.7 g/dl). We present our experience with 23 maintenance hemodialysis patients, all Jehovah's witnesses, in their first session in this center.

Patients and methods
A total of 23 patients, PCV range 14–19%, were dialyzed during the period of April 2018 to November 2018. Patients underwent routine dialysis sessions of 4 h. Ultrafiltration range was determined clinically by level of edema, respiratory distress, and blood pressure. Indications for dialysis were pulmonary edema, uremic encephalopathy, and uremic gastritis with markedly deranged urea and creatinine values.

Results
There were a total of 23 patients dialyzing for the first time during the period under review. There were 11 (47.8%) males and 12 (52.2%) females. Their age range was 16–80 years and mean age was 49.43 years. Mean predialysis blood urea was 170.52 mg/dl, with a range of 103–301 mg/dl. Mean postdialysis urea was 81.57 mg/dl, with a range of 13–167 mg/dl. Predialysis creatinine range was 2.43–28.4 mg/dl, with a mean of 11.46 mg/dl. Postdialysis creatinine range was 0.4–17.4 mg/dl, with a mean of 5.69 mg/dl. Mean urea reduction ratio was 54.67%, with a range of 22.4–91.4%. All the patients tolerated the dialysis sessions well. There were no intradialysis mortality.

Conclusions
Dialyzing patients with anemia who refuse to accept a blood transfusion on account of personal or religious beliefs appears to be generally safe and effective. There is a need to extend dialysis care to these group of our patients, most of whom are Jehovah's witnesses.

Keywords:
anemia, dialysis, Jehovah's witnesses, transfusion

J Curr Med Res Pract 6:373–378

2357-0121

Introduction

Anemia is an almost universal finding in end-stage kidney disease. At this stage of kidney disease, the patient would require renal replacement therapy, which could include hemodialysis, peritoneal dialysis, or a kidney transplant [1].

In Nigeria, the most common form of renal replacement therapy is hemodialysis. Although still in its infancy, it is increasingly being used in many centers across the country [2].

To improve health care outcomes in kidney disease patients, hemoglobin (Hb) values are usually maintained in such a way as to reach target values of 10 g/dl, a figure that in itself anemic.

The improvement of Hb values in patients with kidney disease has generally been made possible with the use of erythropoiesis-stimulating agents [3], and in those who need dialysis and the Hb values are critically low, blood transfusion has been used as a means to raise the Hb levels [4].

There is considerable uncertainty regarding the Hb threshold for the use of red blood cell (RBC) transfusion in anemic patients. For decades, the decision to transfuse RBCs was based on the 10/30 rule, that is, RBCs may be transfused to maintain a Hb of 10 g/dl or a packed cell volume (PCV) of 30%. However, the issue of costs and the need to reduce the adverse effects of blood transfusions caused a

reexamination of transfusion practices in the 1980s and 1990s [5–7].

In a tertiary health center in south-south Nigeria, the minimum acceptable level of hematocrit for patients to dialyses is 20% (Hb 6.7 g/dl). Below this level, patients are transfused predialysis or intradialysis. However, there are a group of patients who refuse blood transfusion on account of conscience and religious beliefs. They are of the Jehovah's witnesses sect [8]. It is well known that one tenet of the Jehovah's witnesses faith is to refuse blood transfusion even at the risk of organ damage or death [7]. However, patients who belong to this religious group are increasingly presenting with end-stage kidney disease requiring dialysis and a number of them with a PCV of less than 20% and therefore are refused dialysis in some centers because they refuse blood transfusion in all circumstances.

The prevalence of end-stage kidney disease in Jehovah's witnesses patients has not been exactly determined. The literature is mainly on case reports and involving less than 20 patients.

The claim of the Jehovah's witnesses is that as students of the bible and as imitators of the first century Christians, they believe that the biblical injunction to abstain from blood applies to transfused blood and its major components [8,9].

Many physicians sometimes wrongly assume that refusal to a blood transfusion by a patient always leads to loss of lives. However, certain studies have shown that blood is usually sometimes administered by physicians with the nearly unchallenged view that failure to transfuse would have dire consequences. However, evidence to support that view is very difficult to obtain [10].

