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RETROSPECTIVE STUDY OF ROLE OF COMPREHENSIVE DIABETES CARE IN KNOWN DIABETIC PATIENTS FROM UTTAR PRADESH REGION.

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ABSTRACT

Background: Global burden of diabetes mellitus has increased consistently since past few decades. India has emerged as a major contributor to this global burden of DM. Comprehensive Diabetes Care (CDC) utilizes combination therapy of Panchkarma, administration of herbal drugs and diet therapy. **Aim and objectives**: The present study was planned to study the effectiveness of CDC therapy along with diet therapy in patients with type 2 DM attending Madhavbaug clinics in Uttar Pradesh, India. **Materials and methods**: This was a retrospective study conducted between September 2018 and September 2019, wherein we identified the data of obese patients suffering from type 2 DM (HbA1c ≥ 6.5%) of either gender and any age, and who had attended the out-patient departments (OPDs) at multiple Madhavbaug clinics located in Uttar Pradesh, India. The data of patients who had been administered CDC with minimum 6 sittings over a span of 12 weeks were considered for the study. **Results**: On analysing the results of HbA1c level in 124 patients who had completed 12 weeks of CDC therapy, it was found that controlled diabetes (HbA1c<5.7) was seen in 58 patients (46%) as compared to baseline (zero patient). The mean HbA1c levels reduced significantly from 8.7 at baseline to 7.03 at 12 weeks of CDC therapy. Other parameters like body mass index, body weight, cardio-pulmonary parameters showed improvement at the end of 12 week CDC therapy. Dependency on conventional allopathic medications was also reduced. **Conclusion**: From the findings of present study, CDC has been found to exert significant euglycemic action, and can serve as potent alternate option for management of DM.

KEYWORDS: Diabetes mellitus, Comprehensive Diabetes Care, CDC, panchkarma, HbA1C, BMI.

INTRODUCTION

DM is a chronic metabolic disorder characterized by derangements in processing of all the key nutrient components i.e. proteins, carbohydrates and fats. The number of cases of DM are rising alarmingly on a global platform. As per 2011 report, the prevalence of DM was found to be 366 million. Type 2 DM comprised of >90% of those cases.[1] It is cited that almost 80% of these diabetic patients are inhabitants of developing, resource poor countries. It is projected that number of diabetic patients will cross 550 million mark by the year 2030.[2]

India has 2nd highest number of diabetic cases in the world. It is estimated that prevalence of DM in India will suffer a massive rise in prevalence of DM by 2.5 times by the year 2030, where the figures are expected to close by 100 million.[2] As per the PODIS i.e. Prevalence of Diabetes in India Study, which was conducted across multiple rural and urban centers in the country, reported the prevalence of DM in the range of 5.5 to 12.5% and 2.5% to 3% in urban and rural populations, respectively.[3] Shockingly, an epidemiological study done in the state of Uttar Pradesh revealed the prevalence of DM to be as high as 17%.[4]

Persistently increased blood glucose levels and insulin resistance in type 2 DM are its hallmark features. The diagnosis of DM is always by laboratory investigations, because the clinical symptoms are non-specific and vague. Measurement of blood sugar levels in fasting and post feeding stage, glycosylated hemoglobin (HbA1c) are the commonly used tests to diagnose DM. Amongst these HbA1c is favored in current scenario, since it reflects the status of blood glucose control over past 2-3 months. Fasting blood glucose (FBG) more than 126 mg/dl, post meal blood glucose levels (PMBG) level more than 140 mg/dl and HbA1c more than 6.5% are diagnostic of DM.[5]

DM is dreaded due to its lethal and morbid after effects. These are broadly categorized into micro and macrovascular complications. Coronary artery disease in the form of myocardial infarction, angina pectoris, unstable angina, peripheral arterial disease in the form of intermittent claudication, other complications like

gangrene, sexual dysfunction in males, amputation, etc. are some of the complications of DM.[6] DM is managed by lifelong therapy of oral hypoglycemic drugs (OHDs) which include biguanides like metformin, sulphonylureas like gliclazide, SGLT2 inhibiters like dapagliflozin, etc. These act by reducing the blood glucose levels.[7]

Continuous use of OHDs is associated with increased adverse effects like fainting, dizziness, pancreatitis, megaloblastic anemia, epigastric discomfort, urinary tract infections, etc. These adverse effects hampers the already reduced quality of life in diabetic patients. Secondly, despite such aggressive conventional therapies already in practice, the prevalence of DM is still increasing at alarming pace.[7] Thirdly, DM is multifactorial disease, therefore its management should be multipronged. Thus, it is dire need of the hour to explore for alternate therapeutic option which will have optimal efficacy and overcome the problems faced with conventional therapy.

