Icodextrin for Long Night Dwell in CAPD in Indian Patients – A Single Centre Experience

Amresh Krishna[1], Prit Pal Singh[2], Harsh Vardhan[2], R K Sharma[3], Amit Gupta[4], Narayan Prasad[4]

ABSTRACT

Introduction: Icodextrin is a glucose polymer derived from starch and has an average molecular weight of 20,000D. It was developed to overcome some of disadvantages of conventional dextrose solution in Continuous Ambulatory Peritoneal Dialysis (CAPD).

Material and Methods: The aim of this study was to analyze the impact of Icodextrin solution on ultra-filtration, blood pressure and blood sugar levels in CAPD patients. Total number of patients in this study was 40.

Results: The mean age of patients was 56.2±9.4 years with a male to female ratio of 3:1. Twenty seven of the subjects were diabetic. 9/40 (22.5%) patients were started on Icodextrin within one month of initiation on CAPD therapy while 31/40(77.5%) were initiated after one month. The reason for starting the Icodextrin was poor ultrafiltration (UF) in 18(45%), inadequate dialysis in 14 /40(35%), better blood pressure control in 44/40 (10%) and poor glycemic control in 4/40(10%) patients respectively. Mean ultrafiltration significantly increased after shifting to Icodextrin (875±450 vs. 1350±525 ml, P=0.001). There was a significant decrease in mean systolic blood pressure (139±41 Vs 128 ±38 mm of Hg, P=0.004) and diastolic blood pressure (87±10 Vs 77±8, P=0.004).The mean requirement of antihypertensive drugs was reduced from 3.5±1 to 2.0 ±0.5. The mean fasting blood sugar also decreased from 158.3±56.5 mg/dl to 132±48.6 mg/dl while post-prandial blood sugar decreased from o mean of 256.7±103.8 mg/dl to 199.3±107.5 mg/dl.

Conclusion: Icodextrin is associated with better UF, better blood pressure control, lesser need of antihypertensive drugs and better blood sugar control.

Keywords: CAPD, Icodextrin, Night dwell, Ultra filtration.

INTRODUCTION

As per current estimates more than 120,000 patients worldwide rely on CAPD as a modality of renal replacement therapy which represents approximately 8% of total patients on Dialysis.[1] Ultra filtration (UF) on CAPD in driven by osmosis. In Peritoneal dialysis (PD), the osmotic gradient of glucose is responsible for fluid removal. With glucose based fluids, dissipation of osmotic gradient may occur during long night dwell, leading to negative UF. The development of Icodextrin based CAPD solutions has been hailed as a major development as it allows adequate UF during long dwell especially in patients with high peritoneal transport characteristics.[3,4,5] Icodextrin is an iso-osmolar glucose polymer derived from starch, with a molecular weight of 20,000 D. It is minimally absorbed from the peritoneal membrane.[6] With Icodextrin, UF is produced by colloidal osmotic pressure and is sustained over prolonged (12 to 16 hour) dwells.[7] Another limitation of glucose based fluids are that they increase the caloric load and may lead to worsening of glycemic control.[8] There are only few studies which has examined the use of Icodextrin in Indian population. The purpose of this study was to report the patient profile of Icodextrin users and its effectiveness in Indian patient.

MATERIAL AND METHODS

Our study was a retrospective analysis of patients with end stage renal disease (ESRD) on CAPD and using Icodextrin solution for long night dwell at Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPIGIMS), Lucknow between 1st January, 2009 to 31st December, 2014. The patients details were collected from our CAPD follow up record.

Inclusion Criteria: Subjects with following criteria were included

1. ESRD patients on CAPD using Icodextrin solution for Long dwell
2. Age more than or equal to 18 years of either sex
3. Regular follow up (at least once every 2 months)
4. Patient on CAPD for at least 6 months

Exclusion Criteria Subjects with following criteria were excluded

1. Recurrent episode of peritonitis (> 2episode in 6 months)
2. Patients with history of noncompliance.
3. Active liver disease
4. Patient with life expectancy of less than 6 months

Study procedure: Patient's medical history and demography was noted from records. Cause of ESRD, duration on CAPD before use of Icodextrin, routine haematological and biochemical variables, net UF before and after use of Icodextrin at 4 month was also noted. Patient compliance

[1]Associate Professor, [2]Assistant Professor, Department of Nephrology, Indira Gandhi Institute of Medical Sciences, Patna, [3]Professor and Head of Department, [4]Department of Nephrology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, U P, India

Corresponding author: Harsh Vardhan, Assistant Professor, Department of Nephrology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India.

