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RESEARCH ARTICLE

PREVALENCE OF HYPERTENSION IN LOW FLUX VERSUS HIGH FLUX MODALITIES OF MAINTENANCE HEMODIALYSIS - A COMPARATIVE STUDY

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Abstract

Background: Hypertension is common in patients on dialysis. Hemodialysis dialyzer membrane may me either High-flux or Low-flux type and biocompatibility of membranes also may be less or more in both these types. There has been no study comparing the control of hypertension across these Low and High-flux modalities with use of same Ultrapure water and same High biocompatible membrane for both the modalities.

Methods: Pre-dialytic BP has been recorded one hour before starting and Post-dialytic BP two hours after finishing Hemodialysis. Intra-dialytic BP has been measured at every 30 minutes interval. All BP recordings have been done for all patients for five hemodialysis sessions and recordings are compared. Number of antihypertensive drugs required in each group have been compared. Fluid overload causing hypertension have been excluded by excluding Intra-Dialytic Weight Gain more than 4.5%.

Results: While comparing Pre-dialytic, Intra-dialytic and Post-dialytic BP across Low and High-flux modalities, the p value obtained in each of the case was greater than 0.05, and requirement of antihypertensive drugs and Intra-Dialytic Weight Gain also have no significant difference across these Low and High-flux modalities.

Conclusions: It has been concluded from this study that both the Low flux and High flux modalities of hemodialysis are equally efficacious in terms of BP control when same Ultrapure water and High biocompatible membrane is used, and there is no difference in requirement of antihypertensive drugs and Intra-Dialytic Weight Gain across these two modalities.

Introduction:-

Chronic Kidney Disease (CKD) is a major health problem, prevalence is around 10% of global adult population.[1] Hypertension is common in CKD patients both in hemodialysis and non-dialysis population. The prevalence of hypertension in dialyzed population being 70-80%.[2]

Dialyzers are commonly performed in low- or high-flux membrane dialyzers. Low-flux membrane dialyzers are defined by an ultrafiltration rate <15 mL/mmHg/h and a β2MG clearance rate <15 mL/min.[3] High flux dialyzer is made of synthetic membranes with a higher permeability of middle molecules compared to low flux dialyzers. High-

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flux dialysis is defined as a β2- microglobulin clearance of over 20 ml/min.[4,5] Ultrapure pure water is a requirement for high flux dialysis to prevent infections in the patients. However, ultrapure water dialysis also provides additional benefits of low inflammation.

There are various studies which has compared Low and High flux modalities in terms of Blood Pressure (BP) control, with Low flux dialyzers made up of less biocompatible membranes and High flux ones of more biocompatible membranes and there are also studies where both Low and High flux dialyzers are made up of same biocompatible membranes. Few studies show superiority of High flux dialyzers over Low flux ones in terms of BP control, but few studies do not support that. However there have been no studies which have compared Low and High flux dialyzers made up of same High biocompatible membranes and both the modalities using same Ultrapure Dialysis Fluid (EDTA-ERA <0.1 CFU/ml and <0.03 EU/ml[6])

Many hemodialysis centers where Hemodiafiltration is not done, uses standard RO water Dialysis Fluid (EDTA-ERA <100 CFU/ml and <0.25 EU/ml[6]), rather than Ultrapure water for Low flux and High flux modalities in Hemodialysis. Ultrapure dialysis water is known to have better hemodynamic stability of patients.[7]

So, this study has been planned to see control of BP using Low and High flux dialyzers made up of same High biocompatible Polyamide or Polysulfone membrane and using same Ultrapure Dialysis Water for both the modalities.

Materials And Method:-

History of all eligible cases regarding cause of CKD, whether kidney biopsy was done or not, drug compliance, compliance to fluid and salt restriction, have been taken.