Ayurvedic therapy consisting of herbal drug administration, panchkarma, and dietary therapy is one of the interesting, potent therapeutic alternative for management of DM along with conventional therapy. Comprehensive Diabetes Care (CDC) is a form of Ayurvedic therapy which utilizes combination of Panchkarma, administration of herbal drugs and diet therapy.

Panchkarma is an intrinsic detoxification process, which consists of 3 key procedures, namely Basti- administration of herbal drugs through rectal route, Swedana- passive heat therapy, Snehana- oleation therapy.[8]

However the clinical data regarding clinical effectiveness is scarce, and therefore the present study was planned to analyze the effectiveness of CDC therapy along with diet therapy in patients with DM attending Madhavbaug clinics in Uttar Pradesh region.

SUBJECTS AND METHODS

This was a retrospective study conducted between September 2018 and September 2019, data of those patients diagnosed with DM attending Madhavbaug clinics in Uttar Pradesh. The patients of either sex, or all ages were included in the study. Data of those diabetic patients who were given CDC therapy for 12 weeks were included in the study. Based on medical records, these patients were given diet kits known as Prameha diet kit, which are low in carbohydrates, fats and contains moderate amount of proteins. Only those medical records were included in the study whose complete relevant data was available at baseline and at week 12. Information like socio-demographic details, anthropometric measurements, glycaemic parameters were noted at both time points and all the data was entered into predesigned and prevalidated data entry form.

Based on HbA1c levels after CDC therapy the patients were categorised as[5]

- Controlled- HbA1c <5.7
- Borderline- HbA1c 5.7-6.5
- Uncontrolled- HbA1c >6.5

Diet box: Diet box was given to the patients, which was 1 month food packing designed to comply with low carbohydrate and low fat diet with daily calorie intake of 800 calories. 1 diet box was designed for 1 month, therefore number of diet boxes were equivalent to number of months on taking the compliance diet. It's a preproportioned calorie restricted to 800cal/day diet box. Based on grade of obesity (sthaulya) we advised diet boxes to all these patients.

The CDC is a 3-step procedure which was performed on the patients of type 2 DM after a light breakfast. One sitting of the procedure took 65-75 minutes, as described in table 1.[8]

Table 1: Study Treatment: Comprehensive Diabetes Care (CDC)

Step of CDC	Type of Therapy	Herbs used for therapy	Duration of Therapy
Snehana	Massage or external oleation (centripetal upper strokes on the body)- Sarvadehik type i.e. whole body	100 ml *Azadirechta indica* (neem) extract processed in sesame oil	20 minutes
Swedana	Passive heat therapy to the body	*Dashmoola* (group of ten herbal roots) with steam at < 40 degrees Celsius	15-20 minutes + 3-4 minutes of relaxation after procedure
Basti kadha	Per-rectal drug administration should be in body for > 15 minutes for maximum absorption	100 ml mixture of 40% *Gudmaar* (*Gymnema sylvestre*), 20% *Daruharidra* (*Berberis aristate)* and 40% *Yashtimadhu* (*Glycyrrhiza glabra*)	10 minutes

Basti chikitsa: Yapana basti chikitsa was done for 7 times, 14 times and 21 times and number of diet kits were given depending on patient's grade of BMI [tables 1 and 2].

Table 2: Basti therapy and diet kits utilized in the present study.

BMI		Number of Basti session	Number of diet kit
Normal	up to 24	7	1
Overweight	24-30	14	2
Obese	more than 30	21	3

Statistical analysis: In this study, data was collected, and entry was done in a Microsoft excel-sheet and analysis was done using Graph Pad in Stat software V3.0. Categorical data were represented in the numeric form and continuous data were presented as the Mean ± SD. Paired t-test was used to assess the difference between baseline values and 90th day after the treatment. P-value <0.05 was considered as statistically significant.

