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Original Research Article

Hypoxemia in patients undergoing first hemodialysis procedure with respect to different clinical and biochemical parameters

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Abstract
Introduction: During hemodialysis, PaO_2 falls about 10-20 mmHg. In seriously ill patients with pre-dialysis hypoxemia, the drop in PaO_2 can be catastrophic. Hypoxemia and fall in PaO_2 do occur during hemodialysis and hence we looked to ascertain the clinical, physiological and biochemical parameters which predisposes such events. Secondly, does it develop post hemodialysis and finally its outcome in patients with hypoxemia?
Methods: A hospital based study was conducted on 120 patients undergoing hemodialysis for first time to know the incidence of hypoxia and its correlation with physiological and biochemical parameters, during and six hours post hemodialysis and their clinical significance in terms of morbidity and mortality. Patients with SpO_2 >95% and not on oxygen support were enrolled in the study. Clinical status of patient's general condition and biochemical parameters were measured as outcome.
Results: Study showed that hypoxia (SpO_2<90%) was the most common complication (22.5%) occurring during and post hemodialysis period of which 55% occurred post hemodialysis in a patient undergoing first dialysis. 27.5% patients had significant fall in PaO_2>25% following hemodialysis. Hypoxia during hemodialysis (especially post dialysis period) was associated with unfavorable outcome mainly due to increased cardiovascular risk in diabetic nephropathy patients and due to multiple organ failure in septicemic patients.
Keywords: Hypoxia, hemodialysis, cardiovascular, septicemia

1. Introduction
Hypoxemia during hemodialysis (HD) is a known phenomenon.[1,2] Although several mechanisms have been proposed, the cause remains unclear. Some studies have attributed hypoxemia during HD to the dialysate, to the non-biocompatible type of membrane used, or to both.[3,4] Ventilation/perfusion (V/Q) mismatch has been proposed as the cause of hypoxemia.[5,6] Dialysis causes lowered blood oxygen levels. It is known that oxygen levels in the arterial blood can drop 5%-23% during dialysis.[7-9] This may go unnoticed but for patients with heart or lung problems, however, it can be catastrophic as HD is a common modality of treatment in renal failure patients. We looked for how clinical, physiological and biochemical parameter predisposes such event which has yet to be ascertained. Does hypoxemia develops post hemodialysis and finally its outcome in such patients?

2. Patients and methods
The present study was a hospital based cross sectional observational study in patients admitted in nephrology unit of medicine department over a period of one year. The study was approved by the ethical committee of the university and informed consent was taken from patients and it confirms to the provision of Declaration of Helsinki (as revised in Tokyo 2004). All patients were enrolled in between August 2014 to June 2015.

Patients who first time presented with the clinical features suggestive of renal failure with the indication of hemodialysis, irrespective of their initial presentation and possible etiology were studied. The inclusion criteria of patients was age ≥ 18 years and required dialysis whereas patient's whose Hb level <6 gm% or Hct <20%, systolic blood pressure <90 mmHg, PaO_2<60 mm of Hg or SpO_2<90% and known patients of pre-exisiting cardiac and respiratory failure

where excluded from the study. Consent was taken from the patient or their close relative (if patient was unable to give consent). Detailed history and examination was done. Patients were investigated thoroughly to find out the cause of renal failure. To avoid dialysis disequilibrium syndrome, short duration of hemodialysis was given for first procedure. Patients underwent hemodialysis for about two and half hours at blood flow @ 200ml/min. and dialysate flow @ 500ml/min using either jugular or femoral intravenous access. One hour prior to hemodialysis, first arterial blood gas (ABG) i.e. 2ml of blood was taken and was repeated during dialysis and post dialysis upto six hours. We used bicarbonate as dialysate fluid and semi synthetic dialyzer membranes (Fresenius Polysulfone Dialyzer F6) in all dialysis procedure. Patient's oxygen saturation of blood was monitored with O_2 saturation probe (pulse oximeter) till post dialysis up to 6 hours. Patients developing hypoxemia (PaO_2<60 mm of Hg or SpO_2<90%) were supplemented with oxygen therapy. Then 3 reports of ABG were collected and analyzed for any significant change in different biochemical parameters.

In the same way, physiological parameters like systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate (PR), respiratory rate (RR) were monitored before the dialysis, every 30 minute during dialysis and hourly up to 6 hours after dialysis and significant changes were recorded and analyzed.

Above patients were managed and their outcome was observed during their hospital stay.

