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Investigation of hemolytic anemia caused by chloramines exposure in dialysis water

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ABSTRACT

This study investigated the relation between hemolytic anemia and the water disinfection schedule of hospitals. Ten dialysis centres in Riyadh, Saudi Arabia, were selected, with a total of 1000 patients undergoing extended hemodialysis/hemodiafiltration (HD/HF). Hemoglobin (Hb) concentration analyses were performed during one year period in 2015. Hb concentrations were compared on days when the water supply was disinfected using chloramines, with data measured on disinfection-free days. Of those patients 650 were males and 350 were females. Their mean ages were 46.74 ± 13.50 years. The results revealed a maximum Hb level of 15.98 g/dL during HD/HF on the disinfection-free days. The Hb level decreased to 9.32 g/dL with maximum value of 11.57 g/dL on the days of water disinfection ($p < 0.001$ compared to disinfection-free days). This study revealed the need for developing effective, less hazardous, less expensive and more suitable alternatives to sterilize dialysis water to ensure the quality of health services provided.

Keywords: dialysis water, hemolytic anemia, chloramines, hemoglobin

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INTRODUCTION

In Middle Eastern countries like Saudi Arabia, data concerning dialysis treatment are lacking. A schematic diagram of water treatment system for hemodialysis (HD) is shown in Figure 1. Drinking water is unsuitable for use in dialysis units. Reverse osmosis (RO) is an additional treatment to minimize contaminant levels and be compatible with specified in national or international standards dealing with water for use in dialysis.[1] Disinfection is vital for dialysis water. Chloramines are oxidant compounds made up of chlorine and ammonia and are used as bactericidal agents throughout the world. The use of chloramines as a disinfectant for dialysis water may result in some undesirable side effects. Oxidation of the Fe^{2+} in hemoglobin (Hb) to Fe^{3+} forms methemoglobin, which is incapable of carrying either O_2 or CO_2. Chloramines can form not only methemoglobin, but can also produce denaturation of proteins within the red cell, thus forming aggregates (Heinz bodies), both by their direct oxidizing capacity and their ability to inhibit red cell reductive (hexose monophosphate shunt activity) metabolism, a mechanism that reduces nicotinamide adenine dinucleotide phosphate (NADPH), which protects the red cells against oxidative damage and thus chloramines make the red cell even more susceptible to oxidant damage. Therefore, acute hemolytic anemia is sometimes observed in uremic patients undergoing HD.[2-4]

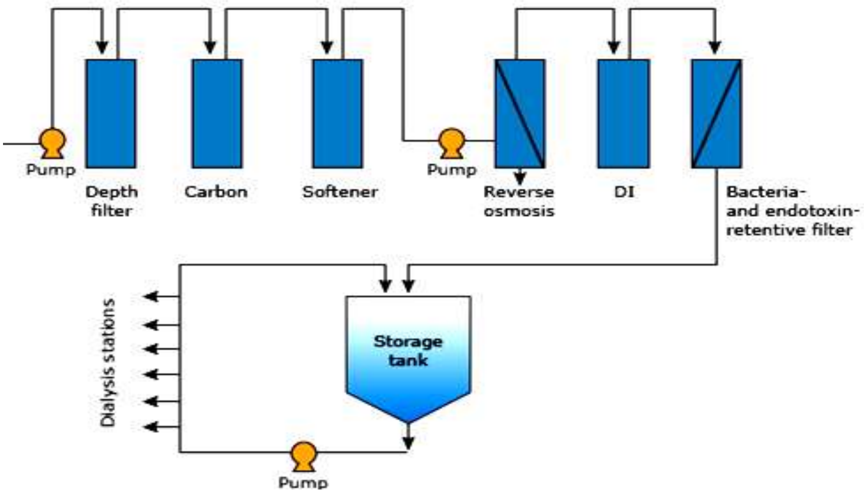

Figure 1: Schematic diagram of water treatment system for hemodialysis; Source: Klein (1986) [3]