RESULTS
In the present study, out of 124 type 2 diabetic patients, 73 were males (59%), while 51 were females (41%), thus male: female ratio was 1.43:1 [figure 1].
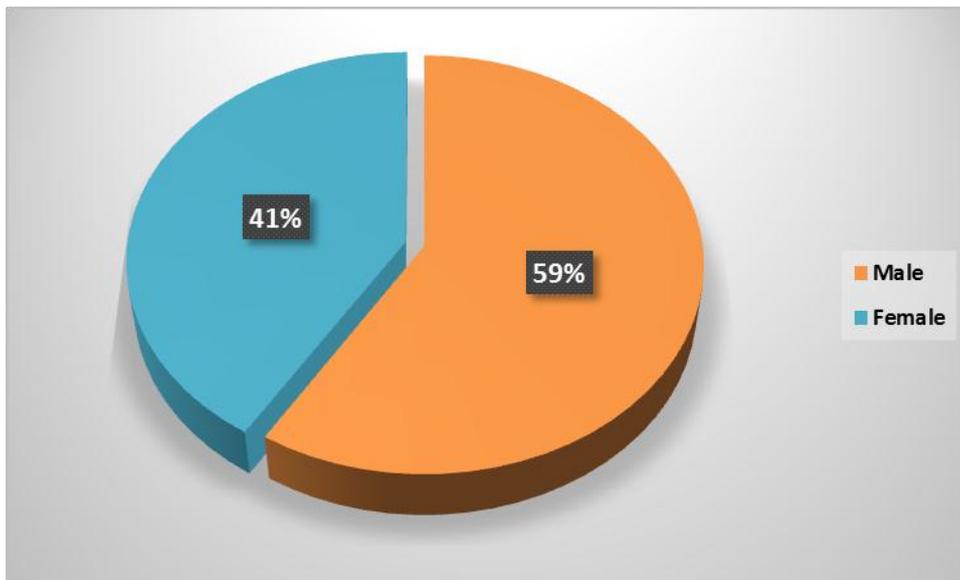
Figure 1: Sex distribution in patients of the present study.

18% of the total patients were not given any diet boxes, while 1 diet box was given to 22%, 2 diet boxes to 23%, 3 diet boxes to 36% and 4 diet boxes were given to 1% of the patients [Figure 2].
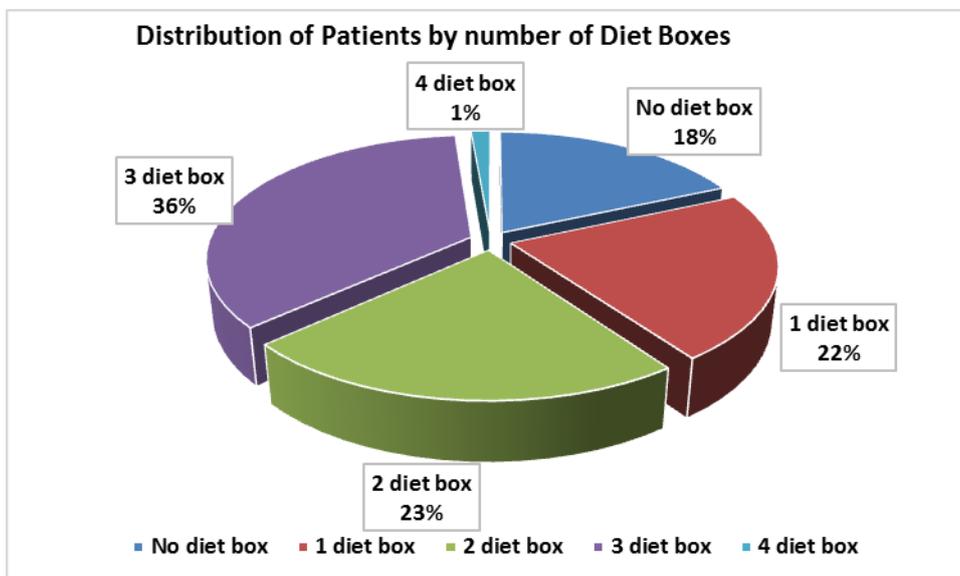
Figure 2: number of diet boxes used by patients of present study.

On analysing the anthropometric parameters in the patients of present study, it was found that body mass index (BMI) was reduced from 26.66 ± 1.08 kg/m2 at baseline to 25.67 ± 1.12 kg/m2 at the end of 12 weeks of CDC therapy, and this difference was statistically significant [p=0.05]. Similarly abdominal girth was reduced from 96.98 ± 3.9 at baseline to 92.05 ± 2.1 at 12 weeks of CDC therapy [p=0.04]. Similarly cardiopulmonary parameters like systolic blood pressure (SBP), diastolic BP (DBP), VO2 peak showed improvements in reading at 12 weeks of CDC therapy, as compared to baseline and these differences were highly statistically significant. Lipid parameters showed similar trends which can be seen in table 3.

