



Pre and post test clinical study to evaluate the combined effect of Snehapana followed by Virechana and Shamanushadhi in reducing FPG, OGTT, and HbA1c in Prediabetes

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ABSTRACT

Background: Prediabetes is the pre diagnosis of Diabetes. The current conventional medical management of Prediabetes includes lifestyle modifications and certain diabetic medications like metformin. But a large population of Prediabetic patients turn out to be diabetic. Prediabetes has similarity with *Kaphaja Pramēha*, owing to its comparable aetiology and clinical features. Progression of Prediabetes to diabetes can be prevented with an early intervention as *Kaphaja Pramēha*, which has a good prognosis. **Objectives:** To assess the combined effect of *Snēhapāna* followed by *Virēcana* and *Śamanaushadhi* in reducing FPG, OGTT and HbA1c levels in Prediabetes. **Materials and Methods:** After the approval from IEC, an open label single arm pre and post-test clinical study was carried out in 20 subjects with Prediabetes diagnosed on the basis of ADA diagnostic criteria for Prediabetes. FPG, OGTT and HbA1c were tested. They were given *Snēhapāna* with *Mūrchita Sarṣapa Taila* followed by *Virēcana* with *Trivṛt tādī Cūrṇa* and *Nisākatakādi Kaṣāya* as *Śamanaushadhi*. **Results:** This study was completed with 20 subjects. Clinical symptoms shown statistical significance with p-value <0.05. FPG, OGTT and HbA1c improved by 33.08%, 16.57% and 11.72% respectively and showed a statistical significance of p-value .0001. Throughout the study, no adverse events were reported. **Conclusion:** The present protocol was effective in reducing the subjective and objective parameters of Prediabetes. Further research can be carried to see long term result of this protocol.

Keywords: Prediabetes, Kaphaja Pramēha, Nisākatakādi Kaṣāya, FPG, OGTT, HbA1c

INTRODUCTION

Lifestyle changes due to urbanisation and modernisation have caused unhealthy diet habits, lack of physical activity and increased stress leading to overweight with higher levels of insulin resistance. India and many other developing countries are going through this scenario and as a result, we notice more of chronic metabolic disorders than communicable diseases posing increasing challenge to the national health. Prediabetes is one among them.

Prediabetes is defined as a condition in which there is impaired glucose tolerance, but elevated blood sugar does not reach the criteria accepted for an outright diagnosis of diabetes [1, 2]. The subjects with Prediabetes are defined by the presence of impaired fasting glucose (IFG) and / or impaired glucose tolerance (IGT) and / or A1C 5.7 – 6.4%. Recently, the term ‘Prediabetes’ has been changed to ‘categories of increased risk for diabetes’.

Prevalence of Prediabetes is increasing worldwide and specialists have projected that quite 470 million people can have Prediabetes by 2030. India which has a large pool of Prediabetic subjects shows a rapid conversion of these high-risk subjects to diabetes. Approximately, 77.2 million people in India are suffering from Prediabetes [3]. The Indian Diabetes Prevention Programme-1 (IDPP-1) has shown an annual incidence of approximately 18% among subjects with Impaired Glucose Tolerance (IGT). There is a long asymptomatic prediabetic stage(s) before the development of diabetes. Several systematic long-term prospective studies from different parts of the world have shown that Prediabetes is largely preventable. Nowadays, modern medical science is depending on diet control and exercise for the management of Prediabetes. In spite of this, a large population of Prediabetic subjects turn out to be diabetic. Recently, in addition to lifestyle modification, some of the subjects are managed with drugs used for the treatment of Type 2 Diabetes Mellitus (metformin) and are often associated with adverse effects [4]. Sedentary lifestyle and improper dietary habits are the major etiological factors described for Prediabetes.

In Ayurvedic classics, *Āsyāsukha*, *Svapna sukha*, excessive intake of *Kapha Varddhaka Āhāra* are mentioned as the *Nidāna* for *Kaphaja Pramēha*. So, the Prediabetes can be compared to *Kaphaja Pramēha* because of the close resemblance of etiology of Prediabetes with *Nidānas* of *Kaphaja Pramēha* [5]. Among *Pramēhas*, *Kaphaja Pramēha* is only curable and Prediabetes is a reversible phase of Diabetes [6]. In our classics it is mentioned that three *Doshas* with predominance of *Kapha* are involved in the pathogenesis of *Kaphaja Pramēha* but vitiation of *Kapha Dosh* is the main causative factor. In *Astānga Sangraha* it is mentioned that *Kapha* associated with *Vata*, *Pitta*, *Mēdas*, *Klēda*, *Mamsa*, *Sukra* and *Rasa* getting localized in the urinary bladder produces *Kaphaja Pramēha*. *Ācārya Caraka* has emphasized that the person inflicted with *Kaphaja Pramēha* should be administered *Apatarpana Cikitsa* due to the involvement of vitiated *Klēda*, *Mēdas* and *Kapha*. Subjects of *Pramēha* have excess accumulation of *Klēda*, *Mēdas* and *Mootra* and diminution of digestive activity [7]. Hence in order to enhance the *Tejo dhātu* and to reduce *Klēda* and *Mēdas*, *Amēda*, *Amootrala* and *Agni Dīpāna Ausadhas* were selected. So, the treatment was planned

