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Research Article

Efficacy and safety of *Tinospora cordifolia* (Tc) as an add-on therapy in patients with type-2 diabetes

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ABSTRACT

Background: Type 2 diabetes has become a global epidemic. *Tinospora cordifolia* is being used in the treatment of type 2 diabetes since ancient times. It is a common misconception that Ayurvedic medicines are always safe. In fact, they also pose serious health risks either in the form of adverse reactions or in the form of drug interactions. Hence this study was undertaken to study the efficacy and safety of Tc on human subjects.
Methods: We recruited 40 type 2 diabetic patients who were on oral hypoglycaemic agents. These patients were then randomly divided into two groups, A and B. Patients in group A continued with their anti-diabetic medications while in group B Tc was given at a dose of 500 mg three times daily along with their conventional medications. The fasting and post prandial blood glucose levels, renal function tests and liver function tests were recorded at baseline, 3 months and 6 months.
Results: During the course of study we observed a decrease in the fasting and post prandial blood glucose levels of the patients. No significant change was observed in the renal function tests and liver function tests and no other event of any adverse drug reactions were recorded.
Conclusion: *Tinospora cordifolia* (Tc) is effective as an add-on therapy in patients with type-2 diabetes. There is no negative impact of Tc on the renal as well as liver function tests.

Keywords: Type 2 diabetes, *Tinospora cordifolia*, Oral hypoglycaemic agents

INTRODUCTION

Diabetes mellitus is a metabolic-cum-vascular syndrome of multiple etiologies characterised by chronic hyperglycemia with disturbances of carbohydrates, fats, and protein metabolism resulting from defects in insulin secretion, insulin action or both. This disorder is frequently associated with long term damage, which can lead to failure of organs like eyes, kidneys, nerves, heart and blood vessels. With the changes in life-style and modernization diabetes is increasing rapidly.[1] With the advancement in the field of medical science, the treatment of diabetes has also advanced on a number of fronts.[2] The regimens presently employed for the management of type 2 diabetes include lifestyle modification, oral-hypoglycemic agents and insulin therapy. However, inspite of the usefulness of these treatments, insulin remains to be the gold standard in diabetes management.[3] It is seen that these oral hypoglycaemic drugs have their own side effects ranging from hypoglycaemia, weight gain, lack of responsiveness, diarrhoea, flatulence, abdominal

discomfort to liver toxicity, and worsening heart diseases.[4-6] Due to adverse effects of these allopathic medicinal agents, there is an obvious need for development of indigenous, economical anti-diabetic crude or purified drugs from botanical or natural sources which have lesser side effects on the body.[6,7]

Nature is an exemplary source of medications, and indigenous remedies have been used in the treatment of diabetes mellitus in many parts of the world since the 6th century BC.[8] In ancient literature more than 800 plant species have been reported to have potent anti-diabetic activity.[9]

T. cordifolia is one such plant which is widely used in Ayurveda for treating diabetes mellitus.[10-12] Guduchi [Tinospora cordifolia] is a large, glabrous, deciduous climbing shrub belonging to the family Menispermaceae[13,14] The notable medicinal properties reported are anti-diabetic, anti-spasmodic, anti-inflammatory, anti-arthritic, anti-oxidant, anti-allergic, anti-stress, anti-leprotic, anti-malarial, hepatoprotective, immunomodulatory and anti-neoplastic activities. The ayurvedic literature report that Tc can cause constipation, if taken regularly at high doses and it has no side effects and toxicity. Yet the safety and the potential in human beings have to be established using modern methods.[15] Hence the present study was undertaken to evaluate the safety profile of *Tinospora cordifolia* in diabetic patients using haematological and biochemical tests.

METHODS

The present study included 40 type 2 diabetic patients (17 males and 23 females), recruited from the medicine and diabetic OPD of King George medical University, Lucknow (U.P.). The study protocol was approved by the institutional ethics committee and written informed consent was taken from all the participants. The procedures followed were in accordance with the institutional ethical committee standards responsible for human experimentation and with the Helsinki declaration. The subjects who were included in this study met the following inclusion criteria:

- A known case of type 2 diabetes mellitus on oral hypoglycaemic drugs
- Patients of age between 30-60 years, of either sex.

Subjects with the following conditions were excluded from the study:

- Type 2 patients on insulin.
- Type 1 Diabetic and Gestational diabetic patients.
- Patients above 60 years of age.
- Patients with Diabetic nephropathy, neuropathy, retinopathy or any other chronic complications.

The selected patients were divided randomly into two groups A and B. The patients in group A were treated as controls and they continued their oral hypoglycaemic drugs while in group B Tc was given as an add-on therapy along with their anti-diabetic medications. Tc was given in the form of immumod tablets which contains extract of Tc. One tablet of 500 mg was given three times daily before meals for six months. The fasting and post prandial blood glucose levels were also estimated at base line, 3 months and after 6 months. The safety assessment of Tc was carried out with the help of biochemical investigations which were assessed at the beginning and after six months. The various tests used for the testing of the safety profile of Tc were as follows:

Blood glucose levels: The fasting and post prandial blood glucose levels of the patients were measured to see the decrease in the blood glucose levels.

