The research for the clinical curative effect through combing traditional Chinese medicine with insulin to cure diabetes

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Abstract: The clinical curative effect is observed through curing type 2 diabetes mellitus with the therapy of combing Traditional Chinese Medicine (TCM) with insulin. Method: Both the insulin prescription and the treatment of traditional Chinese medicine prescription are applied as mutual comparison. And the dosage, time, blood sugar level and curative effect etc are recorded. Healthy human body is taken as comparison for monitoring physical indicators. Results: Through comparing insulin prescription and the combing therapy of insulin and traditional Chinese medicine, the insulin treatment group is better than contrast group ($P<0.05$). For the blending use group, the ISI in each group is significantly lower than that of health control group ($P<0.01$), where accumulation of damp heat in spleen type is the lowest; the BM I, H bA1C of type 2 diabetic patient is higher than health control group, its accumulation of damp heat in spleen type is the highest, TC, TG typical accumulation of damp heat in spleen are higher than other pattern of syndrome. Conclusion: the treatment method of combing TCM with insulin in curing type 2 diabetes mellitus has better effect than using insulin treatment alone; the resistance degree of insulin demonstrates the changing trend of first increase and later decrease with the development of disease course. Accumulation of damp heat in spleen type accounts for the highest proportion in type 2 diabetic patients, and there exists serious insulin resistance.

Keywords: Type 2 diabetes, insulin resistance, traditional Chinese medicine (TCM), TCM syndrome type

INTRODUCTOIN

With the improvement of living standards, especially the popularity of western fast food, bad living habits such as high fat diet, high-calorie diet and so on, it has resulted into abnormal glucose tolerance, lipid metabolic disorder, central obesity and other increasing phenomenon of insulin resistance, then the metabolic syndrome, type 2 diabetes and other diseases follow, so we know type 2 diabetes is the basic characteristics of insulin resistance throughout the whole course of disease. Beforehand, the blending use of traditional Chinese medicine and insulin has been studied in China. Jiarui Wang doctor has proposed that the method of combing traditional Chinese medicine with insulin could be used to cure Type 1 Diabetes in 'cases analysis of curing Type 1 Diabetes through combing traditional Chinese medicine and insulin' (Wang, 2007), Jianghong Xu etc have studied the resistance influence of insulin and the prevention therapy of diabetes mellitus in 'the clinical effect of curing type 2 diabetes mellitus through combing auricular acupuncture and traditional Chinese medicine' (Xu, 2009), as well as its influence on insulin resistance; Zhiming Wang etc think that it has the effect of nursing liver and discharging fire, regulating qi-blood viscera, balancing Yin, Yang and Shui, Mu. They first proposed the theory of curing IR with 'diagnosis and treatment from liver' (Wang, 2006); Yunsheng Xu etc think that IR path mechanism and abnormal lipid metabolism are closely related with spleen deficiency (Xu, 2004), phlegm and blood stasis in traditional Chinese medicine and Pancreatic Su Ling treatment of type 2 diabetes mellitus has the significant effect of tonifying spleen, reducing phlegm and invigorating the circulation of blood. From October 2012 to January 2013, Hospital of traditional Chinese medicine in Shaoxing city of Zhejiang province had made good curative effect in curing patients with type 2 diabetes through adding with the Chinese medicine medicinal broth therapy on the basis of insulin therapy, now report as follows.

This paper involves two experiments, both clinical cases are in accordance with western medicine and TCM diagnosis standards and eliminate serious primary diseases such as acute complications of diabetes, cardiovascular, liver, kidney and malignant tumor etc.

Clinical data

(1) There are 152 cases of hospitalized patients with type 2 diabetes in total in the hospital, they were randomly divided into treatment and control groups, with each group has 76 cases. In treatment group, there are 48 cases of male, 28 cases of female, who are aged between 48 and 66 years of age, disease course is 0. 5~5 years, and their average course is 2.5 years; there are 35 cases of male and 41 cases of female, their age is between 47 and 68, the course is 1 ~ 6 years, its average course is 3. 5 years in the control group. Both groups have main clinical manifestations of being thirsty to drink, too much eating for hunger, frequent urination with much quantity, fatigue strength. Two groups of clinical data are comparable.