The right to refuse transfusion has been questioned in the past. However, it is known that a patient has the right to accept or to refuse different therapies. According to predominant doctrine, giving a transfusion against the wishes of a patient is an illegitimate act, and no one is obliged to receive transfusion treatment [11,12].

Although different groups argue the validity of the Jehovah's witnesses claim that blood transfusion is equivalent to blood consumption, attention has been drawn to a Times Law Report titled 'consumption through injection.' It discusses a case of driving with an excess of alcohol in his body. The alcohol had been consumed when a doctor injected the defendant with Kenalog containing 1.5% benzyl alcohol. The law report defined that as consumption [13].

In a study done at the John Hopkins Medical Center, it was observed that retrospective risk-adjusted clinical outcomes in the bloodless program was similar or better than those who accepted autologous blood transfusion for both their medical and surgical patients. Most clinical guidelines recommend restrictive RBC transfusion guidelines with the goal of minimizing exposure to allogeneic blood. The current evidence support the use of restrictive transfusion triggers in patients who are free of serious cardiac disease and suggest that critically ill patients tolerate anemia well [14–16].

In another study done at the Department of Anesthesia, Cardiovascular Research Institute, University of California, San Francisco, it was found that acute isovolemic reduction in Hb levels to a value of 5 g/dl (PCV 15%) in conscious healthy humans did not produce any evidence of inadequate systemic critical oxygen delivery (TO_2) as assessed by a lack of change in oxygen consumption (VO_2).

This tends to show that healthy patients would tolerate anemia relatively well, even acute anemia [7].

It is well known that one tenet of the Jehovah's witnesses faith is to refuse blood transfusions even at the risk of organ injury or death [17].

There have been examples of Jehovah's witnesses patients refusing blood transfusion after being told that refusal of a blood transfusion may lead to loss of life. A reported case described a witness refusing blood transfusion, preferring death rather than a blood transfusion even if it was to save her life [18].

Physicians come into contact with Jehovah's witnesses and their refusal to accept blood transfusions even when it is needed to save their lives. We must, in our conversations, respect their requests as individuals.

Issues concerning whether they can have hemodialysis have been raised among them. The consensus, however, was that because the blood flow was continuous and is practically an extension of their circulatory system, it was acceptable. However, most do not permit priming of the haemolysis machine with stored blood [insert] so priming is done with saline, and all the blood in the dialyzer can be returned with saline [19].

Patients and methods

Patients who refuse dialysis on account of declining a blood transfusion appear to be on the increase. These patients were referred to a private center, from various hospitals in Benin City, on account of their

being unable to dialyze at other centers because of a PCV less than 20% and their refusal to accept a blood transfusion prior to hemodialysis, where they were dialyzed without transfusion. We retrospectively analyzed a total of 23 patients, having PCVs between 14 and 19%.

An explanation of the risks involved was done in detail to the patient and at least two relatives.

Patients were clinically evaluated.

PCV and Hb were done. Samples were also taken for retroviral screening, hepatitis B surface antigen, hepatitis C antibody, and predialysis electrolytes, urea, and creatinine.

Machine type was the Nikkisso DBB05/06 with automatic noninvasive blood pressure (systolic and diastolic) monitoring. Pulse, systolic and diastolic blood pressure, and mean arterial pressure (MAP) were monitored every 5 min.

Supplemental oxygen was made available in case patient needed oxygen supplementation based on oxygen saturation SpO_2 using a fingertip pulse oximeter less than 90%.

Patients and relative (s) were made to sign a waiver form for the dialysis unit/doctors/nurses after listening to a detailed explanation of why it was desirable to perform a blood transfusion. They were explicitly told that the decision had to be of their own free will, and the waiver was hand written by the patient/relatives. Patients with encephalopathy were not allowed to sign waivers on their own, as full understanding may not be deemed to be present.

Dialysis was started slowly in all patients at 100 ml/min flow rate, gradually increasing to 300 ml/min with pulse, blood pressure, and MAP measured every 5–10 min.

For those with anemic heart failure, ultrafiltration alone was initially started for the first 30 min in the 2 h initial session or 1 h in the 4 h sessions before changing to hemodialysis with ultrafiltration for the rest of the duration of dialysis.