Table 3: anthropometric, cardio-pulmonary and lipid parameters in the patients of present study at baseline and 12 weeks of CDC therapy.

Sr. No.	Parameter	Measurement	Baseline	12 week	p-value
1	Anthropometry	Weight	70.07±4.1	66.60±5.1	0.05
		BMI	26.66 ± 1.08	25.67 ± 1.12	0.05
		ABG	96.98 ± 3.9	92.05 ± 2.1	0.04
2	Cardio-pulmonary	SBP	131.67 ± 5.2	122.69 ± 4.32	0.03
		DBP	81.66 ± 3.8	76.92 ± 3.1	0.05
		VO2 peak	18.24 ± 0.88	24.48 ± 1.1	0.00
3	Lipid profile	Cholesterol	182.50±7.1	105.5±5.21	0.000
		HDL	36.0±1.1	48.0±2.1	0.001
		LDL	136.0±9.1	122.0±7.2	0.001
		TG	185.0±4.96	125.0±6.27	0.000

BMI- Body Mass Index, ABG-abdominal girth, SBP-systolic blood pressure, DBP-diastolic blood pressure, HDL- High Density Lipoprotein, LDL- Low Density Lipoprotein, TG-Triglycerides.

On analysing the results of HbA1c in patients who have completed 12 weeks of CDC therapy, it was found that normal HbA1c was seen in 58 patients (46%), borderline HbA1c was seen in 33 patients (27%) as compared to 59 patients (47%) at baseline, while abnormal HbA1c readings were noted in 33 patients (27%) as compared to 65 patients (52%) at baseline [Figure 3].
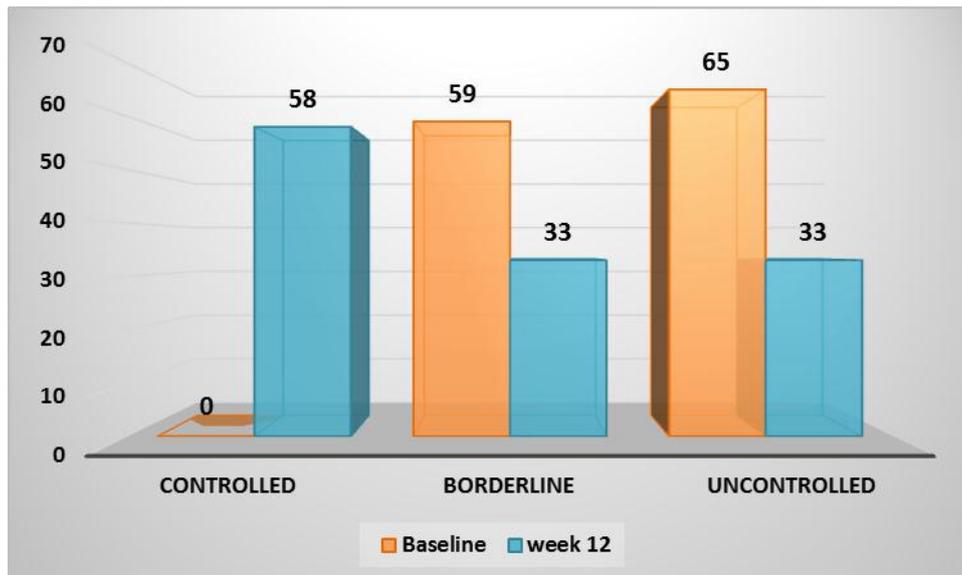
Figure 3: Results of HbA1c in patients who had completed 12 weeks of CDC therapy.