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(2) There are 180 cases of disease in the collection. Among them, 86 cases were male, 96 cases are female, and they are aged between 41and 78 years old. There are 52 cases of Yin deficiency and dryness-heat type, accumulation of damp heat in spleen type has 96 cases, Yang deficiency and dampness stasis type has 32 cases.

Selection criteria of 60 cases in normal control group: physical examination should pass through the detailed medical chest X-ray and inspection of electrocardiogram, blood in urine routine, blood sugar, liver and kidney function, the physical and chemical examination and then they are evaluated to have no major diseases of organ systems and substantial lesions, obvious functional disease in heart, brain, liver, kidney, lung and endocrine system as well. TCM syndrome differentiation demonstrates no partial failure of Yin and Yang. Among them, there are 32 cases of male and 28 cases of female.

Diagnostic criteria

Medical diagnostic criteria: according to the diabetes diagnosis and classification standard recommended by the 1999 world health organization (WHO) (Tong *et al.,* 2011): (1) with diabetes symptoms + any plasma glucose concentration ≥11.1m mol/L. "Any" is defined as any time of day, regardless of the last meal time. The typical symptoms of diabetes include polyuria, polydipsia and unaccountability of declining body quality. (2) FPG≥7.0m m ol/L. Fasting is defined as being with no calorie intake at least 8h. (3) During OGTT, 2h PG≥11.1m mol/L. The experiment should be carried out in accordance with the description in WHO, the use of glucose load should contain the equivalent of 75g anhydroglucose which would be dissolved in water. The question of whether it is in another day and the diagnostic criteria would be confirmed through repeated experiments.

Diagnosis and syndrome differentiation of TCM is with reference to the related content in "guiding principles of clinical research for Chinese new medicine" (Liu *et al.,* 2009) (trial), type 2 diabetes can be divided into Yin deficiency and dryness-heat type, Accumulation of damp heat in spleen type, Yang deficiency and dampness stasis type through combining with clinical type, the diagnosis of syndrome differentiation standard is as follows: (1) Yin deficiency and dryness-heat type: Dry throat and mouth, upset mood and fearing hot, too much drink and food, constipation, reddened tongue, yellow coated tongue, fine and thin pulse. (2) Accumulation of damp heat in spleen type: thoracic and abdominal distension, or full eating, trapped heavy head and body, fat body, depressed mind, lassitude, yellow urine, terrible stool, red tongue, yellow and greasy coated tongue, slippery and rapid pulse. (3) Yang deficiency and dampness stasis type: frequent urine, lumbar debility, fearing cold, cyanoderma lip and nail, limb numbness, body weight of abdominal distension, light red tongue with petechiae, greasy coated tongue, deep and hesitant pulse.

Treatment method

(1) The control group is treated with insulin, specific usage: patients are given subcutaneous injection of 30 R Novolin before breakfast and lunch. The treatment group is added with self proposed drugs on the basis of control group's therapy: 18g *rhizoma anemarrhenae,* 6g *chicken's gizzard-membrane*, 4.5g *radix puerariae*, 9g *radix trichosanthis*, 9g *inseng*, 9g *warf lilyturf*, 6 g *schisandra*, 12 g *pulp of dogwood fruit*, 12g *Chinese yam*, 9 g *rhizoma alismatis*, 9g *cortex moutan*, 9g *poria cocos*, 30g *radix rehmanniae*, 30g *astragalus membranaceus*, 5g *rhizoma coptidis*, 5g *prepared rhubarb*, 15g *euonymus alatus*. Each patient is given 1 dose for 1 day. The medicinal materials are added with 800m water for decoction, its 300 ml medicine juice will be taken orally for twice a day, with each 150ml. Both groups are given continuous administration for 2 weeks in a course of treatment. The pre-dinner and postprandial blood sugar, as well as blood sugar before sleep would be measured every 3 days, by which to adjust the dose of insulin. The target value of lucose (GOD method) is pre-dinner peripheral blood glucose (FPG) <6.1mmol/L, peripheral blood sugar of 2 hours after meal (2hPG) <7. 8 mmol/L.

