

Clinical Observation of Applying ZUTROL to Treat Diabetic Mellitus and its Complications

Bio Life Remedies Inc.

The following is the clinical report of applying ZUTROL to treat diabetes mellitus and its complications with the basic truth of strengthening QI and nourishing YIN, and activating blood and dispelling stasis.

1. General Data

71 cases are selected and randomly distributed into two groups; 50 cases in the Treatment Group and 21 cases in the Contrast Group. All 71 cases diagnosed non-insulin dependent diabetics. Among them, 23 cases (32.4%) are inpatients, 48 cases (67.6%) are outpatients; 29 cases are male patients (40.9%), 42 cases are female patients (59.1%); the patients' age expand from 23 to 71, and the majority of the patients are in the age of 50 to 65 (73.3%). Refer to Table 1. The shortest length of the disease is 3 months, and the longest is 16 years, the majority is among 1 to 6 years. Among the 71 cases, 15 cases are without complications, all others have different complications from 1 to a top of 5 conditions, refer to Table 2.

2. Research Method

1) Criterion of Case Selection

The empty stomach sugar level for all cases selected is greater than 150 mg /dl and all cases diagnosed deficiency in both QI and YIN with the condition of blood stasis. The diagnosis of blood stasis condition refers to the relative standard. The symptoms and physical conditions include dark and purplish tongue or with echymosis, fixed pain, pathological lump, bleeding, dark menstruation with agglomeration for woman, tingling or numbness in hands or feet, hemiplegia, dry mouth and increased thirst, purplish or pale lips, and varix under the tongue, etc., also make reference to special illness history (surgery operation history, induced abortion history, trauma, etc.); If the patient is diagnosed the condition of deficiency in both QI and YIN and have two of the above mentioned blood stasis indication, and laboratory test shows a blood rheological abnormality, the patient is selected for the observation case.

2) Grouping condition:

The 71 cases randomly divided into Treatment Group and Contrast Group (21 cases with 8 males and 13 females, inpatients 7 cases and outpatients 14 cases). There are 50 cases in the Treatment Group and 21 cases in the Contrast Group. In the Treatment Group, 21 cases are male and 29 cases are female, and 16 cases are inpatients and 34 cases are outpatients. In the Contrast Group, 8 cases are male and 13 cases are female, and 7 cases are inpatients and 14 cases are outpatients.

A score system is applied in the Treatment Group, which assigns different score to the symptoms, body conditions, blood rheological index, complications and special illness history, and according to the sum of the score the patients are separated in the Treatment Group into mild, medium and serious types. Among the 50 cases, 17 cases are mild type, 21 cases are medium type, and 12 cases are serious type. The relationship between the seriousness of the illness, the course of the illness and the age of the patients can be seen in Table 3 and Table 4.

It can be seen in the table, as the course of the illness increases, the percentage of the mild type tends to decrease, and the medium type is increasing; but there is no marked tendency with the serious type of illness.

There is a clear co-relationship between the age and the condition of the illness. As the age of the patient increases, the number of mild type decreases and the number of medium and serious type increases.

3) Observation standards

(1) Routine index: Clinical symptoms, body symptoms, empty stomach blood sugar level, 24 hour urine sugar fixed quantity, and blood fat.

(2) The hemorheological index: Apply capillary vessel method with test instrument.

(3) The rate of platelet aggregation (formalin~EDTS Method):

Adding 2 ml of EDTS~formalin thinner (EF thinner) and EDTS thinner (E thinner) into two silicon test tubes respectively, then add respectively 0.5 ml of vein blood extracted by silicon injector and mix evenly, and centrifuge them in low speed; Prepare two glass tubes and fill respectively with 0.4 ml of blood platelets thinner, add respectively 20 microlitre of centrifuged blood sample from the silicon test tubes to the two glass tubes; after leaving them still in room temperature for 15 minutes, start blood platelets number counting.

The formula: rate of blood platelets accumulation = number of blood platelets in EF thinner / number of blood platelets in E thinner × 100%

The descending of the rate of aggregation indicates a decrease in the number of dissociative platelets in the blood reflects a higher aggregation characteristic, and indicates an increase of aggregated matter of blood platelets.

4) Treatment method:

The patients in Treatment Group take 6 pieces of Zutrol each time, 3 times a day. Patients who do not take Western sugar lowering medicine take ZUTROL only; Patients who do use Western sugar lowering medicine will take ZUTROL at the same time and keep taking the same amount of Western medicine. When the condition improves in the process, the quantity of Western medicine to be taken will be reduced gradually; The Contrast Group takes only 80 mg ~ 480 mg of Diamicron per day according to the condition, and no ZUTROL is taken.