BP has been recorded following 2017 ACC/AHA guidelines.[8] BP is measured in supine position, using adult cuff size (16×30 cm) by Auscultatory method, using Aneroid sphygmomanometer. Interdialytic weight gain (IDWG) has been measured by digital weighing machine. High biocompatible Polyamide or Polysulfone dialyzer is used in both Low and High flux modality. Fluid overload causing Hypertension has been excluded by excluding the patients having Intra Dialytic Weight Gain more than 4.5%.

Pre-dialytic BP has been recorded one hour before starting and Post-dialytic BP has been recorded two hours after finishing Hemodialysis. Intra-dialytic BP has been measured at every 30 minutes interval. All BP recordings have been done for all patients for five hemodialysis sessions. The maximum number of Antihypertensive drugs required in each group has been recorded. It has been assumed that all the patients are compliant to their prescribed antihypertensive drugs.

The average readings of five sessions for Pre-dialytic and Post-dialytic BP are taken and presence of Intra-dialytic hypertension more than once out of five sessions is taken to be significant. And all the recordings have been compared in each group.

Interdialytic weight gain (IDWG) has been measured at each session for five sessions for all the patients and average IDWG have been compared in each group.

To calculate antihypertensive requirement, the maximum number of antihypertensive drugs prescribed to the patient for BP control, is taken into account.

Study Setting:
This study is a hospital based study, Department of Nephrology at a tertiary care Hospital.

Study Design:
This study is a prospective cross-sectional observational study.

Study Sample:
Inclusion criteria:
1. CKD patients on maintenance hemodialysis (for at least three months since initiation of hemodialysis)
2. Intra Dialytic Weight Gain within 4.5% of dry weight at each session of dialysis

3. Age more than 18 years
4. HD session three per week

Exclusion criteria:
1. Acute kidney injury due to any cause on hemodialysis, less than three months duration
2. Intra Dialytic Weight Gain more than 4.5% of dry weight at any session of dialysis
3. HD session two per week
4. Age less than 18 years
5. Patients not giving consent to get included in study

Intervention:
No intervention has been done as this study is an observational study.

Data Collection:
History of all eligible cases regarding cause of CKD, whether kidney biopsy was done or not, drug compliance, compliance to fluid and salt restriction, have been taken.

BP has been recorded following 2017 ACC/AHA guidelines.[8] BP is measured in supine position, using adult cuff size (16×30 cm) by Auscultatory method, using Aneroid sphygmomanometer. Interdialytic weight gain (IDWG) has been measured by digital weighing machine. Fluid overload causing Hypertension has been excluded by excluding the patients having Intra Dialytic Weight Gain more than 4.5%.

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Interdialytic weight gain (IDWG) has been measured at each session for five sessions for all the patients and average IDWG have been compared in each group.

To calculate antihypertensive requirement, the maximum number of antihypertensive drugs prescribed to the patient for BP control, is taken into account.

Outcome Measure:
Being an observational study, no intervention has been done, outcome measure is not applicable here.

Sample Size:
The sample size is calculated in discussion with our statistician using the formula of –
$n = (Z_{\alpha/2}+Z_{\beta})^2 [p_1 (1 - p_1) + p_2 (1 - p_2)] / (p_1 - p_2)^2$
Where,
n = Sample Size
$Z_{\alpha/2}$ = Critical value of Normal distribution at α/2 (here, for a confidence level of 90%, Z value is 1.645)
Z_{β} = Critical value of Normal distribution at β (here, for a power of 80%, Z value is 0.84)
p_1 = Proportion of patients having low flux hemodialysis having high BP = 0.56
p_2 = Proportion of patients having high flux hemodialysis having high BP = 0.42
From the formula at 90% confidence interval and 80% of power we get the minimum number of observations required are of 155 in each group. For that, 31 patients have been taken for each group and evaluated for five hemodialysis sessions for a total of 155 observations in each group.

Operational Defination:

HTN in CKD patients on MHD:

As per KDOQI clinical practice guidelines Pre-dialysis BP more than 140/90mm Hg and Post-dialysis BP more than 130/80mm Hg[9] is taken as HTN in CKD patients on MHD.