During the past years, the Kingdom of Saudi Arabia (KSA) faced many challenges due to the scarcity of water resources and to deterioration of their quality, which led to the increased prevalence of several diseases caused by contaminated water, such as kidney failure. Prevalence of patients on dialysis per million populations in Saudi Arabia reached to be 475 during 2009. Therefore, KSA gave priority to meet the challenges of limited water resources and to improve the quality of water in addition to the protection of sensitive groups and upon risk prevention to prevent kidney failure.[5]

The safety of the use of dialyzed water is a basic responsibility for public health authorities for the prevention of complications caused to patients. The Saudi government is making extensive efforts and follow-up to create new dialysis units. It has also placed a priority on the development of HD units to improve the quality of dialyzed water to ensure the quality of health service provided. Therefore, the quality of water in HD units must follow the health and environmental specifications for the establishment, maintenance and sterilization of these units to ensure patients' safety [6]. The aim of this study is to examine the impact of exposure HD patients to chloramines due to disinfection of dialysis water.

MATERIALS AND METHOD

In 2015, data were collected weekly for 12 months from 1000 patients who frequented the ten selected dialysis units, three times a week, Riyadh, Saudi Arabia, on a regular basis.

The concentration of chloramine were determined in 120 dialysis water samples collected monthly from the selected ten dialysis units during the same time period using the analytical standard methods.[7] Determination of the total and free (available) chlorine was performed using colorimetric method (commercial kits). The differences between the total and free (available) chlorine is due to bound chlorine corresponds, which are almost completely chloramines.[7] Also, the concentration of chloramine of the water samples was compared with the chloramine limits specified by the Saudi Ministry of Health (2013) and American Association of Medical Instrumentation (2004) to assess their conformance to the standards for dialysis water quality to ensure the safety of dialysis water to prevent anemia, which is caused by exposure to chloramines.[8,9]

Moreover, Hb concentrations of patients were compared before and after the use of chloramine in the disinfection of dialysis water. The Hb concentrations were determined by CO-oximetry (ABL 825 flex, Radiometer Medical ApS, Brønshøj, Denmark).[10]

Differences between data, obtained on days when the water supply was disinfected and on disinfection-free days, were compared using the chi-square test. A p-value ≤ 0.05 considered to be statistically significant.

RESULTS AND DISCUSSION

Demographic, laboratory and clinical data were recorded in Table 1. It is evident from this table that a total of 1000 HD patients (65% males and 35% females) were included in this study with mean age of 46.74 ±13.50 years; range 35-74 years. Their mean duration on HD was 70 ± 1.54 months. The majority (95%) of cases had thrice-weekly sessions. All patients received 4–6 h per day of HD using volumetric machines and high-flux polysulphone membrane. Two-third (65%) of HD patients had predialysis blood pressure of ≤130/80 mmHg. The mean predialysis systolic blood pressure was 143 ±21.09 mmHg and the mean predialysis diastolic blood pressure was 90.35 ± 19.65 mmHg.

Table 1: Demographic and clinical data of the studied hemodialysis patients

Parameters	$\bar{x} \pm$ SD
Gender	
Male No. (%)	650 (65%)
Female No. (%)	350 (35%)
Age (Years)	46.74 ± 13.50 (35−74)
Predialysis systolic blood pressure (mmHg)	143 ±21.09
Predialysis diastolic blood pressure (mmHg)	90.35± 19.65
Nephrologists to patients ratio	1:39
Nurse to patient ratio	1:4
Dialysis session/nurse/month	48 session (4–6 h)

Table 2 shows that the mean Hb level was 12.38 ± 1.32 g/dL with a range from 11.20 to 15.98 g/dL on the disinfection-free days. The mean Hb level decreased to be 10.21 ± 2.56 g/dL with a range of 9.32-11.57 g/dL on the days of water disinfection ($p < 0.001$ compared to disinfection-free days). More than half (80%) of HD patients had Hb level of ≤11 g/dL while the rest of cases (20%) had a Hb level ≥12 g/dL as shown in Figure 2.

