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Case report

Complementary therapy of traditional Chinese medicine for blood sugar control in a patient with type 1 diabetes

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ABSTRACT

Objective: Using a case study to discuss the effects of traditional Chinese medicine (TCM) treatments on Type 1 diabetes mellitus.
Clinical features: A 4-year-old girl with sudden polyuria and nocturia (fasting plasma glucose level: 270 mg/dL) was diagnosed with type 1 diabetes. Although multiple daily insulin injections were applied, her plasma glucose levels were still unstable. Therefore, she received a complementary TCM therapy by taking modified Liu-Wei-Di-Huang-Wan (3.0 g/day; three times daily) for 3 months. After the treatments, her plasma glucose levels appeared to be more stable. HbA_{1c} 6.5% and insulin injections were reduced to only once a day.
Conclusions: The results suggest that complementary TCM therapy has the ability to assist some patients with type 1 diabetes mellitus in controlling their plasma glucose levels.

1. Introduction

Type 1 diabetes is a disorder in which autoimmune destruction of pancreatic β-cells leads to absolute insulin deficiency. This form of diabetes accounts for 5–10% of all diabetes patients.[1] Type I diabetes is often diagnosed in children and early adolescents. On average, about 50%–60% patients are younger than 18 years old. American Diabetes Association (ADA) diagnostic criteria for diabetes mellitus[2,3] include fasting plasma glucose level ≥ 126 mg/dL or 7 mmol/L under no caloric intake for ≥8 h, hemoglobin A1c (HbA1c) ≥ 6.5%, 2-h plasma glucose ≥ 200 mg/dL (11.1 mmol/L) during an 75-g oral glucose tolerance test (OGTT), or classic symptoms of hyperglycemia or hyperglycemic crisis with a random plasma glucose ≥ 200 mg/dL(11.1 mmol/L). Common symptoms of hyperglycemia include polyuria, polydipsia, blurred vision etc., but marked hyperglycemia is also accompanied by impairment of growth and susceptibility to certain infections associated with chronic hyperglycemia. Diabetes self-management focuses on glycemic control through measuring HbA1c concentrations. Decrease in HbA1c concentrations is associated with lower risk of onset or progression of complications, such as microvascular diseases (e.g., retinopathy, nephropathy, and neuropathy), and macrovascular diseases (e.g., cardiovascular, cerebrovascular, and peripheral vascular disease etc).[4]

The Diabetes Control and Complications Trial (DCCT) showed that intensive insulin therapy (multiple-dose insulin (MDI) injections (three to four injections of basal and prandial insulin per day), continuous subcutaneous insulin infusion (CSII), or insulin pump therapy) can have positive effects on glycemia and type 1 diabetes.[2] In this study, therapy was carried out with short- and intermediate-acting human insulins. But in spite of positive microvascular outcomes, intensive insulin therapy was positively associated with severe hypoglycemia. Therefore, glycemic control, patients self-monitoring of blood glucose (SMBG) or interstitial glucose, and A1C, is important.[2] Three-quarters of all cases of type 1 diabetes are diagnosed in individuals who were younger than 18 years old. Insulin sensitivity changes in children and adolescents with type 1 diabetes because of the following reasons: sexual maturity and physical growth, ability to provide self-care, neurologic

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Table 1
ADA recommendations of plasma blood glucose and A1C goals for type 1 diabetes by age-group.

Age(years)	Plasma blood glucose goal range (mg/dL)		HbA1c
	Before meals	Bedtime/overnight	
0–6	100–180	110–200	8.5%
6–12	90–180	100–180	8%
13–19	90–130	90–150	7.5%

vulnerability to hypoglycemia, and DKA. Therefore, ADA suggested that glycemic goals[2] need to be adjusted according to age and the risk of developing severe hypoglycemia. Its sequelae also need be taken into account (Table 1).

Diabetes Mellitus is similar to *Xiaokezheng* in traditional Chinese medicine (TCM), which results from over consumption of yi fluid leading to production of endogenous heat in the body. Therefore, the clearing heat and engendering fluid method is used to treat Xiaokezheng.[5] It has been well documented that many Chinese herbs, such as *Radix Puerariae*, *Radix Ginseng* etc., may have hypoglycemic effects, and the effects may be mediated via multiple pathways including increasing insulin sensitivity or insulin secretion.[6]

TCM is popular in Taiwan. It has been covered by the national health insurance since 1996. According to statistics, more than 60% Taiwanese used TCM between 1996 and 2001 in Taiwan,[7] and approximately 14.1% used both Chinese herbs and conventional western medicine concurrently.[8] TCM usage in childhood is about 22%.[9] This research reported a case of a child with type 1 diabetes who concurrently used TCM and western medicine to improve plasma glucose sugar levels.