2.1 Statistical analysis

Data were summarized as Mean ± SD. Two independent groups were compared by independent Student's test. Groups were also compared by repeated measures one way analysis of variance (ANOVA) and the significance of mean difference between the groups was done by Tukey's post hoc test. Discrete (categorical) groups were compared by chi-square (χ^2) test. Simple correlation and linear regression analysis was done to see association between the variables. A two-sided (α=2) p value less than 0.05 (p<0.05) was considered statistically significant. All analyses were performed on STATISTICA software (Windows version 6.0).

3. Results

A total of 120 symptomatic patients, age ranged from 18 to 90 years with mean (± SD) 40.3 ± 16.7 years and median 39 years were recruited and evaluated. Most of the patients were younger (below 40 yrs of age - 57.5%) and males (70.0%). Among patients, there were 26 ARF (21.7%) and 94 Acute on CRF (78.3%). Among ARF, septicemia was the most common cause (53.8%). In CRF, chronic glomerulonephritis (60.6%) and diabetic nephropathy was (15.9%) most common. Incidence of various complications in our study group has been shown (Table 1). 55.5% patients developed hypoxia post hemodialysis and in 14.8% hypoxia extended into the post dialysis period (Table 2).

3.1 Association with Hypoxia ($SPaO_2$<90% due to hemodialysis)

Study revealed that hypoxia was not associated with age (p=0.995), sex (p=0.668), type of renal failure (p=0.085) or indications for dialysis (p=0.908). However most of the patients of hypoxia had refractory volume overload and anuria. Septicemia with multiple organ failure and hypertension were more predisposed in developing hypoxia. Patients of CRF had more likelihood of developing hypoxia post hemodialysis. Hypoxia was not significantly associated with final outcome (p=0.312). However unfavourable (expired + LAMA + absconded) outcome was higher in diabetic nephropathy patients developing hypoxia post hemodialysis (Table 2).

3.2 Effect of HD treatment on physiological and biochemical parameters

The pre, during and 6 hours post hemodialysis ABG parameters viz. pH, bicarbonate (HCO_3), PaO_2, $PaCO_2$ of patients and other physiological parameters viz., PR, RR, SBP and DBP of patients are summarized in Table 3. Tukey test revealed that the mean pH, HCO_3 and $PaCO_2$ increased significantly (p<0.001) at during and after dialysis as compared to before dialysis. There was significant fall in PaO_2 (14.78%) compared to baseline and this fall continued 6 hours post dialysis (Table 3).

The association of hypoxia (SpO_2 <90% due to hemodialysis) with physiological characteristics is summarized (Table 4). Comparing the mean level of each characteristic between the two groups (with and without hypoxia), hypoxia showed significant (p<0.05) association with both pH and $S.Na^+$. 27.5% had significant fall in PaO_2>25% from baseline following hemodialysis. Fall in PaO_2 (during dialysis) >25% from baseline was significantly more in patients having high total leukocytes count.

Table 1: Incidence of various complications in the study group undergoing hemodialysis

Types of complications	Number	Percentage
No Complication	68	56.7
Hypotension	10	8.3
Hypoxia	27	22.5
Hypoglycemia	08	6.7
Generalised Pruritis	01	0.8
Nausea/Vomitting	02	1.7
Muscle cramps	02	1.7
Chest pain	01	0.8
Hypocalcemia	01	0.8

Table 2: Patients summary and results who develop hypoxia arising due to hemodialysis

Patients required oxygenation	No. of patients	Age group	Sex group	ARF: CRF	Comorbidity (maximum no. of patients)	Indication (maximum no. of patients)	Final outcome
During hemodialysis	08	60% (above 50 years)	80% male	40:60	Septicemia and hypertension	Refractory volume overload and anuria	100% favourable outcome
Post dialysis period	15	60% (below 40 years)	63% male	20:80	Septicemia, hypertension and diabetes mellitus	Refractory volume overload and anuria	40% favourable outcome
During to post dialysis period	04	All patient below 40 years	100% male	75:25	Septicemia and smoking	Refractory volume overload and anuria	100% favourable outcome

Table3: Changes in physiological and biochemical parameters before, during and after dialysis