5) The treatment course and evaluation standard of the treatment effectiveness:

The treatment course: a single treatment course is 3 months, and the observation time does not exceed one treatment course.

The evaluation standard of the treatment effectiveness: For the convenience of observing the improvement of blood stasis condition, a synthesized evaluation method is adopted:

- Clinical symptom: 0 score for disappearance of the symptoms, 0.5 score for marked improvement, and 1 score for non-improvement;
- Blood sugar and urine sugar level: 0 score is given respectively if empty stomach blood sugar level lowered to normal range, 24 hour urine sugar is under 5 g, or the decreasing percentage of blood and urine sugar level is more than 50% compare to the pre-treatment readings (the index exceeds the normal absolute value, same hereunder). 1

score is given respectively if blood sugar level decreased under 150 mg/dl, 24 hour urine sugar under 10 g, or the decreasing percentage of blood and urine sugar level is more than 30% compared to the pre-treatment readings. 2 score if blood and urine sugar level decreased slightly or no change at all.

- Hemorheological indexes: 0 score if all post-treatment indexes become normal, 0.5 score if one of the abnormal pre-treatment indexes has obvious improvement, 1 score is given if no obvious improvement.
- The standard: 0~3 score: evident effect
3.5~6 score: effective
5.5 score above: no effect.

3. Result

1) Observation of hemorheology:

The comparison of the pre-treatment index of treatment group to the normal reference value indicates that the male patients have a higher specific viscosity of whole blood, and the specific viscosity of plasma is also markedly higher ($p < 0.05$).

The pre-treatment packed red-cell volume is greater than the normal index, but have no marked difference; the indexes of blood sedimentation and fibrinogen are all higher than normal, it has marked difference after statistically processed ($p < 0.01$).

For the female patients, every pre-treatment index is higher than normal and it has marked difference ($p < 0.001$ or 0.01), these results are similar with most academic reports.

After the treatment, the readings of viscosity of whole blood in both high shear and low shear, and fibrinogen of both male and female patients improved markedly ($p < 0.001$ or 0.05); However, the changes in the readings of viscosity of plasma have no statistical meaning;

The readings of packed red-cell volume and blood sedimentation have no apparent change.

The post-treatment readings of each index of the Contrast Group either increase or have minor improvement, it has no statistical meaning ($p < 0.05$).

Refer to Table 5.

2) The result of inspection of platelet aggregation rate:

The result of inspection of platelet aggregation rate of 30 cases of diabetic patients in the Treatment Group indicates that, before the treatment, there has been an increase of aggregated matter of platelets in the blood of the patients which means a lower aggregation rate ($p < 0.05$); After the treatment, platelet aggregation rate has increased apparently, it has clear statistical meaning ($p < 0.01$).

Refer to Table 6.

3) The observation of pre-treatment and post-treatment data of cholesterol and triglyceride:

The pre-treatment readings of cholesterol and triglyceride of the patients in the two groups are all higher than the normal value;

The post-treatment cholesterol readings of the Treatment Group has markedly decreased ($p < 0.01$), the post-treatment readings for triglyceride have no apparent change.

The Contrast Group on the other hand, the post-treatment readings of cholesterol are slightly higher than the pre-treatment readings, but it has no statistical difference; the post-treatment readings of triglyceride is slightly higher than the pre-treatment readings.

Refer to Table 7.

- 4) The comparison of pre-treatment and post-treatment blood sugar reading of empty stomach and 24 hour urine sugar:

After one treatment period, the readings of blood sugar of empty stomach and 24 hour urine sugar of the two groups are decreased markedly.

Refer to Table 8.

- 5) The medicinal usage and clinical effectiveness of the Treatment Group:

In the Group, 10 cases (20%) used only ZUTROL, 29 cases (58%) used ZUTROL and kept the original amount of Western sugar-lowering medicine intake, 8 cases (16%) reduced their Western medicine intake, 3 cases (6%) increased their Western medicine intake.

Using the synthesized evaluation method, the effectiveness of clinical treatment as follows:

- Evident effective is 16 cases (32%);
- Effective is 26 cases (52%),
- No effect is 8 cases (16%),
- Total effectiveness rate is 84%.

- 6) The relationship between the condition of the illness, history of the illness, the age of the patients and the effect of the treatment:

The result of observation indicates the rate of total effectiveness and the degree of blood stasis of the patient is closely related. The mild patients have the best treatment effect and the rate of total effectiveness is 88.24%. The medium patients have the second best treatment effect and the rate of total effectiveness is 85.71%. The serious patients have the least treatment effect, and the overall rate of effectiveness is 75%. Refer to Table 9.

The treatment effect is greater for patients who have a history of the illness under 5 years. There is no clear relationship between the age of the patient and the treatment effect.