Liver Function Tests (LFT): This included AST (Aspartate transaminase), ALT (Alanine transaminase) and ALP (Alkaline phosphatase). These enzymes are markers of liver diseases.

Renal Function Tests (RFT): It included blood urea and serum creatinine levels. An increase in these levels indicates adverse effect on the kidneys.

The normal range for all the above biochemical parameters were taken according to WHO guidelines.

Statistical analysis

The statistical analysis was carried out using 'Unpaired t test' using Graph pad statistical computer software package. Level of significance (P value) was considered less than 0.05.

RESULTS

All the enrolled subjects successfully completed the study. The mean age of subjects in group A was 50.7 ± 9.02 while in group B was 50.05 ± 10.54 (P = 0.8351) which shows that there was no significant difference between the age of the two groups.

1) Fasting blood glucose level: The mean baseline fasting blood glucose in group A was 140.91 ± 52.22 mg/dl and in group B was 143.33 ± 53.54 mg/dl. The P value obtained was 0.8855 showing that there was no significant difference between the two groups at baseline. After three months, it was reduced to 124.02 ± 24.14mg/dl in group A and 123.76 ± 33.43 mg/dl in group B. After 6 months, the fasting blood glucose values were 121.76 ± 29.57 mg/dl in group A and 119.99 ± 34.36 mg/dl. We observed a decrease in the fasting blood glucose levels in both the groups, however this decrease

was not statistically significant since the p value obtained was more than 0.05 (Figure 1).

2) Post Prandial Blood Glucose level: The mean baseline post prandial blood glucose levels in group A was 222.33 ± 84.70 mg/dl while in group B was 208.29 ± 67.69mg/dl. Both the groups were statistically similar as the p value obtained was 0.5648. A decrease in the post prandial blood glucose levels was observed after a period of six months, group A 186.05 ± 50.92 mg/dl, group B 180.61 ± 44.04 mg/dl (Figure 2).

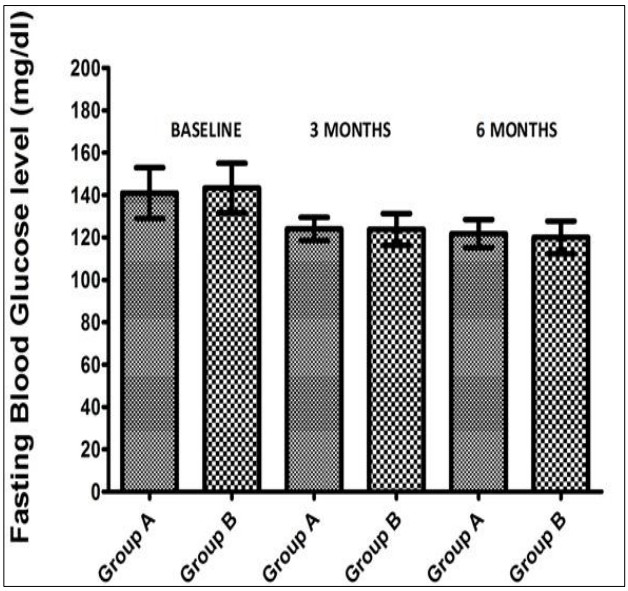

Figure 1: Mean fasting blood glucose levels of group A and B at baseline, 3 months and 6 months.

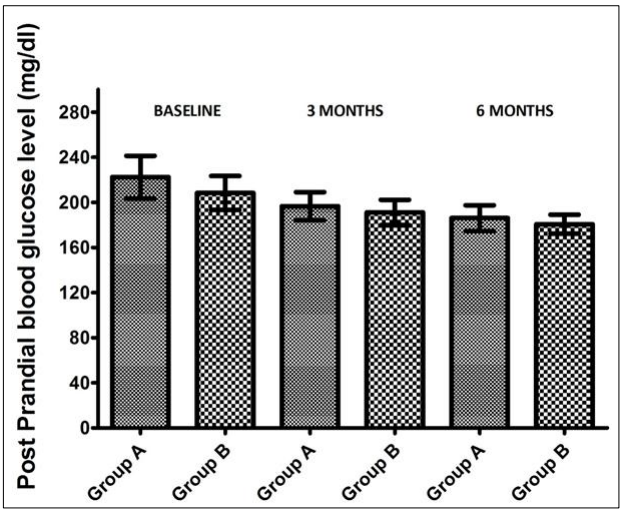

Figure 2: Mean post prandial blood glucose levels of group A and B at baseline, 3 months and 6 months.

3) Renal function tests: The mean baseline serum urea level was 34.22 ± 6.70 mg/dl in group A while 29.17 ± 8.20 mg/dl in group B. Both the groups were statistically similar at baseline. The mean serum urea levels recorded after 6 months were 32.32 ± 10.27 mg/dl and 32.74 ± 6.8 mg/dl in group A and B respectively.

