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EFFECT OF SOYA BASED PROTEIN RICH DIET ON GLYCAEMIC PARAMETERS AND THYROID FUNCTION TESTS IN WOMEN WITH GESTATIONAL DIABETES MELLITUS

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Abstract

Background and Aims: *Medical nutrition therapy plays a major role in the management of gestational diabetes mellitus (GDM). However, control of postprandial blood glucose values is often a challenge in Asian Indian GDM women due to high carbohydrate content in Indian diet.* ***Materials and Methods:*** *Women presenting with GDM diagnosis were randomised to high fiber complex carbohydrate diet and soya based protein rich diet (25% of cereal part in the high fiber, complex carbohydrate diet replaced by soya food) groups.* ***Results:*** *At the end of one week after initiation of dietary intervention, patients who received high fiber complex carbohydrate diet (n=30) had significantly higher postprandial blood glucose levels than those who received soya based protein rich diet (n=32). The need for insulin therapy at the end of one week after initiation of dietary intervention (15.62% vs. 40.0%) and at delivery (18.75% vs. 50%) were significantly lower in soya based protein rich diet group. Maternal thyroid function at diagnosis of GDM and delivery and neonatal TSH were not significantly different between the groups.* ***Conclusion:*** *Consumption of soya based protein rich diet reduced the need for insulin therapy in subjects with GDM. Short term consumption of soya food did not alter maternal and neonatal thyroid functions.*

key words: *Gestational diabetes mellitus, medical nutrition therapy, Soya, thyroid functions*

Background and Aims

The incidence of gestational diabetes mellitus (GDM) is increasing globally with higher incidence in Asian women [1]. Use of the newer International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria may increase GDM incidence by 2-3 fold [2]. A recent study from Tamilnadu, India reported GDM in 14.6% of pregnancies by IADPSG criteria [3]. Gestational diabetes mellitus is associated with increased risks of fetal macrosomia, increased need for primary caesarean delivery, neonatal hypoglycaemia and shoulder dystocia [4,5]. Maternal complications associated with GDM include association with pre-eclampsia and future risk of type 2 diabetes mellitus (T2DM) [4,5]. Treatment of mild

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carbohydrate intolerance significantly reduces serious perinatal events, fetal macrosomia, and neonatal hypoglycaemia [6,7].

Control of postprandial glucose levels may be more important due to their stronger association with fetal macrosomia than fasting plasma glucose levels [8]. In a study from Poland, a low carbohydrate diet significantly reduced postprandial blood glucose levels after breakfast [9]. In a pilot study, a higher number (58.4%) of subjects receiving low glycaemic index (GI) diet achieved the target postprandial plasma glucose levels compared to those who received the control diet (48.7%) [10]. Another study demonstrated that the need for insulin therapy was lower (29%) in GDM women receiving low GI diet than those (59%) receiving control diet [11]. Thus, reduction of GI and/or carbohydrate content in the diet helps to achieve normal postprandial blood glucose values in a higher number of women with GDM.

Control of postprandial blood glucose values is often a challenge in Asian Indian patients due to high (70-80%) carbohydrate content in Indian diet [12]. The recommended carbohydrate intake for diabetic patients is 50-60% of total energy. The carbohydrate portion is further restricted for patients with gestational diabetes (38-45%) and thereby allowing more proportion of proteins (20-25%) and fats (30-40%) [13]. A significant proportion of Asian Indian women with GDM are vegetarians (some are vegans) for whom increasing the fat or animal source protein content in their diet is difficult. Moreover, higher fat intake (which often accompanies consumption of animal source proteins) may increase insulin resistance and negatively affect the glycaemic control [14]. On the other hand, Indian diabetics are estimated to consume only 0.6 g/kg/day of proteins and hence, increase in vegetable source protein intake may be more useful [12]. The staple Indian diet often contains multiple sources of carbohydrate at any one meal (*e.g.*, wheat, rice, dhal, in combination) which may be difficult to curtail for pregnant women [15]. So, addition of a vegetable protein source like soya (protein content: 36.5g protein/100g; carbohydrate content: 30g /100g, glycaemic index: 20) into the staple diet is a useful option for management of Indian women with GDM. This is why we designed a new diet plan by incorporating soya into the previously used high fiber complex carbohydrate diet. However, consumption of soya raises a few concerns. Thus, it may alter thyroid functions especially in those with iodine deficiency [16,17]. Soya may also increase thyroid autoimmunity [18].

In this study, we have compared the effects of soya based protein rich diet and high fiber complex carbohydrate diet on glycaemic parameters and thyroid function tests in subjects with gestational diabetes mellitus.