4. Discussion and understanding

- 1) It is very common with diabetes mellitus that patient suffers blood stasis together with deficiency of QI and YIN; The mechanism of the illness is that the deficiency of YIN and Interior Heat which cause the consumption and burning of YIN blood, and the glutinous and slow down of blood flow forms the condition of blood stasis gradually; Deficiency of QI causes weak blood flow, the obstruction of circulation of QI and blood also contribute to the condition of blood stasis; The deficiency of QI, the deficiency of YIN and the blood stasis condition interact together, make the condition of blood stasis more serious which cause or worsen the condition of blood vessel complications. The research approves that the pathological change of micro-vascular in diabetes mellitus is the result of the abnormal function and forms of micro-vascular and micro-blood circulation; It is the pathological basis of the complications of internal organs.

The traditional understanding of blood stasis is in agreement with the modern research of pathological change of micro-vascular in diabetes mellitus, so we can assume that there is a close relationship between the condition of blood stasis and diabetic vascular complication.

The observation result of hemorheology in this document corresponds with most research reports that the increase of the degree of stickiness of the blood circulation is the main cause, and this is more prominent in female patients. But, we can not tell whether this result is related to the condition that the female's QI and blood are impaired because of child birth and menstruation, as the blood is the essence of female based on the traditional theory. Further research is needed to approve this point.

The observation result in this document also reveal that for the 15 cases with no apparent complications, their hemorheological indexes all increase in different degrees, and the clinical symptom also support the blood stasis diagnosis; therefore, even for deficiency of QI and YIN type diabetic patients with no apparent complication, blood stasis is also very common, and it is feasible to take the approach of "invigorating blood and dispelling stasis" for treatment.

- 2) Increase in the platelet aggregation rate of the diabetics is more apparent in patients with vascular complication, and the rate increases more as the number of blood vessel parts occurring complication increases. It is observed that when the aggregated matter of the circulating blood platelets of the diabetic patients is greater than normal, even the patient is deficient of QI and YIN and with blood stasis condition, the high aggregation state of blood platelets still greatly improves ($p < 0.01$). This indicates that adopting the treating approach of strengthening QI and nourishing YIN and activating blood and dispelling stasis is of definite clinical meaning for improving the hyper-activity of the blood platelets aggregation function.
- 3) The treating principle of ZUTROL is strengthening QI and nourishing YIN and activating blood and dispelling stasis. The mechanism of the diabetes mellitus is that the deficiency of YIN is the essence of the disease. The deficiency of YIN causes a weak process of QI transformation, which leads to the result of QI deficiency. The deficiency of QI and YIN interacts in the occurrence and development of the disease and cause blood stasis which mix up in the course of the disease. Therefore, deficiency is the origin of the disease, and stasis is the superficiality. The treating method of strengthening QI and nourishing YIN, and activating blood and dispelling stasis pay attention to the superficiality of the disease, it also works with the real origin of the disease.

ZUTROL not only relieves the clinical symptoms, it also, in different degrees, promotes the function of metabolism and descends the level of blood and urine sugar. In addition, it improves blood fluidity, lower the hyper-action of blood platelets aggregation, so leads to a better treatment effect. This preparation is most suitable for the treatment of diabetes with deficient YIN and QI and blood stasis.

Since deficiency of YIN always runs through the whole course of diabetes mellitus, and the condition of blood stasis is very common with diabetic patients, most likely the patients suffer abnormal blood fluidity, and their blood platelets adherence and accumulation increase. It is clinically feasible therefore to apply ZUTROL in treating diabetic patient who is deficient of QI and YIN or with deficiency in both YIN and YANG when there is no apparent blood stasis condition. The clinical observation confirms that for this kind of patients, ZUTROL also produces good treatment effect.

4) The judgement of the curative effects of the clinical treatment:

Blood stasis condition is common with diabetic patients, and in the clinical practice the blood rheological indexes are taken for diagnosis of blood stasis condition. Therefore, in observing the curative effects of the clinical treatment for diabetic patients with blood stasis condition, if focussed only on the improvement of clinical symptom, blood sugar and urine sugar, it will not give an objective representation. The synthesized evaluation method adopted in judging the curative effects of the treatment, takes blood rheological index as one of the objective index to score the treatment effectiveness. This makes possible to reflect the clinical treatment effectiveness comprehensively.