Pulse and MAP were measured every 10 min using the automated measurement system in the Nikkisso DBB05/06 machine. Ultrafiltration and blood flow rates were adjusted according to these parameters and patients clinical conditions.

Blood sugar monitoring was done hourly with a portable glucose meter, and 50% dextrose in water was given when blood sugar levels dropped in any of the patients to less than or equal to 70 mg/dl in aliquots of 20 ml into the venous line beyond the dialyzer, and repeat RBS done with a glucometer (accucheck Roche) to assess patient's response.

Supplemental oxygen was made available via oxygen concentrator should SpO_2 drop to or below 90% in room air.

Erythropoietin (4000in) Recomon was given subcutaneously to each of the patients and iron sucrose 200 mg in 150 ml of normal saline slowly over 20–30 min.

A medical officer was in the dialysis room with the patient throughout the duration of dialysis to respond immediately to patient's needs.

Predialysis and postdialysis electrolytes, urea, and creatinine measurements were done for all the patients to assess effectiveness of dialysis, and urea reduction ratio (URR) was calculated as a means of evaluating dialysis adequacy.

Results

There were a total of 23 patients dialyzing for the first time during the period under review. There were 11 (47.8%) males and 12 (52.2%) females.

Indications for dialysis were pulmonary edema (16), uremic gastritis (three), and uremic encephalopathy (four).

Their age range was 16–80 years, with a mean age of 49.43 years.

Mean predialysis blood urea was 170.52 mg/dl, with a range from 103 to 301 mg/dl.

Mean postdialysis urea was 81.57 mg/dl, with a range from 13 to 167 mg/dl.

Predialysis creatinine range was 2.43–28.4 mg/dl, with a mean of 11.46 mg/dl.

Postdialysis creatinine range was 0.4–17.4 mg/dl, with a mean of 5.69 mg/dl.

Mean URR was 54.67%, with a range from 22.4 from to 91.4%.

All the patients tolerated the dialysis sessions well. Patients were significantly clinically better after dialysis. There was no intradialysis mortality.

Indications for dialysis included pulmonary edema, uremic encephalopathy, and uremic gastritis (Tables 1 and 2, Figs. 1–3).

Discussion

Anemia is a common finding in kidney disease. It begins early in chronic kidney disease and is almost universal by the time the chronic kidney disease reaches end-stage kidney disease.

All the patients in the study were severely anemic, with PCV of 14–19%.

Dialysis units traditionally are bothered about dialyzing patients with anemia, and doctors have had to transfuse patients with severe anemia.

The benchmark set for transfusion in anemic patients requiring dialysis is not absolute but renal units have sometimes set their own values. One of the tertiary hospitals in south-south Nigeria set the benchmark at PCV of 20% (Hb 6.7 g/dl) and patient with a blood level less than that are often times required to transfuse predialysis or intradialysis.

Unfortunately Jehovah's witnesses refuse transfusions of blood and blood products even in life-threatening anemia and even when they are in cardiac decompensation. They claim that it is in keeping with their religious beliefs that forbid them from taking blood and blood products.

The issue of blood transfusion has been an ethical issue with health providers and is sometimes a source of frustration for doctors. Some health care providers believe that respect for the nontransfusion demands of the Jehovah's witnesses would be unethical [8,9,18].

There was relatively good urea clearance with dialysis in these patients. Mean URR was 54% (range, 29.7–91.4%). This is significant but not up to the recommended value of 65% (Tables 1). Reasons responsible for this may include the following: first, dialysis was started cautiously in these patients and increasing the blood flow rate was slower than the regimen used for non-anemic patients. Another reason

Table 1 Packed cell volume, urea, creatinine, urea reduction ratio, and indications for dialysis for all participants