Materials and Methods

This study was conducted at Vydehi Institute of Medical Sciences and Research center, Bangalore, Karnataka. All patients who consulted the department of Endocrinology with the diagnosis of gestational diabetes mellitus between July 2014 and December 2015 were screened and those who consented were recruited for the study. GDM was diagnosed using the IADPSG criteria [19]. The participants were randomised using computer-generated random numbers to a high fiber complex carbohydrate diet group or a soya based protein rich diet group. The study was approved by the institutional ethics committee. Patients with primary hypothyroidism, pre-gestational diabetes and chronic medical illness were excluded from the study.

Both types of diets included a total energy intake of 1600-2000 kCal/day and a minimum carbohydrate intake of 175 g/day. All subjects were advised to take 3 major meals (350-400 kCal) and 3-4 snacks (150-200 kCal). Soya based protein rich diet was same as the high fiber complex carbohydrate diet except for replacement of 25% of the cereal part in each major meal by soya (beans, chunks, granules or flour). Dietary counselling of all patients was done by a single nutritionist at diagnosis and adherence to the suggested diet was ensured at 1-2 weekly intervals. Subjects were instructed to perform self monitoring of blood glucose (SMBG) at least six times a day: before and 2-h after each major meal and those who did not achieve target ranges (pre-meal SMBG < 90 mg/dl and 2-h postprandial SMBG < 120 mg/dl) on more than 3 occasions per week with the same pattern by the end of first week were initiated on insulin therapy.

All subjects underwent thyroid function tests and thyroperoxidase (TPO) antibody tests at diagnosis of GDM, thyroid function tests at monthly intervals thereafter till delivery and TPO antibody at delivery. All neonates born to subjects in both groups were tested for thyroid function between day 3 and day 7 of life.

Statistical analysis Data were represented as mean ± SD or percentages as applicable. Comparison of parameters between two groups was performed using student's independent t test. Comparison of thyroid function tests at GDM diagnosis and at delivery were compared using student's paired 't' test. A p value < 0.05 was considered statistically significant.

Results

There were 32 subjects in the soya based protein rich diet group and 30 subjects in the high fiber complex carbohydrate diet group. The baseline characteristics including age, pregestational weight, weight at diagnosis of GDM, glycaemic parameters at diagnosis [(75-g oral glucose tolerance test (OGTT) values, glycated haemoglobin, SMBG values on the previous day of initiation of medical nutrition therapy (MNT)] were not different between the two groups and are summarised in Table 1.

At the end of one week after initiation of suggested diet, patients who received the high fiber complex carbohydrate diet had significantly higher postprandial blood glucose levels than those who received soya based protein rich diet (Table 2). Fasting and pre-meal blood glucose values although tended to be lower in the soya based protein rich diet group but they did not differ significantly from those of high fiber complex carbohydrate diet group (Table 2).

In the high fiber complex carbohydrate diet group, 12 (40%) subjects failed to achieve the glycaemic targets compared to four (12.5%) subjects in the soya based protein rich diet group. In addition, one patient in the soya based protein rich diet group, although achieving glycaemic targets, complained of intolerance (nausea and increased flatulence) to the diet and preferred to receive insulin. Thus, at one week after diagnosis, 12 (40%) patients in the high fiber complex carbohydrate diet group and five (15.62%) patients in the soya based protein rich diet group received insulin therapy.

Weight gain from the diagnosis to delivery and the weight at delivery were not significantly different between the groups (Table 3). The glycaemic parameters were also not different between the groups at delivery (Table 3). At the time of delivery, 15 (50%) patients had received insulin therapy in the high fiber complex carbohydrate diet group compared to six (18.75%) in the soya based protein rich diet group.

All mothers in the soya based protein rich diet had live births with twin delivery in one mother whereas one mother in the high fiber complex carbohydrate diet had a stillbirth. Birth weight of the neonates, although lower in soya based protein rich diet group, did not differ significantly from that in high fiber complex carbohydrate diet group. The prevalence of large for gestational age, shoulder dystocia and neonatal hypoglycaemia requiring IV infusion were not different between the groups (Table 3). There was no significant difference between the two groups with respect to neonatal TSH. None of the neonates in either group had TSH > 15 μIU/ml.

Table 1. Baseline characteristics of subjects in the two different groups.