Parameters	Before dialysis	During dialysis	After dialysis	% mean change (pre to post)	p value
pH	7.29 ± 0.10	7.36 ± 0.10	7.38 ± 0.09	1.2%	<0.001**
HCO_3 (mmol/L)	12.41 ± 5.21	16.58 ± 10.53	17.19 ± 4.46	27.8%	<0.001**
PaO_2 (mm Hg)	103.79 ± 22.28	93.12 ± 27.68	89.01 ± 25.93	14.78%	<0.001**
$PaCO_2$ (mmHg)	24.71 ± 7.16	26.68 ± 8.43	28.20 ± 6.48	12.4%	<0.001**
PR (per minute)	94.33 ± 8.18	95.83 ± 9.25	96.90 ± 9.38	2.6%	0.022*
RR (per minute)	20.94 ± 4.23	19.03 ± 3.57	17.73 ± 3.79	15.0%	<0.001**
SBP (mm Hg)	144.53 ± 26.59	132.42 ± 27.09	128.50 ± 22.68	11.1%	<0.001**
DBP (mm Hg)	87.62 ± 15.20	79.25 ± 24.01	80.22 ± 16.74	8.4%	<0.001**

** highly significant (p<0.001), * significant (p<0.05), PaO_2 – partial pressure of oxygen, $PaCO_2$ - partial pressure of oxygen, SBP – systolic blood pressure, DBP – diastolic blood pressure, PR – pulse rate, RR – respiratory rate, HCO_3 - bicarbonate

Table 4: Association of hypoxia with physiological and biochemical parameters at presentation

Parameters	Without hypoxia (n=93)	With hypoxia (n=27)	P value
pH	7.28 ± 0.11	7.33 ± 0.09	**0.019***
HCO_3	12.14 ± 5.07	13.33 ± 5.65	0.299
PaO_2	105.02 ± 21.21	99.96 ± 25.04	0.297
$PaCO_2$	24.40 ± 6.58	25.78 ± 8.95	0.380
Hb	7.78 ± 1.62	8.03 ± 2.17	0.520
TLC	10548.47 ± 4809.48	10711.11 ± 4534.08	0.876
S. Urea	207.92 ± 97.29	211.45 ± 98.92	0.869
S. Creatinine	12.13 ± 6.97	10.67 ± 4.64	0.309
S. Na^+	134.42 ± 7.43	137.74 ± 6.48	**0.038***
K^+	4.81 ± 1.26	4.71 ± 1.13	0.707
PT	15.90 ± 5.79	16.91 ± 8.97	0.489
INR	1.29 ± 0.59	1.40 ± 0.97	0.442
PR	94.86 ± 8.61	92.52 ± 6.27	0.192
RR	20.75 ± 4.40	21.22 ± 4.89	0.635
SBP	146.00 ± 27.19	139.48 ± 24.20	0.264
DBP	87.51 ± 15.98	88.00 ± 12.42	0.882

* significant (p<0.05), PaO_2 – partial pressure of oxygen, $PaCO_2$ - partial pressure of oxygen, SBP – systolic blood pressure, DBP – diastolic blood pressure, PR – pulse rate, RR – respiratory rate, HCO_3 - bicarbonate

4. Discussion

Hypoxia arising from hemodialysis was the most common complications in our study followed by hypotension and more than 50% patients developed hypoxemia post hemodialysis. This was also reported from the study of Dhakal *et al*[10], although their study subjects were very small in number. One of the cause of hypoxia was hypoventilation in our study, it was revealed by significant fall in PaO_2 (p<0.001) and this was significantly co-related with decrement in respiratory rate and increased in $PaCO_2$ (p<0.001). The findings of the present study was matched with other studies.[11,12] Not only hypoventilation, other causes are also responsible for hypoxia during hemodialysis like rapid correction of metabolic acidosis during hemodialysis, where significant rise of HCO_3 and pH (p<0.001) was found. Heparin an anticoagulant given during hemodialysis for prevention of thrombosis in AV lines is also responsible for hypoxia. Similar results were also shown by other studies.[13-15]

In the present study, hypoxia was observed in younger patients (median age 39 years) and such patients have lesser chances of pre-existing cardiac or respiratory failure. Septicemia with multiple organ failure were more predisposed in developing hypoxia may be attributed to pulmonary leak syndrome.[16] When we analyzed the patients who showed significant drop in $SPaO_2$ (<90%) post hemodialysis, it was more in acute on CRF than ARF (4:1) i.e. showing many chronic factors i.e. metabolic and endocrine changes also responsible for this fall in CRF. Patients of diabetic nephropathy had unfavourable outcome as they had increased chances of cardiovascular mortality. Findings of our study correlated with many different studies done in past.[17-20]

Though survival and quality of life of dialysis patients are strictly dependent on the quality of the haemodialysis (HD) treatment but identification of underlying risk factors of patients underlgoing HD is also important.[21] This study showed that hypoxia also occurs commonly in post-dialysis period than intradialysis period, hence patients in post dialysis period also require strict $SPaO_2$ monitoring otherwise it would be fatal. In high risk patients hypoxia can be prevented by oxygen inhalation. Our study has limitations as its observational nature, which prevents conclusions concerning causality. We have no data that would allow us formulate above in greater detail. Further studies are needed with longer duration and with more sample size in age matched population for more validation of results to address the hypotheses.