Intradialytic Hypertension:

As per KDOQI clinical practice guidelines an increase of MAP from Pre-dialysis BP to more than or equal to 15 mm Hg at any time during four hours of hemodialysis[10] is taken as Intra-dialytic Hypertension.

Results:-

1. It shows that among 62 patients on dialysis, 60% (n=37) are male and 40% (n=25) are female.
2. Among 62 patients on Hemodialysis, combining Low and High-flux modality, 31% (n=19) are Diabetic nephropathy, 16% (n=10) are Hypertensive nephropathy, 8% (n=5) are Biopsy proven glomerulonephritis / interstitial nephritis and 45% (n=28) are of unknown cause. (Figure – 1)
3. In Low-flux modality 3% (n=1) of the patients are having Controlled and 97% (n=30) are having Un-controlled Pre-dialytic BP.
4. In Low-flux modality 19% (n=6) of the patients are having Controlled and 81% (n=25) are having Un-controlled Intra-dialytic BP.
5. In Low-flux modality 3% (n=1) of the patients are having Controlled and 97% (n=30) are having Un-controlled Post-dialytic BP.
6. In High-flux modality 13% (n=4) of the patients are having Controlled and 87% (n=27) are having Un-controlled Pre-dialytic BP.
7. In High-flux modality 16% (n=5) of the patients are having Controlled and 84% (n=26) are having Un-controlled Intra-dialytic BP.
8. In High-flux modality 10% (n=3) of the patients are having Controlled and 90% (n=28) are having Un-controlled Post-dialytic BP
9. The study shows that in both Low-Flux and High-Flux dialysis, majority of the observations are having uncontrolled Pre-dialytic BP. Here the p-value obtained is 0.3 (greater than 0.05). Hence, it has been concluded that there does not exist any statistically significant difference between Low-flux and High-flux modalities of hemodialysis with respect to controlled Pre-dialytic BP.
10. The study shows that in both Low-Flux and High-Flux dialysis, majority of the observations are having uncontrolled Intra-dialytic BP. Here the p-value obtained is >0.9 (greater than 0.05). Hence, it has been concluded that there does not exist any statistically significant difference between Low-flux and High-flux modalities of hemodialysis with respect to Intra-dialytic hypertension.
11. The study shows that in both Low-Flux and High Flux-dialysis, majority of the observations are having uncontrolled Post-dialytic BP. Here the p-value obtained is 0.6 (greater than 0.05). Hence, it has been concluded that there does not exist any statistically significant difference between Low-flux and High-flux modalities of hemodialysis with respect to controlled Post-dialytic BP.
12. While comparing Intra Dialytic Weight Gain (IDWG), the p-value obtained is 0.098 (greater than 0.05). Hence, it has been concluded that there does not exist any statistically significant difference in IDWG across Low-flux and High-flux modalities of hemodialysis. (Table – 1)
13. While comparing the number of requiring antihypertensives in Low and High flux modality, the obtained p value is 0.57 (greater than 0.05). Hence it has been concluded that there is no statistically significant difference in antihypertensive requirement across Low or High flux modality. (Figure – 2)

Discussion:-

Hypertension is common in CKD patients on dialysis. **Velasquez MT, von Albertini B, Lew SQ, Mishkin GJ, Bosch JP**[11]has concluded that the average BP did not differ significantly between conventional low-flux dialysis and high-flux dialysis. Similar type of results has been obtained from this study also. **HEMO study**[12] has also concluded the same.

In contrary, **El Arbagy AR, Koura MA, El Barbary HS, Abou El Nasr AE**[13] has concluded that Post-dialysis MAP decreased significantly after use of high-flux dialysis. But here the present study has not found high-flux modality to be better than low-flux modality in managing hypertension.

Giorgia Bianchi , Vanja Salvadé, Barbara Lucchini, Sibylle Schätti-Stählin, Igor Salvadé, Michel Burnier, Luca Gabutti[14]has concludedthat the low-flux membrane correlated to higher BP levels compared with the high-flux ones.But this has not been found in this study.