	Soya based protein rich diet group (n=32)	High fiber complex carbohydrate group (n-30)	P value
Age (years)	29.43±2.98	29.17±3.38	0.740
Weight (kg)	69.95±5.95	69.89±5.64	0.962
Gestational age (weeks)	25.19±1.92	25.56±1.69	0.413
Gravida (1/≥2)	14/18	16/14	0.61
Fasting plasma glucose (mg/dl) in OGTT	104.00 ± 13.74	107.76 ± 13.10	0.274
1-h plasma glucose (mg/dl) in OGTT	213.12 ± 21.59	214.56 ± 21.89	0.795
2-h plasma glucose (mg/dl) in OGTT	167.06 ± 22.03	170.36 ± 20.39	0.542
Fasting SMBG (mg/dl)	102.81 ± 11.41	103.40 ± 11.95	0.844
2-h after breakfast SMBG (mg/dl)	164.31 ± 26.92	167.03 ± 24.95	0.681
Before lunch SMBG (mg/dl)	100.12 ± 13.78	102.00 ± 13.06	0.584
2-h after lunch SMBG (mg/dl)	158.56 ± 21.98	164.16 ± 20.56	0.304
Before dinner SMBG (mg/dl)	100.31 ± 11.37	101.34 ± 11.26	0.720
2-h after dinner SMBG (mg/dl)	167.75 ± 25.54	170.73 ± 23.61	0.634
Glycated hemoglobin (%)	5.91 ± 0,24	5.93 ± 0.23	0.776

Table 2. Glycemic parameters and proportion of patients receiving insulin therapy during second week after initiation of therapeutic diets.

	Soya based protein rich diet group (n=32)	High fiber complex carbohydrate group (n-30)	P value
Fasting SMBG (mg/dl)	89.86 ± 7.31	93.41 ± 6.99	0.056
2-h after breakfast SMBG (mg/dl)	111.90 ± 10.44	123.98 ± 16.15	0.001
Before lunch SMBG (mg/dl)	89.68 ± 9.54	94.26 ± 9.16	0.058
2h-h after lunch SMBG (mg/dl)	114.48 ± 14.30	127.80 ± 20.30	0.005
Before dinner SMBG (mg/dl)	88.52 ± 10.34	93.79 ± 10.43	0.051
2-h after dinner SMBG (mg/dl)	116.14 ± 16.06	130.87 ± 22.39	0.005
Number of subjects requiring insulin therapy	5 (15.62%)	12 (40%)	0.046

Free T3, free T4 and TSH at GDM diagnosis were not different between the groups. These thyroid function parameters were also not different between the groups at delivery (Table 4). Within the soya based protein rich diet group, thyroid function tests at diagnosis and delivery were not significantly different. Two patients in each group had a TSH > 3 µIU/ml (3-6 µIU/ml) during follow-up visits and received thyroxine supplementation till delivery. Follow-up evaluation of these four patients during postpartum period revealed a TSH of < 4 µIU/ml in all. At baseline three patients in the soya based protein rich diet group and two in the high fiber complex carbohydrate group had positive thyroid peroxidase autoantibodies. None of the remaining subjects in either group turned positive for TPO antibodies at delivery.

Table 3. Maternal characteristics at delivery, mean glycemic parameters during last week prior to delivery and early neonatal characteristics of off-springs in two different groups.

	Soya based protein rich diet group (n=32)	High fiber complex carbohydrate group (n-30)	P value
Gestational age at delivery(weeks)	37.37±2.22	37.23±2.11	0.798
Weight change from GDM diagnosis (kg)	6.36±1.23	6.81±1.68	0.230
Weight at delivery (kg)	76.06±5.80	76.7±4.97	0.643
Mode of birth (Vaginal/LSCS)	26/6	23/7	0.76
Fasting SMBG (mg/dl)	83.91 ± 3.52	85.53 ± 3.53	0.076
2-h after breakfast SMBG (mg/dl)	108.78 ± 7.13	112.55 ± 14.49	0.215
Before lunch SMBG (mg/dl)	86.80 ± 4.51	87.56 ± 4.80	0.526
2-h after lunch SMBG (mg/dl)	112.81 ± 4.53	113.25 ± 4.73	0.710
Before dinner SMBG (mg/dl)	84.72 ± 2.86	85.79 ± 3.60	0.204
2-h after dinner SMBG (mg/dl)	113.79 ± 4.80	113.74 ± 4.86	0.967
Glycated hemoglobin (%)	5.43 ± 0.13	5.46 ± 0.13	0.513
Need for insulin therapy	6 (18.75%)	15 (50%)	0.015
Birth weight (kg)	2.86±3.07*	3.07±0.39	0.05
Large for gestational age	1 (3.03%)*	2 (13.3%)	0.601
Shoulder dystocia	1 (6.25%)*	1 (10%)	1.00
Neonatal hypoglycemia	1 (3.03%)*	2 (13.3%)*	0.595
Neonatal TSH	8.14±3.33	8.01±3.2	0.866

*n=33 for neonates in the soya based protein rich diet group since one mother gave birth to a twin babies and n=29 for neonatal hypoglycemia analysis in the high fiber complex carbohydrate group since one mother had a stillbirth.