in two phases- *Sodhana Cikitsa* and *Samana Cikitsa*. Before *Sodhana*, for *Amapācana* and *Agnidipāna*, *Trikatu Cūrna* was administered. Followed by *Sarsapa Taila Pāna* having qualities like *Katu Rasa*, *Usna Vīrya*, *Kapha Vātahara* and *Mēdhoharatvā* in escalating dosage. *Moorcchana* was performed to prevent *Amadosha*. *Vīrēcana* was done with *Trivrt Cūrna*, which is specifically mentioned for *Kapha Adhikya Avasthās* and also helps in *Agnidipti* [5]. *Nisākatakādi Kasāya* which is indicated for *Pramēha*, having *Kapha Vatahara* action was selected as *Shamanaushadhi*.

METHODOLOGY

Study design and Duration :

An open label single group clinical study with pre & post-test study design in which 20 patients satisfying inclusion and exclusion criteria were selected. Pre and post testing according to subjective and objective parameters.

Study setting :

The study was carried out in OPD (Out Patient Department) and IPD (In Patient Department) of Amrita Ayurveda Hospital, Vallikkavu, Kollam, Kerala under the Postgraduate department of Kayachikitsa.

The subjects were admitted and are administered with *Trikatu Curna* as *Dipanapacana* for 3 – 5 days, *Murcchita Sarsapa Taila* as *Snehapana* for 5 – 7 days and then *Sarvanga Abhyanga* with *Tila Taila* for 3 days and after that *Virechana* will be done on the last day with *Trivrit Curna* along with *Peyadi krama* according to *Sudhi* and subjects was discharged. Following *Virechana* and *Peyadi Krama*, subject was administered with *Nisakatakadi kasaya*, twice daily before food till 90th day at OP level. On 91st day, reassessment will be done with objective parameters.

Diagnosis

Diagnosis was done according to ADA diagnostic criteria for Prediabetes [8]. After proper diagnosis, case was recorded in clinical case proforma specially designed for the present study.

Inclusion Criteria

1. Either gender of age group of 20 – 70 years
2. HbA1c : 5.7% - 6.4%
3. FPG : 100 mg/dl – 125 mg/dl
4. OGTT : 140 mg/dl – 199 mg/dl
5. Subject fit for *Snehapana* and *Virechana Karma*.

Exclusion Criteria

1. Type II Diabetes Mellitus (NIDDM) with and without complications.
2. Type I Diabetes Mellitus (IDDM) associated with and without complications.
3. Subjects suffering from any other systemic diseases.

4. Subjects unfit for *Snehapana* and *Virechana karma*.
5. Subjects who are under diabetic medication.
6. Certain genetic syndromes sometimes associated with Prediabetes e.g. Down's Syndrome, Klinefelter's Syndrome, Turner's Syndrome etc.

Assessment

Objective Parameters :

1. FPG
2. OGTT
3. HbA1c

Therapeutic Intervention

a. Pūrva Karma (Pre-operative measures) :

Āma Pācana: For *Āma Pācana*, *Trikaṭu Cūrṇa* was given at a dose of 6gm twice daily before food for a period of 3-5 days at OP level.

Snēhapāna: For *Snēhapāna*, subjects were admitted in the IPD. They were given *Mūrchita Sarṣapa Taila* starting with 30 ml at 6 am on empty stomach. They were allowed to take food only after attaining good appetite and clear belching, indicating the full digestion of *Snēha* (medicated oil). Subjects were advised to take hot water frequently after taking *Snēha*. When subjects felt hunger, only light food in the form of rice gruel was given in the afternoon and night. Next day dose was calculated according to the per hour digestion based on the time of administration and time of hunger. This was continued till the appearance of *Samyak Snigdha Lakṣanas* (features of optimal oleation) like *Vatanulōmana* (normal movement of vata), *Agni Dīpti* (increase in appetite), *Asamhata Varcha* (loose stools), *Anga Laghava* (lightness of body), *Snehōdvēga* (aversion to *Snēha*), *Gātra Snigdhatta* (unctuousness of body) and *Glāni* (un-exertional tiredness)