2. Case report

A 4-year-old girl, who was a healthy and active child, was found malaise appearance, poor activity, poor attention, nocturnal enuresis, polyuria and polydipsia without polyphagia by her family. On May 26, 2013, her family noted that there were ants around stool-bucket after her urination. Therefore, she was carried to an outpatient department (OPD) of a medical center in Southern Taiwan. Laboratory examinations showed that her plasma blood sugar was 270 mg/dL. Type1 Diabetes mellitus was diagnosed and she was then hospitalized. The doctor used regular insulin (Actrapid HM Penfill) and NPH (Insulatard HM Penfill) 5U (daytime) (twice injection a day) to control hyperglycemia. The fasting plasma blood sugar levels ranged from 58 to 452 mg/dL during her hospitalized period from May 26 to June 3 2013 (Table 2). She received antidiabetic treatment by using adjusted doses of regular insulin and NPH injection twice a day in OPD after discharge (Table 3).

She visited our clinic in search of a complementary treatment of TCM for controlling her plasma glucose levels on June 5, 2013. During our four examinations of TCM, the patient appeared to be thin and her lip was reddish color. Her activity was weak and she tended to stay in her mother's arm. Tongue body was tender-soft and red. Tongue fur was thin and white, and most of the furs located on the top of tongue. The pulse was sting-like, quick and soggy. The cubital skin was hot upon touch examination. Together, the patient was categorized as "dual deficiency of qi and yin with internal heat" according to TCM pattern. Thus, the Chinese medical doctor used Liu-Wei-Di-Huang-Wan (3.0 g/day; SUN TEN PHARMACEUTICAL CO.,LTD), a formula of TCM granules, which consists of Shu-Di-Huang (*Radix Rehmanniae Praeparata*), Shan-Zhu-Yu (*Fructus Corni*), Shan-Yao (*Rhizoma Dioscoreae*), Mu-Dan-Pi (*Cortex Moutan*), Fu-Ling (*Poria*) and *Ze-Xie (Rhizoma Alismatis*), together with Huang-Qi (*Radix Astragali*; SUN TEN PHARMACEUTICAL CO.,LTD) 0.3 g/day, and Tian-Hua-Fen (*Trichosanthis Radix*; SUN TEN PHARMACEUTICAL CO.,LTD) 0.2 g/day, three times daily, to control her levels of plasma of glucose (Table 4). The serum glucose became acceptable based on plasma blood glucose goal range for type 1 diabetes by age groups, after Liu-Wei-Di-Huang-wan treatment for 23 days (from 5 to June 27, 2014). We can see the frequency of plasma blood glucose over 180 (mg/dL) decline (52%, before TCM treatment, 34.3%, after 7-days TCM treatment, 14.2%, after 14-days TCM treatment, 12.5%, after 22-days TCM treatment). (Table 5) Furthermore, western medical doctors changed regular insulin and NPH injection from twice a day to qd (one time per day) after 11-days TCM treatment, and continued to reduce the dose (Table 3). After 3 month of combined treatment, HbA1C is 6.5% (Table 3).

3. Discussion

Type 1 diabetes is usually associated with premature mortality due to both acute and chronic complications, such as renal complications and cardiovascular disease, in spite of the advances in diabetes care.[10] A decrease in chronic complications of diabetes during the first 20 years of diabetes can help explicate the better survival rate for patients with the early onset (age 0–14 years) type 1 diabetes.

HbA1c $\geq$ 10.5%[11] was found to be associated with increased risks of heart failure in patients with type 1 diabetes. Also, microalbuminuria[12] was associated with the risk of developing nephropathy. Importantly, both of them will be reduced remarkably with an ideal blood glucose levels control. Therefore, how to control as an ideal blood glucose level is critical. This study also argued that HbA_{1c} levels can be used as an indicator to evaluate the state of blood glucose levels.[11] However, despite better microvascular outcomes, intensive insulin therapy was positively associated with the rate of developing severe hypoglycemia. Notably, most children couldn't react to or were unaware of hypoglycemic symptoms. This places them at greater risk of severe hypoglycemia and its sequelae.