(2) The general condition of selected patients (name, gender, age, course of disease, height, body mass, etc.) will be collected. The patients' indicators of fasting blood glucose (FPG), 2 h postprandial blood sugar (PPG), triglycerides (TG), total cholesterol (TC), fasting insulin (FINS), glycosylation hemoglobin (H bA1C) etc would be checked after being hospitalized, and the body mass index (BM I) and insulin sensitive index (ISI) will be calculated, the calculation of ISI is performed with the method introduced by Li Guangwei etc (Zhou *et al.,* 2009) which is the reciprocal of product of fasting glucose and insulin, as it is of the non-normal distribution, so the analysis is to apply the negative natural logarithm, namely ISI=-In (FPG×FINS), the unit of blood glucose is mmol/L, the unit of insulin is m Iu/L.

STATISTICAL METHODS

The counting data is denoted with case number, the measurement data is denoted with $\bar{x} \pm s$. Two groups of measuring data are compared, t-test is applied in normal distribution; rank sum test is applied in abnormal distribution. 2 tests are applied in groups of counting data, Person correlation analysis is applied in single correlation analysis. When it is applied with SPSS13.0 software package, the significance level is defined with $P < 0.05$.

The results of experiment one

Criterion of Therapeutical Effect

Representing effect: peripheral blood sugar before meal (FPG) <6. 1mmol/L, Peripheral blood sugar 2 hours after meal (2hPG) <8.0mmol/ L. Effect: FPG 6.1~7.0 mmol/L,

2hPG 8.0~10mmol/L. Ineffectiveness: FPG >7.0 mmol/L, 2hPG > 10mmol/L.

RESULTS

The curative effect of treatment group is better than that of control group, as shown in table 1. When two groups of blood sugar attain the effect, the insulin (Kim *et al.,* 2012) used in treatment group has reduced 20% than control group, treatment days and the frequency of hypoglycemia is lower than the control group. The difference was statistically significant, as shown in table 2.

Table 1: Curative effect comparison between two groups

Grouping	N case	Demonstrating effect	Effect	ineffectiveness	Total effective rate (%)
Treatment group	76	50	18	8	89.47
Control group	76	24	28	24	69.42

Table 2: Comparing the indicators for the two groups before and after treatment (x±s)

Grouping	N case	Insulin dosage/(U/d)	Hypoglycemia (time/person)	Total treatment days/day
Treatment group	76	20.0±9.5	0.8±0.3	9.0±3.5
Control group	76	28.7±10.8	1.4±0.9	20.6±4.5

Compared with control group, P<0.05 ， P<0.01.

Table 3: The TCM syndrome distribution of 180 patients with type 2 diabetes

TCM syndrome	Case number	Constituent ratio (%)
Yin deficiency and dryness-heat type	52	28.9
Accumulation of damp heat in spleen type	96	53.3
Yang deficiency and dampness stasis type	32	17.8

Table 4: Changes of age and duration in patients with type 2 diabetic of different TCM syndrome type ($\underline{x}$ ±s)

TCM syndrome	Case number	Age (year)	Duration (years)
Yin deficiency and dryness-heat type	52	47.82±9.68	3.02±1.43
Accumulation of damp heat in spleen type	96	50.91±9.01	4.68±3.68
Yang deficiency and dampness stasis type	32	60.22±8.79	10.75±2.16

Note: compared with Yin deficiency and dryness-heat type, P<0.01; compared with accumulation of damp heat in spleen type, P<0.01.

Table 5: The comparison of FPG, FINS, ISI in each group ($\underline{x}$ ±s)

Grouping	Case number	FPG (m mol/L)	FIN (m IU/L)	ISI
Healthy control group	60	4.76±0.87	7.58±3.81	-3.46±0.27
Yin deficiency and dryness-heat type	52	8.67±1.12	14.96±3.20	-4.31±0.27
Accumulation of damp heat in spleen type	96	11.42±1.87	23.31±8.47	-4.93±1.08
Yang deficiency and dampness stasis type	32	10.36±1.38	19.91±4.75	-4.45±0.39

Note: Compared with healthy control group, P<0.01; compared with Yin deficiency and dryness-heat type, P<0.01, P<0.05; compared with accumulation of damp heat in spleen type, P<0.05.