HigH IDWG is associated with hypertension, which has been also found by **Ipema K.J.R. Kuipers J. Westerhuis R. Gaillard C.A.J.M. van der Schans C.P. Krijnen W.P. Franssen C.F.M**[15]. So, to compare the efficacy of low flux and high flux modalities of dialysis in controlling hypertension, the patients in both the groups have been advised to be strictly compliant to fluid and salt restriction as prescribed. The compliance of the patients have been reflected in their IDWG. According to EBPG guidelines, 4.0-4.5% IDWG as percentage of dry weight may be acceptable in patients with an optimal nutritional intake and salt restriction.[16] In this study the average IDWG of patients for both Low and High flux variety is well below 4.5%.

So, from the discussion it is clear that there are studies which favor High flux membranes over Low flux for control of hypertension and there are also studies which do not. However, there has been no study comparing the control of hypertension across these Low and High-flux modalities with use of same Ultrapure water and same High biocompatible membrane for both the modalities, which this study does. Ultrapure dialysis water is known to have better hemodynamic stability of patients.[7]It has been concluded from this study that both the Low flux and High flux modalities of hemodialysis are equally efficacious in terms of BP control and there is no difference in requirement of antihypertensives dose across these two modalities when same Ultrapure water and High biocompatible membrane is used and Intra-Dialytic Weight Gain has also no significant difference across these two modalities.