Sarvāṅga Abhyaṅga (external oleation) and *Uṣṇa jala snāna* (hot water bath): After attaining *Samyak Snēhana*, subjects were subjected to *Sarvāṅga Abhyaṅga* (full body massage) with *Tila taila* (sesame oil) and *Uṣṇa jala snāna* for a period of 3 days.

b. Pradhāna Karma (Operative measures) :

Virēcana: On the third day after *Sarvāṅga Abhyaṅga* and *Uṣṇa jala snāna*, *Virēcana Oushadi* (purgative drugs) *Trivṛ tādī Cūrṇa* 12 gm was given on empty stomach at about 7 am along with honey. Subjects were asked to take *Uṣṇa Jala* (hot water) frequently in small quantities. *Pravara* (excellent), *Madhyama* (medium) and *Avara Śudhi* (least) were assessed at the end of *Virēcana Karma*. *Virēcana Vēgās* (Passage of purgative bouts) ranging from 1-10, 11-20, & 21-30 is considered as *Pravara*, *Madhyama* and *Avara* type of *Śudhi* respectively.

c. Paschāt Karma (Post-operative measures) :

Samsarjana Krama (diet following purgation): It was followed according to the type of *Śudhi* observed.

d. Śamanoushadi :

After *Virēcana* and *Samsarjana Krama*, subjects were administered *Niśākatakādi Kaṣāya Curnā*. As per requirement, *Kaṣāya* (decoction) was prepared with drugs and water taken in the ratio 1:16 and reduced to 1/8th. Then they were advised to consume 48 ml *Kaṣāya* twice daily before food till 90th day at OP level. Subjects were advised to continue their normal diet and physical activities, which they were routinely performed. On 91st day, the subjects were reassessed with both subjective and objective parameters to evaluate the effect of the treatment protocol administered.

TABLE 1

Procedure	Drug	Dose	Duration
<i>Pūrva Karma</i>			
<i>Āma Pācana</i>	<i>Trikaṭu Cūrna</i>	6 gm twice daily before food	3-5 days
<i>Snēhapāna</i>	<i>Mūrchita Sarṣapa Taila</i>	Ascending dose according to per hour digestion	5-7 days or till the appearance of <i>Samyak Snigdha Lakṣanas</i>
<i>Sarvāṅga Abhyaṅga</i>	<i>Tila taila</i>	3 days	30 minutes
<i>Pradhāna Karma</i>			
<i>Virēcana</i>	<i>Trivṛ tādi Cūrṇa</i>	12 gm with honey	1 day
<i>Paschāt Karma</i>			
<i>Samsarjana Krama</i>			Acc to type of <i>Śudhi</i> (<i>Avara Śudhi</i> , <i>Madhyama Śudhi</i> , <i>Pravara Śudhi</i>)
Oral Medications			
<i>Śamanoushadi</i>	<i>Niśākatakādi Kaṣāya</i>	48 ml twice daily before food	Till 90 th day

RESULTS

In the present study, total 20 subjects of Prediabetes were registered and completed the treatment protocol. Statistical analysis was done using SPSS VER.20. Wilcoxon signed rank test and Paired samples t-Test were used for statistical analysis of the collected data.

FPG : The mean value of FPG before treatment was 113.80 and reduced to 91.85 after treatment with a mean difference of 21.9500 and found to be statistically significant with *P* – value .0001.

TABLE 2

Paired samples test for FPG

Paired Samples Statistics						
	Mean	N	MD	Std. Deviation	t-value	P-value
FPG-BT	113.8000	20	21.95000	7.88386	12.451	.0001
FPG-AT	91.8500	20				

OGTT : The mean value of OGTT before treatment was 156.60 and reduced to 130.65 after treatment with a mean difference of 12.00647 and found to be statistically significant with P-value .0001.

TABLE 3

Paired samples test for OGTT

Paired Samples Statistics						
	Mean	N	MD	Std. Deviation	t-value	P-value
OGTT-BT	156.6000	20	25.95000	12.00647	9.666	.0001
OGTT-AT	130.6500	20				

HbA1c : The mean value of HbA1c before treatment was 5.9700 and reduced to 5.2750 after treatment with a mean difference of 0.69500 and found to be statistically significant with P-value .0001.