PCV	PreUR (mg/dl)	PostUR (mg/dl)	PreCR (mg/dl)	PostCR (mg/dl)	URR	IND. HD.
15	103.9	13.2	2.43	1.47	87.3	Pulmonary edema
18	213	101	21.9	13.4	78.2	Pulmonary edema
18	296	167	28.1	17.4	43.6	Encephalopathy
18	122	68	5.4	3	44.3	Pulmonary edema
19	259	144	10	6.2	44.4	Encephalopathy
15	169	112	10.1	6.7	33.7	Pulmonary edema
16	141	22	6.7	0.7	84.4	Pulmonary edema
18	116	35	13.7	5.5	69.8	Pulmonary edema
16	155	109	28.4	9.8	29.7	Pulmonary edema
15	120	39	8.6	3.1	67.5	Pulmonary edema
14	144	87	4.3	1.8	39.6	Gastritis
18	116	90	9.4	6.3	22.4	Gastritis
16	198	101	11.7	4.1	49	Pulmonary edema
14	157	66	12.8	5.8	58	Pulmonary edema
19	113	48	9	3.6	57.5	Pulmonary edema
18	282	147	11.7	6.4	49.9	Encephalopathy
15	301	152	19.4	9.6	49.5	Encephalopathy
14	146	89	11.4	6.2	39	Pulmonary edema
17	167.4	108.6	13.2	9.9	35.3	Pulmonary edema
18	150.6	67.2	9.4	5.3	55.3	Encephalopathy
16	186	16	2.5	0.4	91.4	Pulmonary edema
18	161	52	8.7	2.2	67.7	Pulmonary edema
18	105	42	4.7	2.1	60	Pulmonary edema

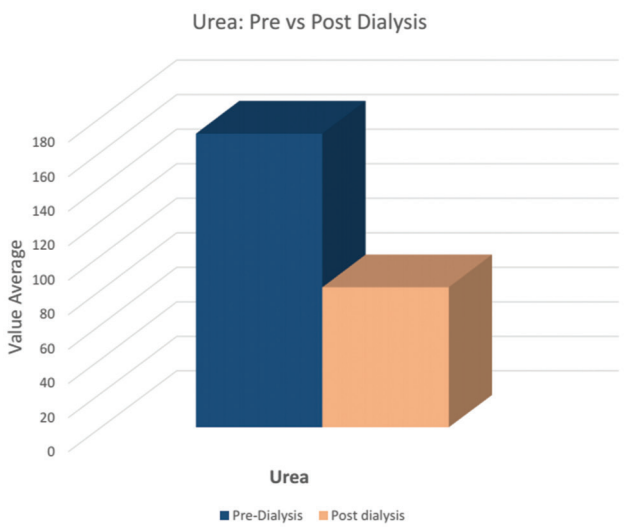
IND. HD., indications for dialysis; PCV, packed cell volume; PostCR, postdialysis creatinine; PostUR, postdialysis urea; PredCR, predialysis creatinine; PredUR, predialysis urea; URR, urea reduction ratio.

Table 2 Packed cell volume, urea, creatinine, urea reduction ratio, and indications for dialysis by gender

Sex	Number	Age	PCV	PredUR	PostUR	PredCR	PostCR	URR
Male	11	58.36±12.93	16.5±1.69	159.55±54.02	78.89±36.39	13.12±6.00	5.93±2.75	-
Female	12	41.25±15.22	16.75±1.71	180.58±67.48	84.02±53.14	9.94±7.86	5.48±5.26	-
Total	23	49.43±16.38	16.65±1.67	170.52±60.98	81.57±44.95	11.46±7.07	5.69±4.16	54%

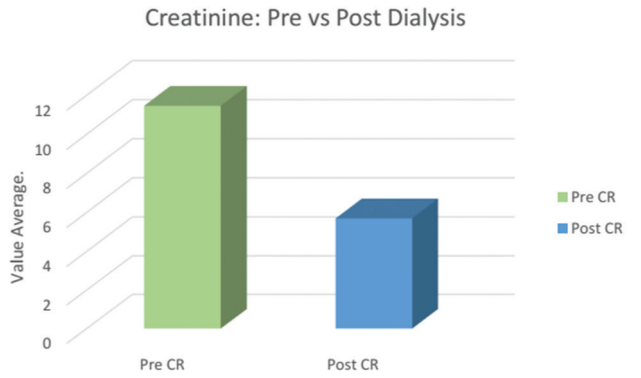
PCV, packed cell volume; URR, urea reduction ratio.