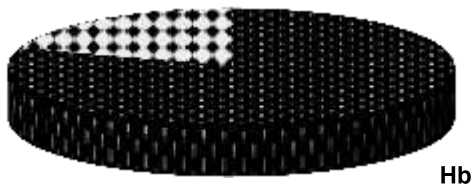

Figure 2: Percentage of hemoglobin levels in the studied hemodialysis patients

Table 2: Hemoglobin concentrations in patients during sessions of extended hemodialysis/hemodiafiltration

Parameters	Extended hemodialysis/ hemodiafiltration on days with water disinfection	Extended hemodialysis/ hemodiafiltration on disinfection-free days	χ^2 (*p*-value)
	$\bar{x} \pm$ SD	$\bar{x} \pm$ SD	
Number of sessions	60	144	
Hemoglobin concentrations (g/day)	10.21±2.56 (9.32-11.57)	12.38±1.32 (11.20-15.98)	10.119 (0.000***)

***$p \leq 0.001$

Chemical analysis of dialysis water revealed that it is incompliant with Saudi MOH and AAMI guidelines (≤ 0.1 mg/l) as presented in Table 3. All the study HD centers used RO to treat the water used in dialysis. In the present study, total chlorine concentration was extending from 0.53 to 0.87 mg/l. In addition, a percentage of chloramines ranged from 15% on the disinfection-free days to 70% on the days of water disinfection (Table 3). A significant correlation was observed between Hb concentrations in HD patients and chloramines concentrations in dialysis water (Figure 3).

Correlation Coefficient	-0.976*
Sig.(2-tailed)	0.000
*Correlation is significant at the 0.05 level	

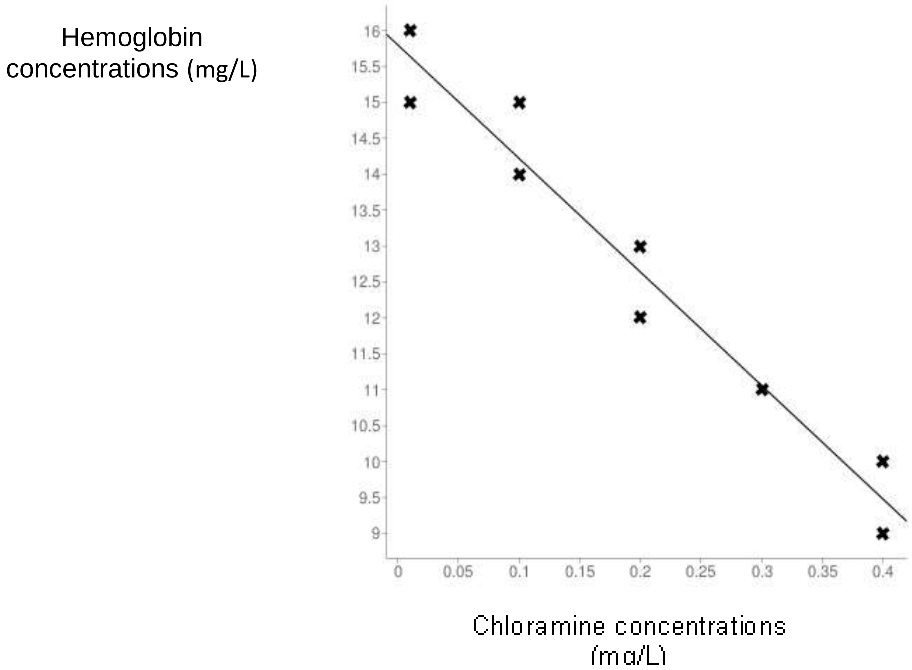

Figure 3: Correlations between hemoglobin levels in hemodialysis patients and chloramines concentrations in dialysis water

Table 3: Chloramines concentrations in hospitals' water during sessions of extended hemodialysis/hemodiafiltration