Glycosylated hemoglobin (HbA1c) reduced from 8.7 at baseline to 7.03 at week 12 of completion of CDC therapy, and the difference was statistically significant [figure 4].
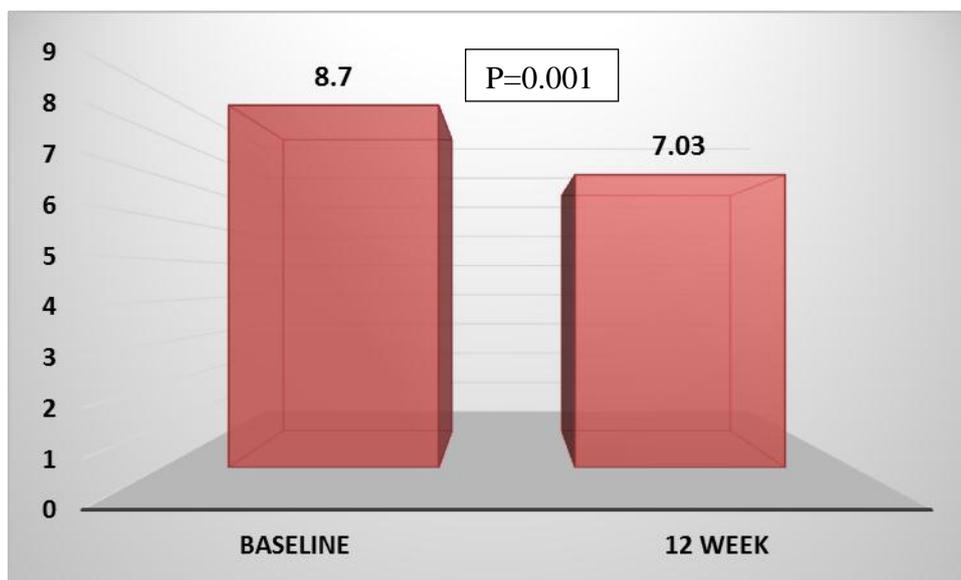
Figure 4: Glycosylated haemoglobin (HbA1c) in patients of present study at baseline and at 12 weeks of taking CDC therapy.

On analysing the variation in diet boxes and HbA1c levels at week 12, it was found that there was significant reduction in mean HbA1c levels at week 12 as compared to baseline in all groups and this reduction was greater in patients receiving more number of diet boxes [table 4].

Table 4: Variations in number of diet kits and mean reduction in mean HbA1c levels.

No. of diet kit	No. of patients	HbA1c (mean ± SD)			
		Baseline	**Week 12**	**Reduction**	**p-value**
0	22	7.58 ± 1.02	6.6 ± 1.12	0.98	0.05
1	27	7.94 ± 0.96	6.93 ± 1.0	1.01	0.04
2	28	8.70 ± 1.03	7.32 ± 1.45	1.38	0.01
3	45	8.86 ± 1.24	6.88 ± 0.99	1.98	0.001
4	2	8.92 ± 2.0	6.71 ± 1.86	2.21	<0.001

Medication history was available in 121 patients, out of which majority of the patients were taking biguanide and sulfonylureas (SU). The number of tablets/patient ratio reduced from 1.21 at baseline to 0.51 at week 12 of CDC therapy, thus there was 58% reduction in number patients taking allopathic medications after 12 weeks of CDC therapy, with major reduction seen in intake of biguanides and SU [table 5].

Table 5: Consumption of allopathic medications by the patients in the present study at baseline and at 12 weeks of CDC therapy.

No. of patients taking allopathic medicines				
Sr. No.	**Medication**	**Baseline**	**Week 12**	**p-value**
1	β blocker	10	5	0.13
2	ARB	20	10	0.001
3	CCB	10	6	0.22
4	Diuretic	5	2	0.38
5	SU	31	17	0.001
6	Biguanide	44	14	0.001
7	Antiplatelet	4	3	0.9
8	DPP4 inhibitor	8	3	0.001
9	Statins	17	4	0.001
10	Tablet/patient ratio	1.21	0.51	0.05

ARB-angiotensin receptor blocker, CCB-calcium channel blocker, SU-sulfonylurea, DPP4- dipeptidyl peptidase.

On analyzing HbA1c status at end of week 12 of CDC therapy, it was found that number of patients with controlled DM status increased and that with uncontrolled status reduced at week 12. The greatest

changes were observed in patients with duration of DM > 10 years [table 6].

Table 6: HbA1c results and duration of DM.

Duration of DM	Period of CDC therapy	HbA1c status			N
		Controlled	Borderline	Uncontrolled	
<2 yrs	Baseline	0	20	12	32
	week 12	19	6	7	32
2-10 yrs	Baseline	0	22	23	45
	week 12	18	17	10	45
> 10 yrs	Baseline	0	23	24	47
	week 12	21	10	16	47

DISCUSSION

Despite the availability of variety of conventional antidiabetic drugs and extensive guidelines for the management of DM, the prevalence of disease is rising alarmingly to the epidemic levels. This disturbing fact urges the physicians to search for alternate potential therapy which will have optimal effectiveness and at the same time it overcomes the shortcomings associated with the use of conventional therapy.