Table 2
Fasting plasma glucose levels during admission period (mg/dL).

TIME DATE (2013)		3:00	8:00	12:00	18:00	22:00	Insulin Injection	Time and DOSE
							12:20	18:30
5/26	5/27	283	120	161	58	236	RI:3U NPH:5U	RI:2U NPH:2U
5/28		198	267	282	217	186	RI:3U NPH:5U	RI:1U NPH:2U
5/29		75	220	124	204	317	RI:3U NPH:5U	RI:1U NPH:2U
5/30		80	298	294	183	89	RI:3U NPH:5U	RI:1UNPH:1.5U
5/31		130	254	60	209	259	RI:3U NPH:5U	RI:1UNPH:1.5U
6/1		452	308(R,9:00)	328	87 (R,19:00)	286	RI:3.5UNPH:6U	RI:1UNPH:1.5U
6/2		343	239	246	115(R,19:00)	124	RI:3.5UNPH:6U	RI:1UNPH:1.5U
6/3		69					RI:3U NPH:6U	RI:1UNPH:1.5U

3:00: 3 am; 8:00: 8 am; 12:00: 12:00 P.M.; 18:00: 6:00 P.M.; 22:00: 10:00 P.M.; insulin injection executed at 12:20 pm and 18:30.
RI: regular insulin; NPH: NPH insuln; R: Random plasma glucose test.

Table 3
Fasting plasma glucose test in the outpatient door after discharge (unit:mg/dL).

TIME Date(2013)	3:00	8:00	12:00	18:00	22:00	Insulin Injection	Time & Dose
						9:00	18:30
Before TCM intervention							
6/3	70	180	91	270	185	RI:3U	RI:1U
6/4				170	132	NPH:6U	NPH:1.5U
						RI:4U	“
						NPH:6U	
After TCM intervention							
6/5	236	254	133	184	88	“	“
6/6	261	274	197	98	165	“	“
6/7	371	312	115	228	368	RI:2U	RI:1.5U
6/8	148	168	73	86	180(R)	(I, 10:00)	NPH:1.5U
						RI:4U (8:30)	RI:1U
						NPH:6U	NPH:1.5U
6/9	125	143	71	83	87(R)	“	“
6/10	82	366	67	247	80	RI:4U (8:30)	RI:1.5U
						NPH:6U	NPH:1.5U
6/11	193	172	115	79	102	RI:4U (8:30)	RI:1U (19:00)
						NPH:6U	NPH:1.5U
6/12	219	120	75	249	156(R)	RI:3U	RI:1U (19:00)
						NPH:5.5U	NPH:1.5U
6/13	71	112	46	233	100	“	“
6/14	273	183	75	90	98	RI:3U	RI:1U
						NPH:5U	NPH:1.5U
6/15	176	105	66	78	172	RI:3U	
						NPH:5U	
						Only one time insulin use left due to resonable serum glucose	
6/16	113	137	175	66	223	RI:2U (9:00)	NPH:4U
6/17	85	141	92	73	205	“	
6/18	97	141	156	76	151	“	
6/19	71	93	142	140	173	“	
6/20	122	119	146	87	130	RI:2U (10:30)	NPH:4U
6/21	70	100	148	52	116	“	
6/22	97	97		162	321	RI:2U (10:30)	NPH:3U
6/23	233	72		70	98	“	
6/24	128	138	95	65	193	“	
6/25		120		64	131	“	
6/26		112		157	196	RI:2U	NPH:2.5U
6/27		110		118	151	“	
9/3	HbA1c:6.5%						

3: Fasting plasma glucose test at AM 3:00.
8: Fasting plasma glucose test at AM 8:00.
18: Fasting plasma glucose test at PM 18:00.
22: Fasting plasma glucose test at PM 22:00.
AC: Fasting plasma glucose test.
R: Random plasma glucose test.
I:Injection time.
“:the same with the former dose.
TCM: Traditional Chinese Medicine.
BID: insulin injection twice per day.
QD: insulin injection once per day.