Parameters	**Extended hemodialysis/ hemodiafiltration on days with water disinfection**	**Extended hemodialysis/ hemodiafiltration on disinfection-free days**	**Saudi Ministry of Health Standards (2013) (mg/l)**	**American Association of Medical Instrumentation (2004) (mg/l)**
	$\bar{x} \pm$ **SD**	$\bar{x} \pm$ **SD**		
Number of sessions	60	144		
Total chlorine concentrations (mg/l)	0.87±0.045	0.53±0.001	0.5	0.5
Chloramines concentrations (mg/l) and (%)	0.29 (70%)	0.10 (15%)	0.1	0.1

DISCUSSION

The blood pressure results is consistent with results obtained by Al Saran et al. (2011) who found that blood pressure were adequately controlled in 91.8% of HD patients. Moreover, cardioprotective medications such as angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and *β*-blockers were given to almost HD patients in Prince Salman Center for Kidney Diseases, Riyadh, KSA.[11]

The results of Hb concentrations contradicts the results obtained by Al Saran et al. (2011), indicating that intravenous iron and erythropoietin therapy were provided by the administration on regular and frequent bases and management of anemia to the target of 11–12 g/dL was achievable in 79.45% of prevalent dialysis cases.[11] Our results are also in contrast with the findings reported by Locatelli et al. (2004) in the Dialysis Outcomes and Practice Patterns Study. The highest mean Hb levels (12 g/dL) found to be in Sweden; Hb ≥11 and Hb <12 g/dL in the United States, Spain, Belgium, Canada, Australia/New Zealand, Germany, Italy, the United Kingdom, and France; and Hb = 10.1 g/dL in Japan.[12] However, similar results were obtained by Bek et al. (2009); the mean Hb concentrations of patients during extended HD/HF were slightly, but statistically significantly, lower on days with water disinfection.[10] Botella et al. (1977) found that increase of the total chlorine to 3.5 ppm resulted in a serious decline of the mean haematocrit to 20.80 +/- 5.22 SD (*p* less than 0.0001).[13] In addition, Yoon et al. (2014) revealed that acute hemolysis associated with HD is a rare complication; however, if it's not recognized early and managed adequately, it can be associated with life-threatening complications such as hyperkalemia and even myocardial infarction.[14]

Chemical analysis of dialysis water of the present study is consistent with those reported by Vorbeck-Meister et al. (1999).[15] In contrast, a study carried out by Botella et al. (1977) found that total chlorine concentration and percentage of chloramines varies from 0.5 to 1.1 ppm and from 40 to 95%, respectively.[13] Suhail (2005) reported that laboratory evidence of hemolysis, Heinz body anemia, is suggestive and the presence of chloramines in water or dialysate is confirmatory.[16] In Australia (1982), there was an outbreak of Heinz-body-positive haemolytic anaemia among patients who were undergoing dialysis in Sydney Hospital. This appeared to be due to excessive chloramines in and inadequate carbon filtration of, the water used for haemodialysis.[17] Epidemiologic investigation demonstrated that the mortality rate among dialysis center patients increased during the 5 months after chloramine exposure when compared with the 12 months before chloramine exposure.[18] Pérez-García and Rodríguez-Benítez (1999) showed that chloramine concentrations above 0.2–0.25 mg/l in the dialysis water may cause real `epidemics' of anaemia in dialysis units.[4] An anemia outbreak was identified in HD unit. The dialysate chloramine levels had risen from < 0.1 mg/mL to 0.27

mg/mL during 4 months while other parameters of water quality were within accepted standards.[19]

A negative correlation of Hb levels with chloramines concentrations may indicate a common source of pollution during dialysis water disinfection. Neilan et al. (1978) found that ascorbic acid addition effectively neutralize chloramines in vitro and in patients dialyzed with the single batch dialysis delivery system.[20] Rigorous control of water quality in HD services is extremely important in order to guarantee a better quality of life of the patients submitted to this treatment.[21]

CONCLUSION

In conclusion, association between hemoglobin levels in hemodiaysis patients and disinfection of dialysis water using chloramines was found. Decline in patients' hemoglobin level during exposure to chloramine- disinfection was detected. These results suggest the need for developing effective, less hazardous, less expensive and more suitable alternatives to sterilize dialysis water to ensure the quality of health services provided.

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