TABLE 4

Paired samples test for HbA1c

Paired Samples Statistics						
	Mean	N	MD	Std. Deviation	t-value	P-value
HbA1c -BT	5.9700	20	.69500	.15720	19.772	.0001
HbA1c -AT	5.2750	20				

TABLE 5

Effect of Therapy on Objective Parameters (Change in mean values)

SI No	Variables	Mean BT	Mean AT	Percentage of improvement
1	FPG	113.80	91.85	33.08%

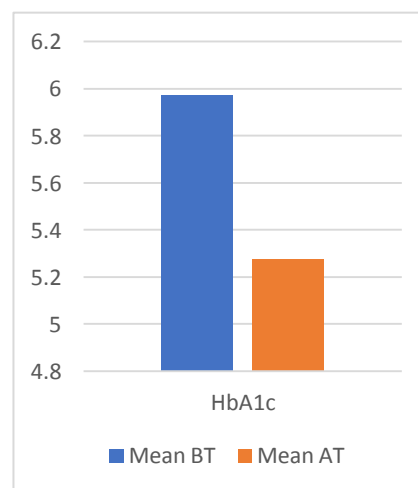
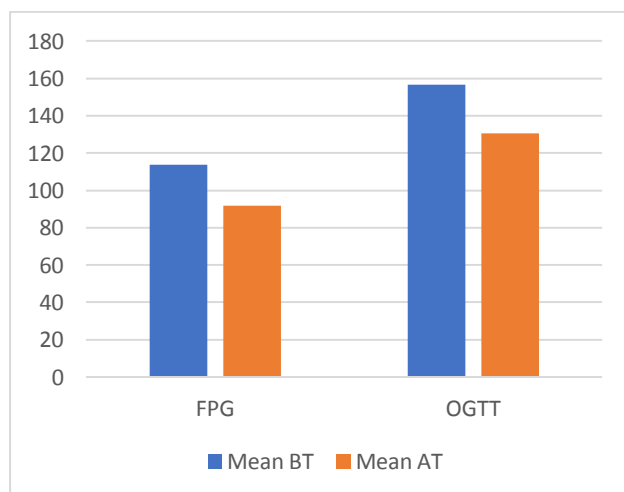
2	OGTT	156.60	130.65	16.57%
3	HbA1c	5.9700	5.2750	11.72%

FPG : There was a reduction in mean values of fasting plasma glucose levels from 113.80 (BT) to 91.85 (AT) with an improvement percentage of 33.08

OGTT : There was a reduction in mean values of OGTT from 156.60 (BT) to 130.65 (AT) with an improvement percentage of 16.57

HbA1c : There was a reduction in mean values of HbA1c levels from 5.9700 (BT) to 5.2750 (AT) with an improvement percentage of 11.72

Chart showing Effect of therapy on objective parameters (Change in mean values)



DISCUSSION

Prediabetes is a clinical condition with an impaired blood glucose level lesser than a diabetic blood profile. It can be compared to *Kaphaja Pramēha* described in the context of *Pramēha* in *Ayurvēdic* classics due to similarity in etiological factors. The major etiological factors are (1) genetic and hereditary factors and (2) unhealthy dietary habits and lack of physical activities. In our classics it is mentioned that three *Dosha* with a *Kapha* dominance are involved in the pathogenesis of this clinical condition.

Majority of the subjects in this study showed positive family history of diabetes. This indicated presence of either of *Sukra* or *Shonita Dushti*. The genetic predisposition (*Bija Dushti*) contributed to the onset of *Kaphaja Pramēha*.

Most of the subjects in this study consumed meat, curd, sugarcane products, junk foods and had untimely food habits. The above said food items are all *Abhisyandi* in its action. *Abhisyandi Ahārās* vitiated *Kapha* and produced *Agnimāndya* and *Ama*. Untimely food habit provoked a *Sannipāta Kopa*. Most of the subjects slept during day and lacked physical activities. Excessive day sleep caused *Kaphapitta Kopa* where as sedentary habits produced accumulation of *Kapha* in the body. A *Sannipāta Dosha Dushti* with *Kapha* dominance in the form of *Bahudrava Avastha* prevailed with the above said *Nidanās*.

The etiological factors like intake of excess *Madhura Ahārā* in the form of sugarcane products and *Abhisyandi Ahārās*, habit of day sleep and sedentary life style produced *Medodhatvāgni Māndya* which subsequently led to *Medovaha Srotodushti*. The vitiated *Kapha* dominant *Tridosha* got lodged in the vitiated *Medo Dhatu*. The compactness of *Medo Dhatu* got lost due to the interaction of *Bahudrava Dosha Avastha* with the *Medo Dhatu*. The *Badha Mēda* got converted into *Abadha Mēda*. This series in pathogenesis lead to the production of excessive *Klēda* in the body. The *Klēda* so produced, reached *Vasti* and resulted in *Kaphaja Pramēha*. Since the elimination of *Klēda* is through *Mutra*, *Bahumutrata* is one of the cardinal features in this condition.