Table 6: The comparison of BMI, HbA1C, TC, TG in each group ($\underline{x}$ ±s)

Grouping	Case number	NM I (kg/m2)	HbA1C (%)	TC (m mol/L)	TG (m mol/L)
Healthy control group	60	22.68±1.26	4.09±0.82	4.43±0.80	1.22±0.38
Yin deficiency and dryness-heat type	52	25.38±1.92	7.38±1.02	5.48±0.70	2.13±0.72
Accumulation of damp heat in spleen type	96	26.43±1.84	9.31±1.60	6.01±0.47	2.83±0.94
Yang deficiency and dampness stasis type	32	22.81±1.30	8.02±1.17	5.31±0.58	2.32±0.73

Note: Compared with healthy control group, P<0.01; compared with Yin deficiency and dryness-heat type, P<0.01; compared with accumulation of damp heat in spleen type, P<0.01, P<0.05.

The results of experiment two

1. The TCM syndrome distribution of type 1 diabetic patients is shown in table 3. Table 3 shows that for the TCM syndrome distribution of patients with type 2 diabetes, the type of dampness heat in trapped spleen is the most, the type of Yin deficiency and dryness-heat is the second, the type of Yang deficiency and dampness stasis is the least.

2. Changes of age and duration in patients with type 2 diabetic of different TCM syndrome type as shown in table 4. Table 4 indicates that the average age of Yin deficiency and dryness-heat type is the youngest, the average age of Accumulation of damp heat in spleen type is the second, and the average of Yang deficiency and dampness stasis type is the oldest. As it could be seen from the course of the disease, Yin deficiency and dryness-heat type has the shortest course, which was statistically significant ($P<0.01$) when compared with the other two types. Yang deficiency and dampness stasis type has the longest duration. Through the comparison among types, the difference among their course of disease and age was statistically significant ($P<0.01$).

3. The comparison of FPG, FINS, ISI in each group as shown in Table 5. Table 5 represents that the FPG, FINS of every syndrome in type 2 diabetes were all higher than healthy control group, their difference has statistical significance ($P<0.01$), of which the accumulation of damp heat in spleen type is the highest, it has statistically significant difference when compared with the other two groups ($P<0.01$ or $P<0.05$), Yang deficiency and dampness stasis type is the second and has statistically significance when compared with Yin deficiency and dryness-heat type ($P<0.01$). The INS in syndrome type of Diabetes mellitus type is significantly lower than that in healthy control group ($P<0.01$), where accumulation of damp heat in spleen type is the lowest and has statistical significance when compared with the other two types ($P<0.01$or $P<0.05$), Yang deficiency and blood stasis type is the second, as it is compared with Yin deficiency and dryness-heat type, their difference has statistical significance ($P<0.05$).

4. The comparison among BM I, H bA 1C, TC, TG in each group as shown in Table 6.We could know from Table 6 that, the BM I, H bA 1C, TC and TG in the TCM syndrome types of patients with type 2 diabetes are all higher than healthy control group ($P<0.01$); the BM I, H bA1C, TC and TG in accumulation of damp heat in spleen type are all higher than other syndrome types, their difference have statistical significance ($P<0.05$ or $P<0.01$), through comparing the BM I, H bA1C, TC, TG in Yin deficiency and dryness-heat type with Yang deficiency and dampness stasis type, their difference has no statistical significance.