Table 4. Thyroid function tests at diagnosis of GDM and at delivery in the two groups.

	Soya based protein rich diet group (n=32)	High fiber complex carbohydrate group (n-30)	P value
Free triiodothyronine at diagnosis (ng/ml)	2.51±0.51	2.43±0.53	0.563
Free thyroxine at diagnosis (ng/dl)	0.83±0.11	0.84±0.11	0.841
Thyroid stimulating hormone at diagnosis (µIU/ml)	1.74±0.72	1.96±0.65	0.214
Free triiodothyronine at delivery (ng/ml)	2.57±0.47	2.52±0.47	0.707
Free thyroxine at delivery (ng/dl)	0.81±0.11	0.83±0.11	0.594
Thyroid stimulating hormone at delivery (µIU/ml)	2.15±1.03545	2.10±1.03	0.838

Discussion

This is the first study that demonstrates that soya based protein rich diet significantly improves the glycaemic parameters at the end of first week of MNT compared to control diet. Higher number of subjects in the soya based protein rich diet achieved target ranges, especially for postprandial glucose levels. Hence, the need for insulin treatment was significantly lower in the soya based protein rich diet group. Although low carbohydrate diet reduced the postprandial plasma glucose values after breakfast in a study from Poland, the results were not supported by other studies [9,20]. The benefits of low GI diet have consistently been reproduced by a few studies [10,11,21]. A recent systematic review has concluded that it is not the reduction of carbohydrate content in diet that reduces the need for insulin but low GI diet [22]. Hence, it is likely that the reduced need for insulin therapy in soya based protein rich diet group is largely due to its effect on reduction in GI of the diet.

The proportion of GDM women who need insulin therapy varies from 13% to 65.1% [22]. In a recent community based Indian study, only 9.7% of GDM women required insulin therapy [23]. Higher need for insulin therapy in both of our study groups is likely to be due to referral bias, with only those GDM women with relatively higher hyperglycaemia getting referred to our center. In another Indian study in which GDM was diagnosed using the older ADA criteria with baseline glycaemia comparable to that of our cohort, 65.5% of GDM women required insulin therapy [24].

There was no effect of soya based protein rich diet on thyroid function tests of the mother. Studies have reported variable results on the effect of soya on maternal thyroid functions [17]. Earlier it was suggested that excessive soybean ingestion may cause goiters in healthy people, depending on the duration of the treatment [16]. However, later studies did not support these results. A study in postmenopausal women reported that the consumption of isoflavones for three years did not affect the thyroid functions [25]. A recent review concluded that in euthyroid, iodine-replete individuals, soy foods, or isoflavones do not adversely affect thyroid function [17]. Although iodine status in our subjects was not estimated, pregnant women from Bangalore are considered as iodine sufficient [26]. However, in iodine deficient areas women receiving soya based diet should be supplemented empirically with iodine. Soya consumption may increase the prevalence of thyroid autoimmunity due to alterations in the structure of thyroid peroxidase [27]. A study in infants who were fed on soy feeds, had higher incidence of developing thyroid autoimmunity during adolescence [18]. Interestingly, a study of soya consumption up to more than three times per week in pregnant women has been proven to be safe with no effect on thyroid functions or thyroid autoimmunity [28]. In our study also, there was no effect of soya based protein rich diet on maternal thyroid function tests and TPO antibodies. Consumption of soya during pregnancy may have additional benefits. It decreases rates of eczema at six months in their off-springs [29]. Moreover, fermented soya consumption during pregnancy helps to circumvent the further decrease of iron status among iron-deficient pregnant women [30]. However, larger studies are required to demonstrate the safety of long term consumption of soya food on maternal thyroid functions, thyroid autoimmunity and thyroid functions and neurodevelopmental outcomes in the off-springs.

Conclusions

Significantly greater proportion of GDM women achieved target postprandial blood glucose levels at the end of one week after initiation of a diet rich in soya based protein compared to women who consumed a high fiber complex carbohydrate diet. The need for insulin therapy was significantly lower in the soya based protein rich diet group at the end of one week after initiation of dietary intervention as well as at delivery. Short term consumption of soya based protein rich diet did not alter maternal thyroid functions. However, larger, long term studies are required to ensure the lack of negative effects of soya on thyroid functions.

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