Samprapti Vighatana is the main aim of any treatment. In *Kaphaja Pramēha*, treatment modalities should aim to decrease *Kapha* and *Klēda* and correct *Agni* at the level of *Koshta* and *Medo Dhatu*.

Discussion on probable mode of action of therapies :

Pācana - Dīpāna with Trikatu Cūrna

Mandāgni and *Āma* formation initiated the *Samprāpti* in *Kaphaja Pramēha*. *Trikatu Cūrna* which contained *Pippali*, *Marica* and *Nāgara* were given for *Pācana-Dīpana* as the first line of management. *Trikatu Cūrna* is *Usna Virya*, *Katu Rasa* and possess *Laghu*, *Ruksha* and *Tīkshna Gunas*. It would have corrected the *Agni* and ensured proper *Rasa* formation. *Dīpāna* drugs kindled the gastric fire where as *Pācana* drugs cooked the undigested food. *Hēmādri* commenting on it said that, *Pācana* does digestion of *Āma* and *Dīpana* does separation of *Dosha* from *Dhātu*. Thus the combined effect resulted in correction of *Agni* and thus *Ahara*

Paka. This reduced the over accumulation of *Malarūpa Kapha* or *Kledāmsha* and also to an extent corrected *Medo Dhātvāgni*.

Snēhapāna with Murcchita Sarsapa Taila

Pramēha is a disease where *Rasādi Dhātus* (tissues of the body) are involved in the *Samprāpti*. *Snēhapāna* was done to extract the *Klēda* (waste) from the *Dhātus* and bring to *Kōṣṭha* for elimination. *Snēhapāna* was done with *Mūrccchita Sarṣapa Taila*. *Sarṣapa Taila* is *Kaṭu* (pungent), *Uṣṇa* (hot in potency) and possess *Tīkṣṇa* (sharp) and *Laghu Guṇa*. It pacified *Kapha* and *Mēdas* by *Klēda Śōṣaṇa* (diminution of excessive waste) owing to its *Kaṭu Rasa* (pungent taste) and *Vāta* by its *Snigdha* (oily) and *Uṣṇa Guṇa* [9, 10]. *Sarṣapa Taila* showed hypoglycemic effect [11].

Virēcana with Trivrt Cūrna

The *Virēcana Dravyās* (*Pippali*, *Nāgara*, *Trivrt* and *Yavaksāra*) have properties like *Usna*, *Tīksna*, *Sukshma*, *Vyavayi*, *Vikāshi* etc. Due to the *Vyavāyi* and *Vikāsi* qualities of *Yavaksāra*, the *Virecana Dravya* entered into circulation into large and small channels of the body. *Vikāsi Guna* helped in detaching the *Malās* from *Dhātus*. *Ushna* and *Tīksna* properties of *Nāgara*, *Trivrt* and *Yavaksāra* caused liquefaction and disintegration of the accumulated *Doshas*. Because of *Suksma Guna* of *Lavana Rasa*, the *Malas* or *Doshas* floated and passed through the smallest channels and reached *Pakvāsaya*. And then it was eliminated out of the body.

Virēcana eliminated the morbid *Kapha* and *Pitta*, thereby reducing the *Klēda* level in the body. The process also resulted in *Amulomana* of *Vata* and correction of *Agni*.

Nisākatakādi Kashāya as Samanaushadhi

Kasāya, *Tikta Rasa* predominance; *Laghu*, *Rūksha*, *Tīksna Guna*, *Katu Vipāka* and *Kapha Vata Hara* nature of this yoga facilitated *Soshana* of *Kleda* and *Medas*. Ellagic acid, one of the major chemical constituents present in *Āmalaki* exerted anti-diabetic activity through the action on Beta-cells of pancreas that stimulated insulin secretion and decreased glucose intolerance and [12] Curcumin in *Haridrā* showed anti-diabetic activity. It also reduced blood glucose and the levels of glycosylated hemoglobin through the regulation of polyol pathways [13]. *Nisākatakādi Kashāya* also had antihyperglycemic activity [14].

CONCLUSION

Prediabetes showed similarity in etiological factors and clinical symptoms to that of *Kaphaja Pramēha*. Conversion of a Prediabetic individual to diabetes can be prevented with an early intervention as *Kaphaja Pramēha*, which has a good prognosis. FBS, OGTT and HbA1c improved by 33.08%, 16.57% and 11.72% respectively and showed a statistical significance of P-value .0001.

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