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Conflicts of interest: None

References

[1] Kishimoto T, Tanaka H, Maekawa M, Ivanovich P, Levin N, Bergstrom J, Klinkmann H. Dialysis-Induced Hypoxemia. *Nephrol Dial Transplant* 1993; 8 [Supp.2]: 25-29.

[2] De Broe ME. Hemodialysis-Induced Hypoxemia. Nephrol Dial Transplant 1994; 9 [Supp. 2]:173-175.

[3] De Backer W, Verpooten GA, Borgonjon Dj, *et al*. Hypoxemia during hemodialysis: Effects of different membranes and dialysate compositions. *Kidney Int* 1983; 23:738-743.

[4] Igarashi H, Kioi S, Gejyo F, *et al*. Physiologic Approach to Dialysis-Induced Hypoxemia: Effects of Dialyzer Material and Dialysate Composition. *Nephron* 1985; 41: 62-69.

[5] Craddock PR, Fehr J, Dalmasso AP, *et al*. Hemodialysis Leukopenia: Pulmonary Vascular Leukostasis Resulting from Complement Activation by Dialyzer Cellophane Membranes. *J Clin Invest* 1977; 59: 879-888.

[6] Bischel MD, Scoles BG, Mohler JG. Evidence for Pulmonary Microembolization during hemodialysis. *Chest* 1975; 67: 335-337.

[7] Rodriguez-Roisin R, Barbera JA. Pulmonary complications of abdominal disease. In: Mason RJ, Broaddus VC, Murray JF, Nadel JA, editors. Murray and Nadel's textbook of respiratory medicine. *Philadelphia: Elsevier Saunders*, 2005: 2223–2241.

[8] Patterson RW, Nissenson AR, Miller J, *et al*. Hypoxemia and pulmonary gas exchange during hemodialysis. *J Appl Physiol* 1981; 50: 259–264.

[9] Pierson DJ. Respiratory considerations in the patient with renal failure. *Respir Care* 2006; 51: 413-22.

[10] Dhakal MP, Kallay MC, Talley TE. Hemodialysis associated hypoxia extends into the post-dialysis period. *Int J Artif Organs* 1997; 20: 204-207.

[11] Barstow TJ, Landaw EM, Springer C, Cooper DM. Increase in bicarbonate stores with exercise. *Respir Physiol* 1992; 87: 231-242.

[12] Lefebvre A. [A hemodialysis bath with bicarbonate improves comfort and ultrafiltration]. Nephrologie 1983; 4: 200. French.

[13] Nath CR. Hypoxemia during Hemodialysis. *J Natl Med Assoc* 1984; 76: 627–629.

[14] Quebbeman EJ, Maierhofer WJ, Piering WF. Mechanisms producing hypoxemia during hemodialysis. *Crit Care Med* 1984; 12: 359-363.

[15] Romaldini H, Faro S, Stabile C, *et al*. Pulmonary gas exchange and ventilation during hemodialysis. *Braz J Med Biol Res* 1982; 15: 395-404.

[16] Ritz E. Leaking Capillaries and White Lung in Sepsis—Is Angiopoietin 2 the Culprit? *J Am Soc Nephrol* 2006; 17:1207–1217.

[17] Chen T, Freidman H, Belmonte M, Smith A. Hemodynamic changes during hemodialysis: Relationship to arterial pO_2. (abstract) 9th Ann Clin Dial Transplant Forum, Boston, 1979, p.30

[18] Burns CB, Scheinborn DJ: Hypoxemia during dialysis. *Arch Int Med* 1983; 142: 1350–1353.

[19] Hunt JM, Chappell TR, Henrich WL, Rubin LJ. Gas exchange during dialysis. Contrasting mechanisms contributing to comparable alterations with acetate and bicarbonate buffers. *Am J Med* 1984; 77: 255–260.

[20] Francos GC, Besarab A, Burke JF, Peters J, Tahamont MV, GEE MH *et al*. Dialysis–induced hypoxemia: Membrane dependent and membrane independent causes. *Am J Kidney Dis* 1985; 5: 191–198.

[21] Locatelli F, La Milia V, Violo L, Del Vecchio L, Di Filippo S. Optimizing haemodialysate composition. *Clin Kidney J*. 2015 Oct; 8(5): 580-9.