Plethora of herbal drugs are found to possess same action as that of conventional antidiabetic drugs i.e. lowering of blood glucose levels.[10] Thus, Ayurvedic therapy serves as potential form of therapy which can help to control the elevated HbA1c levels as well as reduce the adverse effects encountered with the use of antidiabetic drugs. CDC utilizes combination of Panchkarma and diet kit therapy in diabetic patients.[10] This was an first attempt to understand efficacy of this comprehensive program which includes preportioned calorie restricted diet and (Yapna) basti chikitsa with Snehana and Swedana.

CDC is postulated to act via reduction in intrinsic production of glucose through the process of gluconeogenesis, increased glycolysis, and reduction in wear and tear of vascular endothelium.[11] Basti chikitsa utilized in CDC therapy consisted of kadha of Gudmaar/ Gymnema sylvestre which has proven insulin secretagogue action[12], Yashtimadhu/ Glcerrhiza glabra which has shown hypolipidemic action[13] and Daaruharidra/ Berberis aristata which has shown to prevent adipogenesis.[14] These actions might help to reduce the HbA1c levels. BMI, body weight, abdominal girth were significantly reduced in the present study at the end of 12 weeks. Similarly, most critical parameter in type 2 diabetes i.e. glycosylated haemoglobin was also significantly reduced after CDC therapy. Also, the number of patients allopathic medications reduced drastically at the end of 12 weeks, which means that dependency on conventional medications was significantly reduced after CDC therapy.

Prior to popular belief, that HbA1c reduction will reduce the risk of complications and thus improve the prognosis in terms of reduction in mortality and morbidity, the results of landmark clinical trial in DM i.e. ACCORD trial has enabled the physicians to readdress the importance of HbA1c as the major target for treatment. In this multicentric trial the effect of intensified HbA1c control regimen was compared with usual HbA1c control regimen on cardiovascular outcomes, which are a major cause of mortality in diabetic patients. The clinical trial found out that intensified HbA1c reduction actually increased the risk of cardiovascular complications by 3.5 times as compared to usual regimen. Intensified regimen utilized use of multiple antidiabetic drugs, while usual regime used least possible antidiabetic drugs along with lifestyle modifications.[15,16,17]

Thus, one deduction from these findings can be dine in relation to HbA1c reduction and user of conventional drugs- if HbA1c reduction is possible to by other conventional possible therapeutic options with minimum possible use of conventional antidiabetic drugs, the cardiovascular outcomes can be better. In the present study, patient's dependency on allopathic medications was reduced, as well as there was significant reduction in HbA1c levels, thus CDC can serve as viable therapeutic option with better prognostic outcomes.

In the present study, greater improvement was seen in patients with chronic DM. Key changes in patients with long standing DM are reduction in insulin mediated glucose uptake by the tissues and reduction in insulin secretion.[18] The therapies in CDC are known to augment insulin release by acting as insulin secretagogue as well as reduce glucose production.[10,12,13,14]

Variations in blood glucose levels are considered to be the major cause of tissue damage due to glucose levels. Glycaemic variability is the variations in blood glucose levels ranging from hyperglycaemic peaks to hypoglycaemic troughs. It has been well cited in literature that higher the glycaemic variability higher is the risk of developing micro as well as macrovascular complications.[19] Usually physicians target blood sugar levels or HbA1c for optimal therapeutic regimen, but glycaemic variability is given increasing weightage in current scenario in most of the guidelines, in addition to HbA1c.[19] Thus, any form of therapy which maintains the steady optimum levels of blood sugar is anticipated to minimize the risk of developing vascular complications and thus improve the prognosis. In this regards, CDC has shown to maintain almost steady blood

sugar levels in the present study, with very less fluctuations, and hence CDC can be expected to have a good prognosis.

To achieve glycemic control regular use of OHA/Insulin is needed rather augmented dose is needed. But here within 12 weeks Hba1c has shown good glycemic control along with reduction in dose of OHAs/Insulin.

However, we recommend that such studies should be carried out prospectively at multiple centres all over India, which aid in comparison and validation of current study findings.

CONCLUSION
CDC reduced glycosylated haemoglobin, body mass index, abdominal girth and also the patient's dependency on conventional medications, at the same time number of patients with euglycemic status were more at the end of therapy. Thus, it can be concluded that CDC will not only serve as effective option to manage type 2 DM, but it will also improve the prognosis, as well as patient compliance.

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