How to cite this article: Amresh Krishna, Prit Pal Singh, Harsh Vardhan, R K Sharma, Amit Gupta, Narayan Prasad. Icodextrin for long night dwell in CAPD in Indian patients – a single centre experience. International Journal of Contemporary Medical Research 2018;5(1):1-4.

was assessed from patient diary. The primary outcome of the study was net UF during overnight Icodextrin dwell at end of 4 months of study. The net UF was obtained by subtracting weight of Icodextrin solution administered in night dwell from that of effluent drained at the end of long dwell. One gram of fluid was considered equivalent to one millilitres of fluid for volume estimation. Blood pressure, blood glucose level urine output and numbers of antihypertensive at the initiation of Icodextrin and at the end of study was also noted. Any adverse events occurring during the study were also noted.

STATISTICAL ANALYSIS

Statistical analysis was done using software SPSS 15.0. Statistical method for study included repeated measures analysis of variance, Pearson chi-square test, Fisher exact test, and Student paired t-test.

RESULTS

This study was a retrospective observational study conducted at Department of Nephrology, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow (India) between 1st January, 2009 and 31st December, 2014. 48 patients were started on Icodextrin solution at our centre. After exclusion 40 patients could be included in this study. Baseline patient characteristics have been shown in Table-1. The mean age of patients was 56.2 ±9.4 years. Male patients outnumbered female patient by a ratio of 3:1. 67.5% of patients were diabetic ESRD. Among nondiabetic patients chronic interstial nephritis and hypertensive nephropathy was the leading cause of ESRD (Table2).The mean duration of initiation on CAPD prior to use of Icodextrin solution was 20.99±19.2 months. 9/40 (22.5%) patients were started on Icodextrin within 1 month of initiation on CAPD therapy while 31/40(77.5%) after 1 month because of one or more reasons. 75% of subjects were high transporters or high average transporters while 25% were low average transporters The Creatinine clearance at base line was 63.63±26.02 L/ week at base line. The peritoneal transport characteristics and Creatinine clearance did not change during the study. The reasons for use of Icodextrin solution in our study was poor ultra-filtration in 45% of patients with dextrose based solutions, to achieve adequacy of dialysis in 35%, for better blood pressure control in 10% of patients, and for better glycemic control in 10% of patients each respectively (Table 3). After 4 months of Icodextrin use significant change in systolic blood pressure, diastolic blood pressure, weight of the patient and blood glucose level were noted (Table 4). The mean systolic blood pressure decreased from 139±41 mm of Hg to 128± 38 mm of Hg (P=0.004) while mean diastolic blood pressure decreased from 87± 10 mm of Hg to 77 ± 8 mm of Hg(P=0.004). The weight of patient decreased from 62.50±12.7 kg to 58±14.1 kg (P=0.001) while UF increased from a baseline value of 875±450 ml/day to 1350 ±525 ml/day (P=0.001). At base line the mean requirement of antihypertensive drugs were 3.5±1 which came down to 2.0±0.5 at the end of 4 month of Icodextrin use (P=0.005). A better glycemic control was noted with use of Icodextrin solution in night dwell and mean fasting blood glucose levels which were 158.3±56.5 mg/dl at baseline, decreased to 132.0±48.6 mg/dl at the end of 4th month (P=0.001) while

Profile	Mean ± SD
Age (in years)	56.2±9.4
Male : Female	3:1
Diabetic : non diabetic	2.1:1
Duration on CAPD before initiation on Icodextrin (in months)	20.99± 19.2
CrCl (L/week)	63.65 ± 26.02
Kt/v	1.84 ± 0.56
Transport characteristics High and high average : Low average transporters	30/40(75%): 10/40(25%)
D/P Cr	0.72 ± 0.13
CrCl - Creatinine clearance, K - dialyzer clearance of urea, t - dialysis time V - volume of distribution of urea, D/P Cr Dialysate-to-plasma ratio creatinine.	

Table-1: Demographic profile of patients (N=40)

Etiology	Numbers (%)
Diabetic nephropathy	27(67.5%)
Chronic Interstitial nephritis	6 (15%)
Chronic Glomerulonephrits	2 (5%)
Hypertensive nephropathy	4(10%)
Polycystic kidney disease	1(2.5%)

Table-2: Etiology of ESRD

Reason	Number (%)
Poor ultra-filtration	18(45%)
To achieve adequacy	14(35%)
For better blood pressure control	4(10%)
Glycemic control	4(10%)

Table-3: Reason for starting Icodextrin (N=40)