Figure 1



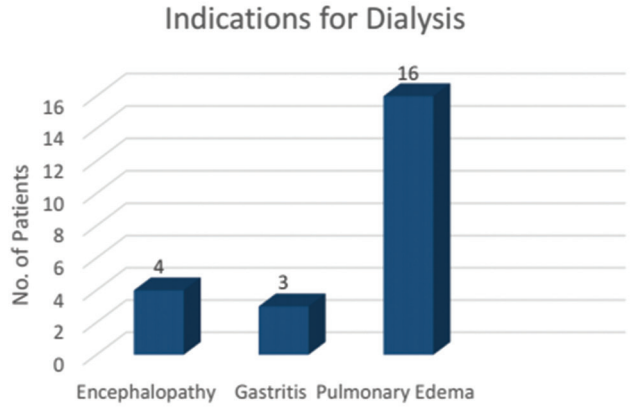
Pre-dialysis Urea vs Post dialysis urea for all subjects

Figure 2



Pre-dialysis Creatinine vs Post dialysis Creatinine for all subjects

Figure 3



Indications for Dialysis

may have been that most patients evaluated were in severe pulmonary edema and the initial focus was to commence the patients on isolated ultrafiltration to maximize fluid removal before commencing the patient on dialysis with ultrafiltration. Although this enabled greater amounts of fluid removal from the patients while minimizing cardiovascular disturbances, it may also have reduced the level of urea removal from dialysis.

The outcome of the dialysis was remarkably good in all the patients. There was no intradialysis mortality in all the patients. Morbidity improved in all the patients, and all the patients were stable clinically in both the immediate and 24-h postdialysis period.

Six patients needed supplemental oxygen during dialysis. All six had presented in severe pulmonary edema. However, as ultrafiltration progressed, the supplemental oxygen given at a flow rate of 4–6 l/min was discontinued, as oxygen saturation of over 95% at room air was achieved without supplemental oxygen. This usually occurred after 2–2.5 l of ultrafiltration.

It is important that medical doctors view the refusal of Jehovah's witnesses patients to accept a blood transfusion as a medical challenge rather than being a point of contention. This will enable physicians to work toward responding to those challenges in other ways to provide care for this group of patients while at the same time respecting their personal and religious rights and saving lives at the same time.

Conclusion

Dialyzing anemic patients with ESRD who object to transfusion is possible and remarkably safe at least in the PCV range of 14–19%, if care and adequate precautions are taken, such as SpO_2 monitoring and availability of supplementary oxygen and resuscitation equipment.

Patients will die anyway of uremic complications if not dialyzed at all. This is especially true in patients who present with pulmonary edema, in which ultrafiltration is required on an emergent basis. Dialysis in these groups of patients is lifesaving and life prolonging, and removing them out of the uremic milieu, in our patients, enables the majority to respond to erythropoietin and iron sucrose therapy, which would lead to marked improvements in their Hb profiles.

It is suggested that dialyzing this group of patients is viable and practicable as well as relatively safe, provided adequate precautions are taken, including those outlined here such as adequate monitoring of patient, emphasis being on noninvasive blood pressure monitoring, oxygen saturation, blood sugar, and provision of emergency intervention medications that includes supplemental oxygen, 50% dextrose water

and normal saline infusions, blood volume expanders, antiarrhythmic medications, and all the basic things needed for resuscitation.

It is also advised that a meeting should be held with the patients and relatives explaining in detail the possible risks associated with refusing a blood transfusion in the circumstances the patient is in.

A signed waiver should be obtained from the patient and relatives clearly stating that they have been offered blood transfusion, that the possible consequences of not accepting a blood transfusion has been explained to them, and they have refused the blood transfusion after adequate information has been provided to them. It should also include a waiver that protects the health institution from any legal consequences of not transfusing the patient with blood. In all cases, Jehovah's witnesses and their relatives willingly and readily signed all the necessary waivers.

In addition, recombinant human erythropoietin should be commenced. It was commenced in all the patients in this group. Iron sucrose was also started at the same time. This may not change the immediate prognosis but will be expected to improve erythropoiesis in the longer term.

We recommend that all centers should dialyze patients who object to blood transfusion on grounds of conscience with precautions taken to avoid loss of life in this category of patients, as this report has shown that dialyzing this group of patients appear to be a viable and safe procedure, at least in the group with PCVs in the range of 14–19%.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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