DISCUSSION

Insulin resistance's and secretion's defects are the two basic links and characteristics of type 2 diabetes disease's mechanism. Evidence-based medicine has demonstrated that when the diagnosis of type 2 diabetes was established, there had already existed 50% impaired islet cells; about 90% of type 2 diabetes mellitus are associated with insulin resistance. For the treatment of type 2 diabetes mellitus, early insulin use is tended to be used at home and abroad currently, thus making islet B cells have a good rest is the new treatment strategy to improve islet B cell function. In curing diabetes mellitus type with traditional Chinese medicine (Zheng *et al.,* 2012), the treatment of insulin resistance must be studied. Pharmacological studies have verified that *ginseng, astragalus membranaceus* have good hypoglycemic effect, as it can increase the body's immune function, strengthen body resistance and tissue repair ability at the same time. Water extract of *Ginseng* can play its role by increasing insulin sensitivity to the *glucose. Coptis chinensis* mainly contains *berberine,* which could significantly enhance the effect of insulin sensitivity in experimental rats (Chen *et al.,* 2012); Rhubarb could improve the insulin resistance of rat model in diabetes mellitus type and improve blood flow dynamics and microcirculation through acting on insulin receptor (Zhou *et al.,* 2009); *Euonymus alatus* can stimulate the islet cell hyperplasia, promote insulin secretion and reduce blood sugar. The doctor of traditional Chinese medicine thinks, the early diabetes is given priority to hot and saliva injury, its basic pathogenesis is Yin deficiency and dryness-heat, thus the treatment should follow the principle of clearing heat and promoting the secretion of saliva or body fluid. *Radix rehmanniae, cornus, yam, alisma, cortex moutan, poria cocos* is the combination of Six glutinous rehmannia pill, which can increase the glycogen content in mice, significantly reduce the blood sugar level of experimental hyperglycemia mice. *Radix astragali, radix puerariae and radix trichosanthis* could nourish Yin and promote the secretion of saliva or body fluid, *schisandra chinensis* could seal renal clearance, *endothelium corneum gigeriae galli* could cure stomach gas (Fu *et al.,* 2010). The results of this group indicates that combined use of traditional Chinese medicine can reduce the dosage of insulin, and better improve glycemic control in patients at the same time, reduce the occurring of hypoglycemia, so as to shorten the hospitalization days and reduce the hospitalization expenses.

We could see from the case analysis (2) of this study that, accumulation of damp heat in spleen type accounts for a large proportion (53.3%) in diabetes mellitus type (Chen *et al.,* 2009) and there exists more serious insulin resistance in patients with this TCM syndrome. Accumulation of damp heat in spleen type is an important stage in type 2 diabetes. For the role of damp heat in

diabetes, generations of Chinese medicine have discussed a lot. It first appeared in “Plain Questions”. The theory of “strange disease proposed that “fat is an internal heat, sweet could fill abdominal distension, so the gas overflows and transforms to diabetes”. The wet and sticky damp could block Qi function, harm spleen and stomach, thus makes the operation weak, intrinsic damp, then enter into heat-transmission through gloomy mood, and the internal and external evil emerge, hot damp is deep and more touching, damp and heat sealing is more stalemate, which are more likely to lead to hot and humid trapped spleen. The patients of accumulation of damp heat in spleen type mainly have serious obesity, lipid metabolic disorder and insulin resistance, the method of clearing heat and removing dampness should be reused in this phase to improve the patient's internal environment, alleviate or eliminate insulin resistance, which has important significance in the control of lowering blood sugar and diabetes complications. There is already clinical research evidence verifying that the TCM curative effect of "hot damp" treatment (Fu *et al.,* 2010).

CONCLUSION

This study results show that the BMI in patients with accumulation of damp heat in spleen type is obviously higher than other groups, the difference was statistically significant, and there exists serious blood lipid metabolism disorders in accumulation of damp heat in spleen type, because of overweight, fat accumulation, metabolism disorder of blood lipid, which resulted into the reduction of insulin receptor's quality and quantity, thus led to the occurrence of severe insulin resistance, so the insulin sensitive index of accumulation of damp heat in spleen type was significantly lower than other model. After the occurrence of type 2 diabetes, it can also cause abnormal lipid metabolism. Due to insulin resistance, the synthesis of lipoprotein lipase and the activity would decline, which would lead to slow hydrolysis of triglycerides, extending time of lipoprotein and its residual particles that are rich with triglycerides, which would cause higher level of triglycerides and total cholesterol, suggesting that there is a close relationship between insulin resistance and blood lipid metabolism.

The level determination of TCM syndrome in related indicators should be considered in clinical diagnosis, which helps to make the combination of macroscopic and microcosmic differentiation, thus better guide clinical diagnosis and treatment work, the therapy of traditional prescription added with improved insulin resistance is applied in the treatment to relieve clinical symptoms, improve the patients' quality of life and reduce the case of fatality rate.

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