Research has demonstrated that TCM has positive effects on type 1 diabetes.[13,14] This research presented the first case that uses complete plasma glucose recordings to illustrate the effects and safety of Liu-Wei-Di-Huang-Wan adjunctive treatment. According to a TCM theory, symptoms and signs, such as a thin body contour, low weight, a preference for ice, a red lip, red tongue with peeling fur and rapid pulse, can lead to the diagnosis of “deficiency of yin with internal heat” pattern. Sitting up late may aggravate this pattern. The visceral manifestation theory of TCM suggests that type 1 diabetes usually happens at young age,[2,3] and the pattern of constitutional insufficiency at birth is called “kidney deficiency.” This is because the root of innate endowment comes from kidney. Therefore we chose Liu-Wei-Di-Huang-Wan to be the major formula to treat the patient and also used Tian-Hua-Fen to resolve the spleen heat (usually appearing in “wasting-thirst”, the Chinese medicine domain which diabetes belong to). Heat on her skin can explain this, because muscles belong to spleen according to TCM theories. Also, some symptoms such as poor activity and a tender-soft tongue with a soggy and soft pulse imply “deficiency of qi”. Therefore, we added Huang-Qi (Radix Astragali) to tonify qi. In addition, previous studies also showed that intervention[15] or prevention of astragalus polysaccharide (APS) can lower the incidence of diabetes, the degree of the lymphocytic inflammation of pancreatic islets.[16]

It should also be noted that a so-called honeymoon or remission period would take place soon after clinical diagnosis and initiation of insulin therapy. It refers to reduced exogenous requirement because the remaining functional beta cells secrete some endogenous insulin.[17] But the incidence rates of remission and duration of remission vary. Multiple factors, such as the C-peptide level, serum bicarbonate level at the time of diagnosis, duration of Type 1 diabetes mellitus symptoms, HbA1C levels at the time of diagnosis, sex, and age, could influence the remission rates and duration. However, they are still questionable because the mechanism of remission is not clearly understood. The honeymoon phase would not appear on every person. These jointly indicate that our TCM may play a role in stabilizing glycemic levels, and protecting insulin secretion.

This case report has a number of limitations. First, the herbal formula used in this case was strictly for the “dual deficiency of qi

Table 4
Ingredients and dosages of the prescribed TCM herbal formula and single herbal granules.

Chinese name	Scientific name	Dosages (g)
Liu-Wei-Di-Huang-Wan (3 g of concentrated herbal formula contain the following raw herbs)		
Shu-Di-Huang	*Radix Rehmanniae Praeparata*	0.77 g
Shan-Zhu-Yu	*Fructus Corni*	0.38 g
Shan-Yao	*Rhizoma Dioscoreae*	0.38 g
Mu-Dan-Pi	*Cortex Moutan*	0.29 g
Fu-Ling	*Poria*	0.29 g
Ze-Xie	*Rhizoma Alismatis*	0.29 g
Single herbal granules (0.3 g of concentrated herbal granules contain the following raw herbs)		
Huang-Qi	*Radix Astragali*	0.5 g
Single herbal granules (0.2 g of concentrated herbal granules contain the following raw herbs)		
Tian-Hua-Fen	*Trichosanthis Radix*	0.35 g

Table 5
The frequency of plasma blood glucose over America Diabetes Association-considered glycemic goals in 0–6-years children.

Date	Stage	The frequency of plasma blood glucose over 180 mg/dL
5/27–6/5	Before TCM use	52%
6/6–6/12	During 7-days TCM use	34.3%
6/13–6/19	During 14-days TCM use	14.2%
6/20–6/27	During 22-days TCM use	12.5%

and yin with internal heat". Second, more time should be allowed to observe the change of plasma glucose in order to exclude the honeymoon phase. Moreover, the findings of a single case cannot be generalized; further evaluation of experimental clinical trials is needed.

Regardless of the limitations, this research argued that it may be beneficial to patients to receive care from both the pediatrics and TCM. TCM may be helpful to some degree and the possible adverse risks could be monitored by pediatricians.

4. Conclusion

We reported a successful case of using complementary and alternative therapy to treat Type 1 diabetes mellitus. The results of this case provide an alternative option and warrant further studies of TCM for treatment of Type 1 diabetes mellitus.

Conflict of interest

The authors declare that they have no conflict of interest.

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