Parameters	Before Icodextrin	After Icodextrin	P-value
SBP (mm of Hg)	139± 41	128 ± 38	0.004
DBP (mm of Hg)	87±10	77±8	0.004
Weight of patient (in Kgs)	62.50±12.7	58.25±14.1	0.001
Ultra filtration (ml/24hr)	875±450	1350±525	0.001
Number of antihypertensive drugs	3.50±1.0	2.0±0.50	0.005
FBS (mg/dl)	158.3±56.5	132 ± 48.6	0.001
PPBS(mg/dl)	256.7±103.8	199.3± 107.5	0.001
SBP- Systolic blood pressure, DPB-Diastolic blood pressure, FBS- Fasting blood sugar, PPBS- Post prandial blood sugar			

Table-4: Change in Clinical parameters after starting Icodextrin (N=40)

Adverse effect	Number of patient (%)
Headache	1(2.5%)
Peritonitis	2(5%)
Hypotension	1(2.5%)
Skin rash	3(7.5%)
Exit site infection	1(2.5%)

Table-5: Adverse effects (N = 40)

post prandial blood sugar decreased from 256.7±103.8 mg/dl at baseline to 199.3± 107.5 mg/dl (P=0.001).As shown in Table 5 a total of 6 adverse events were noted in the subjects, none of which required withdrawal of Icodextrin solution. Skin rash was most common adverse event reported. It was seen in 7.5 % of patients. The rash was self-limiting, transient and appeared between 3-6 weeks of Icodextrin use and subsided without any treatment. Peritonitis was observed in 5% of the patients while hypotension, headache and exit site infection each was noted in 2.5% of subjects.

DISCUSSION

CAPD is the third most common modality of renal replacement therapy worldwide. At present, it is estimated that over 120,000 patients worldwide are on CAPD.[1] Our study validates the safety and efficacy of Icodextrin in Indian Population. The result of present study indicate that Icodextrin use in long night dwell is associated with (1) an increase in net Ultra filtration (2) better blood pressure control (3) lesser requirement of antihypertensive agent and (4) better glycemic control. The study also indicates that the most common adverse effect associated with Icodextrin use in a self-limiting transient macular rash. The mean age of patients on Icodextrin was 56.2±9.4 years which was similar to other patients on CAPD in our centre and to that of patients on CAPD elsewhere [9].The percentage of patients on CAPD with diabetic nephropathy as cause for ESRD was similar to that reported by Johnson et al from Australia [10]. The Systolic Blood Pressure and the diastolic blood pressure of the patient of the present study were similar to patients on CAPD in other studies. [11] The number of female patients on CAPD in this study was much less than that reported from developed countries. [9, 10] This can be explained by lack of education and poor socioeconomic condition in India. The transport characteristics of the peritoneal membrane of patients in our study were similar to those in other studies.[9]There was a significant increase in the UF in patients after treatment with Icodextrin. The improvement in UF tended to be higher in patients with high and high average transport characteristics and all patients were able to achieve adequate UF with Icodextrin solution. This finding is consistent with other studies from west. [5, 6, 9, 10,11] The increase in UF can be explained by difference in mechanism of action of Icodextrin which acts as a colloid to generate osmotic pressure small pores while dextrose based solutions generate osmotic pressure across ultra-small pores[12]. Our patients showed a significant decrease in body weight after use of Icodextrin solution at 4 month which reflects probably the better fluid removal with Icodextrin. One year study by Wolfsan et al [9] had shown that there is no weight gain in patients who are using Icodextrin for 1 year, while other studies have shown that long term treatment on peritoneal dialysis with dextrose based solutions is associated with weight gain.[13] The improved UF also offers improved fluid management in patient on CAPD who exhibit fluid overload. It has been shown by Ates et al that patients on CAPD who are volume overloaded have decreased survival.[14]However further studies are needed to evaluate that whether improvement in fluid balance is translated into better survival in Indian patient.

The present study clearly demonstrates better blood pressure control and reduction in antihypertensive drugs with use of Icodextrin solution. These results are similar to other study in west [9,15]. The reduction in blood pressure and requirement of antihypertensive drugs have been attributed to better volume control which is achieved with Icodextrin. [16] Günal et al. expressed that an efficient volume control can even eliminate the need for antihypertensive agents. [17]As shown by Johnson et al the present study too shows that use of Icodextrin for CAPD in associated with better glycemic control. While Johnson et al[10] showed that there was reduction in HbA_1C and insulin requirement, our study concludes that there was reduction in fasting as well as post prandial blood sugar. In comparison to glucose Icodextrin is absorbed at slower rate and also has a slower rate of intra cellular metabolism. [18]

The most common adverse effect associated with Icodextrin our study was skin rash. The skin rash associated with Icodextrin use has been described as macular or macula-papular lesion. It may be associated with peeling of skin of palm and sole of feet. [19] However these rashes did not require withdrawal of Icodextrin. In a similar study by Wolfson et al incident of rash was shown to be around 18%. [9]

CONCLUSION

The present study shows that use of Icodextrin for long night dwell is associated with better ultra-filtration, better blood pressure control, lesser need of antihypertensive drugs and better blood sugar control. These effects may translate into improved survival with Icodextrin use. The adverse effects associated were trivial and did not require withdrawal.