Figures

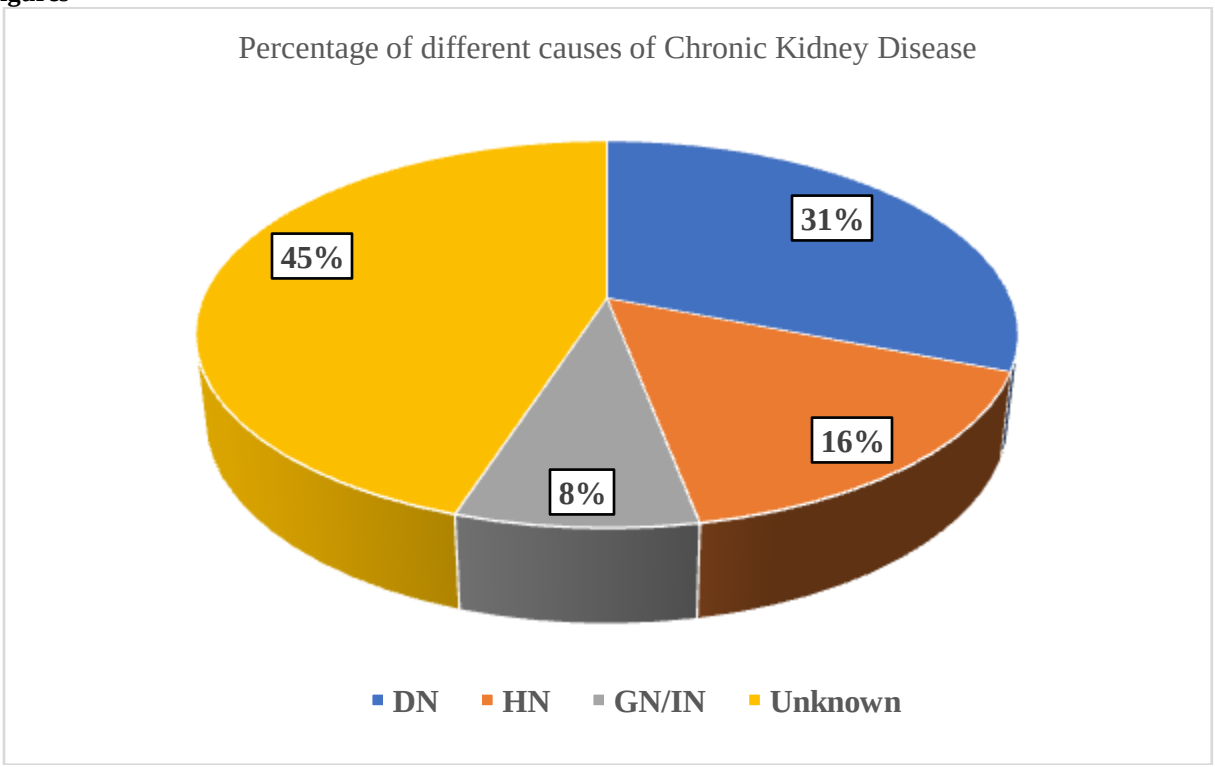

Figure 1:- Percentage of different causes of Chronic Kidney disease in patients on Dialysis.

DN – Diabetic Nephropathy, HN – Hypertensive Nephrosclerosis, GN/IN – Glomerulonephritis/ Interstitial nephritis (biopsy proven)

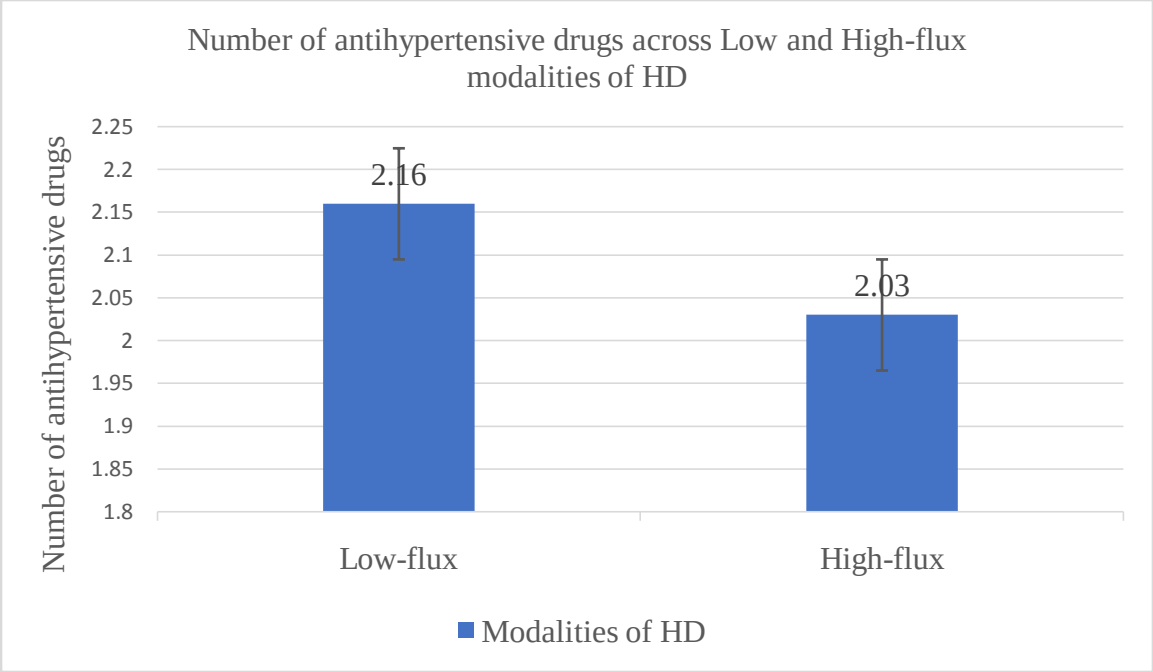

Fig 2:- Antihypertensive requirement across Low-flux and High-flux modality.

Tables:-

	Average Dry weight (Kg)	Average IDWG (Kg)	Percentage increase	P-value
Low-Flux (n=31)	58.27	1.94±0.28	3.3%	0.098
High-Flux (n=31)	63.01	1.78±0.42	2.8%	

Table 1:- Comparison of IDWG across Low-flux and High-flux modality.

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Conflict Of Interest:
Nil.

Authors Contributions:
Dr. Samaresh Paul (Primary author): Writing the protocol, data collection, data analysis, writing the manuscript

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Data is available with the Primary author in soft copy form

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