Similarly, the mean baseline serum creatinine level in group A was 0.88 ± 0.17 mg/dl while in group B was 0.84 ± 0.20 mg/dl. The serum creatinine levels recorded after 6 months of Tc intervention was 0.77 ± 0.12 mg/dl and0.82 ± 0.17 mg /dl respectively. No significant change in the serum urea and serum creatinine levels was observed (Table 1).

Table 1: Showing comparison of urea and creatinine levels between group A and B at baseline, 3 months and 6 months.

		Baseline		3 month		6 month	
		Group A	**Group B**	**Group A**	**Group B**	**Group A**	**Group B**
Serum urea (mg/dl)	Mean ± SD	34.22 ± 6.70	29.17 ± 8.20	34.02 ± 6.78	32.65 ± 7.94	32.32 ± 10.27	32.74 ± 6.8
	P value	0.3397		0.5599		0.8804	
Serum creatinine (mg/dl)	Mean ± SD	0.88 ± 0.17	0.84 ± 0.20	0.82 ± 0.17	0.84 ± 0.21	0.77 ± 0.12	0.82 ± 0.17
	P value	0.4681		0.6909		0.2529	

4) Liver function tests: The mean baseline value for AST in group A was recorded as 30.68 ± 24.87 IU/L while in group B was 33.47 ± 22.0 IU/L. The values obtained after 6 months of Tc administration were 23.67±10.94 IU/L in group A and 33.34 ± 23.86 IU/L group B. The mean baseline serum ALT level in group A was 30.94 ± 22.94 IU/L and in group B was 35.60 ± 21.59 IU/L and after 6 months they were recorded as 26.02 ± 6.44 IU/L in group A and 34.06 ± 26.06 IU/L in group B.

Similarly the mean baseline ALP values observed were 108.48 ± 67.75 IU/L and 127.72 ± 65.37 IU/L in group A and group B respectively. The values obtained at the end of six months were 88.83 ± 13.37 IU/L in group A and 118.89 ± 53.06 IU/L in group B.

We did not observed any significant change in the liver function tests of the patients in both the groups (Table 2).

Table 2: Showing comparison of AST, ALT and ALP levels between group A and B at baseline, 3 months and 6 months.

		Baseline		3 month		6 month	
		Group A	Group B	Group A	Group B	Group A	Group B
AST (IU/L)	Mean ± SD	34.22 ± 6.70	29.17 ± 8.20	34.02 ± 6.78	32.65 ± 7.94	32.32 ± 10.27	32.74 ± 6.8
	P value	0.3397		0.5599		0.8804	
ALT (IU/L)	Mean ± SD	0.88 ± 0.17	0.84 ± 0.20	0.82 ± 0.17	0.84 ± 0.21	0.77 ± 0.12	0.82 ± 0.17
	P value	0.4681		0.6909		0.2529	
ALP (IU/L)	Mean ± SD	108.48 ± 67.75	127.72 ± 65.37	88.31 ± 15.23	122.86 ± 48.51	88.83 ± 13.37	118.89 ± 53.06
	P value	0.4987		0.4324		0.3187	

DISCUSSION

The results obtained from the present study shows that there is no significant increase or decrease or any adverse effect on the renal function tests. Tc has been described as useful in *mutrakriccha* (urinary trouble) separately and in the form of various formulations in Ayurveda. In a scientific study on rats and human volunteers, *T. cordifolia* was found to have diuretic effects.[16] It was also found effective in modulation of morphology and some gluconeogenic enzymes activity in diabetic rat kidney.[17]

Similarly no significant change was observed in the liver profile of the patients during the course of the study. On the other hand various studies have shown hepatoprotective role of Tc. A clinical study has shown that *Guduchi* plays an important role in normalization of altered liver functions (ALT, AST).[18] The antihepatotoxic activity of Tc has been demonstrated in CCl_4 induced liver damage, normallising liver function as assessed by morphological, biochemical (SGPT, SGOT, serum alkaline phosphatase, serum bilirubin) and functional (pentobarbitone sleep time) tests.

Tc revealed hepatoprotective action in goat. [19] Tc prevents antitubercular drugs[20,21] and bile salts[22] induced hepatic damage, x and obstructive jaundice.[23] The extract has also exhibited *in vitro* inactivating property against hepatitis B and E surface antigens in 48 to 72 hours.[24]

Similarly other studies conducted on the safety profile of Tc show no significant side effects or adverse reactions in the dosage mentioned.[25]

CONCLUSION

The findings of the present study suggest that there is no negative impact of Tc on the renal as well as liver function tests. The results obtained were similar to the previous studies conducted on animal models as well as human beings. We therefore conclude that the administration of Tc at the dose of 500 mg three times a day can be done safely.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee (Ref No-291/R-Cell-12)

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