Limitation: lack of a parallel control group

REFERENCES

1. Moeller S, Gioberge S, Brown G: ESRD patients in 2001: Global overview of patients, treatment modalities and development trends. Nephrol Dial Transplant 2002; 17:2071-2076.
2. Keshaviah P: Relationship between body size, fill volume and mass transfer area coefficient in peritoneal dialysis. J Am Soc Nephrol 1994; 4:1820-1826
3. Wolfson M, Ogrinc F, Mujais S: Review of clinical trial experience with icodextrin. Kidney Int 2002; 62: S46–S52.
4. Abu-Alfa AK, Burkart J, Piraino B, Pulliam J, Mujais S: Approach to fluid management in peritoneal dialysis: A practical algorithm. Kidney Int: 2002; 62: S8–S16.

5. Krediet R, Mujais S: Use of icodextrin in high transport ultrafiltration failure. Kidney Int: 2002; 62: S53–S61.
6. Mistry CD, Gokal R, Peers E: A randomized multicenter clinical trial comparing isosmolar icodextrin with hyperosmolar glucose solutions in CAPD. MIDAS Study Group. Multicenter Investigation of Icodextrin in Ambulatory Peritoneal Dialysis. Kidney Int 1994; 46:496-503.
7. Krediet RT, Ho-dac-Pannekeet MM, Imholz AL, Struijk DG: Icodextrin's effects on peritoneal transport. Pent Dial Int 1997; 17:35-41.
8. Davies SJ, Phillips L, Naish PF, Russell GI: Peritoneal glucose exposure and changes in membrane solute transport with time on peritoneal dialysis. J Am Soc Nephrol 2001; 12: 1046–1051.
9. Wolfson M, Piraino B, Hamburger RJ,Morton AR: A Randomised controlled trail to evaluate the safety and efficacy of Icodextrin in peritoneal dialysis. Am J of Kid.dis 2002; 40:1055-1065.
10. David Wayne Johnson, Mary Arndt, Amanda O'Shea, Rhonda Watt, Jan Hamilton and Kaia Vincent: Icodextrin as salvage therapy in peritoneal dialysis patients with refractory fluid overload. BMC Nephrology 2001, 2:2.
11. Davies SJ, Woodrow G, Donovan K,et al. Icodextrin Improves the Fluid Status of Peritoneal Dialysis Patients: Results of a Double-Blind Randomized Controlled Trial. J Am Soc Nephrol 2003; 14: 2338–2344.
12. Rippe B, Stelin G, Haraldsson B:Computer stimutation of peritoneal fluid transport in CAPD. Kidney Int 1991;4:315-325.
13. Jolly S, Chatalsingh C, Bargman J, Vas S, Chu M,Oreopolus DG:Excessive weight gain during peritoneal dialysis. Int J Arti Organs 2001;24:197-202,
14. Ates K, Nerizoglu G, Keven K, et al: Effect of fluid and sodium removal on mortality in peritoneal dialysis patient. Kidney Int 2001; 60:767-776.
15. Gunal AI, Duman S, Ozkahya M, Toz H, Asci G, Akcicek F, Basci A: Strict volume control normalizes hypertension in peritoneal dialysis patients. Am J Kidney Dis 2001; 37: 588–593.
16. Konings CJ, Kooman JP, Schonck M, Gladziwa U, Wirtz J, van den Wall Bake AW, et al. Effect of icodextrin on volume status, blood pressure and echocardiographic parameters: a randomized study. Kidney Int 2003; 63:1556–1563.
17. Gunal AI, Ilkay E, Kirciman E, Karaca I, Dogukan A, Celiker H. Blood pressure control and left ventricular hypertrophy in long-term CAPD and hemodialysis patients: a crosssectional study. Perit Dial Int 2003; 23:563–567.
18. Bredie SJ, Bosch FH, Demacker PN, et al: Effects of peritoneal dialysis with an overnight icodextrin dwell on parameters of glucose and lipid metabolism. Perit Dial Int 2001; 21:275–281.
19. Goldsmith D, Jayawardene S, Sabharwal N, Cooney K. Allergic reactions to the polymeric glucose-based peritoneal dialysis fluid icodextrin in patients with renal failure. Lancet 2000; 355:897.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 30-12-2017; **Accepted:** 01-02-2018; **Published:** 10-02-2018