Table 1 The Age Distribution							
Group	~30	~40	~50	~60	~65	~70	Total
Treatment	2	1	6	21	14	6	50
Contrast	0	2	2	13	3	1	21
Total	2	3	8	34	17	7	71

Table 2 Complications of the 71 cases												
Group (n)	Hyper-tension	Coronary heart disease	Cerebro-vascular disease	Diabetic renal disease	Retinal disease	Cataract	Glaucoma	Pathological change of peripheral nerve	Vascular disease of lower limb	Pruritus	Periodon-titis	Others
Treatment (50)	15	9	6	8	17	18	3	5	7	11	4	9
Contrast (21)	7	6	0	1	13	6	0	2	0	2	3	3
Total (71)	22	13	6	9	30	24	3	7	1	13	7	12

Table 3 The relationship b/w the condition and the course of the illness – Treatment group				
Course (Year)	Condition			Total
	Mild (%)	Medium (%)	Serious (%)	
~2	7 (43.75)	5 (31.25)	4 (25.0)	16
~6	7 (35.0)	8 (45.0)	5 (20.0)	20
6~	3 (21.43)	8 (57.14)	3 (21.43)	14
Total	17	21	12	50

Table 4 The relationship b/w the condition and the age of the patients – Treatment group

Age	Condition			Total
	Light (%)	Medium (%)	Serious (%)	
~50	4 (44.45)	3 (33.33)	2 (22.22)	9
50~	8 (38.10)	8 (38.10)	5 (23.80)	21
60~	5 (25.0)	10 (50.0)	5 (25.0)	20
Total	17	21	12	50

Group		Cases/number	Viscosity of whole blood		Viscosity of plasma	Packed red-cellvolume	blood sedimentation	Fibrinogen
			Centipoise	Centipoise	Centipoise	(%)	(mm/h)	(mg%)
Treatment	Pre-treatment	Male	*	*	*		***	***
		21	4.30±1.18	9.03±3.7	1.77±0.14	49.67±4.93	16.81±11.2	545.48±165.2
		female	***	**	**	***	***	***
		29	1.09±1.01	7.61±2.12	1.79±0.10	48.17±6.52	3.69±9.50	579.13±144.6
	Post-treatment	Male	△	△				△
		21	3.75±0.76	7.04±1.67	1.70±0.11	49.81±5.01	18.33±10.21	470.95±80.8
		female	△△△	△△				△
		29	3.17±0.76	6.09±1.34	1.79±0.12	46.90±5.20	27.13±13.01	517.17±155.5
Contrast	Pre-treatment	Male					**	***
		8	3.94±1.08	8.27±2.48	1.77±0.15	48.50±4.72	19.50±12.08	505.00±97.06
		female					***	***
	Post-treatment	13	3.67±0.69	7.05±2.07	1.73±0.14	45.316.07	31.16±11.13	620.40±18.91
		Male						
		8	4.01±1.13	8.15±3.01	1.83±0.09	49.00±4.99	18.25±12.09	503.80±135.8
Normal		female						
		13	3.78	7.01	1.810.12	45.23	30.28.73	605.20±170.1
		Male						
		35	3.88±0.68	7.66±1.46	1.70±0.17	48.51±2.72	6.68±6.98	
		female						
		30	3.44±0.73	6.40±1.41		42.96±3.50	15.06±8.25	

* indicates a comparison with the normal group: * means p<0.05, ** means p<0.01, and *** means p<0.001

△ indicates a comparison between the results of pre-treatment and post-treatment: △ means <0.05, △ △ means p<0.01, and △ △ △ means p<0.001

Group	treatment	Blood platelets accumulation rate (%)	d	p
Treatment	Pre-treatment	30	0.68±0.023	
Treatment	Post-treatment	30	0.4±0.22	0.16<0.01
Total		23	0.84±0.16	

Group		Number of cases	Cholesterol	Triglyceride
Treatment	Pre-treatment	50	223.66 ± 30.84	162.46 ± 76.38
	Post-treatment	50	211.25 ± 28.87	163.02 ± 75.51
Contrast	Pre-treatment	21	211.51 ± 41.41	176.27 ± 52.12
	Post-treatment	21	216.57 ± 30.44	181.56 ± 59.38

Δ : Comparison between the data of before and after the treatment, p < 0.01

Group (cases)		Blood sugar (mg/dl) pp	Urine sugar (g) pp
Treatment (50)	Pre-treatment	190.78 ± 5.82	31.6 ± 5.18
	Post-treatment	147.40 ± 5.48<0.001	21.58 ± 3.05<0.01
Contrast (21)	Pre-treatment	219.12 ± 7.22	54.22 ± 12.75
	Post-treatment	178.29 ± 1.63<0.05	37.02 ± 10.20<0.05

Table 9 the relation between the effect and condition of the Treatment Group

Type	Evident effect (%) cases	effective (%) cases	No effect (%) cases	Overall effective rate (%)
Mild	6 (35.29)	9 (52.95)	2 (11.76)	98.24
Medium	7 (33.33)	11 (52.39)	3 (14.29)	85.71
Serious	3 (25.00)	6 (50)	3 (25.00)	75
Total	16	26	8	