Preliminary results of highly localized plantar irradiation with low incident levels of mid-infrared energy which contributes to the prevention of dementia associated with underlying diabetes mellitus

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Background and aims: The incidence of vascular dementia (VD) and Alzheimer's disease (AD) has recently increased and the prevention of progression of these diseases is very difficult.

Results: The application of pinpoint plantar long-wavelength infrared light irradiation (PP-LILI) to a patient's sole, at the point where the line drawn between the first and second metatarsal heads intersects with the vertical line from the medial malleolus, was effective in increasing blood flow to the facial artery, elevating high-density lipoprotein cholesterol (HDL-C) levels, and reducing insulin resistance.

Conclusions: We found that these effects of PP-LILI might be helpful for preventing VD and AD, conditions that are becoming a social problem in an aging Japanese society.

Introduction

In recent years, increasing attention has been paid to the co-morbidity of diabetes mellitus and dementia, diseases whose morbidity increases with age. In particular, it has been reported that the incidences of vascular dementia (VD) and Alzheimer's disease (AD), known as major causes of dementia, are higher in patients suffering from diabetes.¹⁻⁸⁾

We have established Stress-free Therapy® (SF Therapy: Trademark Registration No. 5495960; Patent Application No. PCT [Patent Cooperation Treaty]/JP [Japan] 2012/073972), a drug-free therapy aimed at improving diabetes in an attempt to prevent dementia. This therapy elevates the patient's peripheral deep body temperature, increases blood flow, stabilizes blood pressure, and significantly decreases stress hormone levels (e.g., adrenocorticotrophic hormone [ACTH] and cortisol). In pinpoint plantar low-wavelength infrared light irradiation (PP-LILI), low incident levels

of light energy are applied to the patient's sole in a pin-point manner, at the point where the line drawn between the first and second metatarsal heads intersects with the vertical line from the medial malleolus.¹⁾ We previously reported that PP-LILI was useful for the treatment of early dementia, as it increased blood flow to the head and had significant beneficial effects on glycemic control and insulin resistance in patients with type 2 diabetes.^{2), 9-12)} In the present study, we examined whether PP-LILI could change blood flow to the facial artery and influence blood glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and stress hormone (ACTH and glucocorticoid [cortisol]) levels in patients with type 2 diabetes.

Methods

PP-LILI was performed in 15 patients with type 2 diabetes (nine men and six women; mean age, 62.0±7.2 years) in whom glycemic control was difficult to achieve with medications.

After the patients rested in the supine position for

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15 minutes, PP-LILI was bilaterally applied to the sole at the point where the line drawn between the first and second metatarsal heads intersected with the vertical line from the medial malleolus for 15 minutes using the PP-LILI device (Controlled Medical Device Approval No. 224AFBZX00075000: highly localized probe 20 mm in diameter, mid infrared wavelength 9000-12000 nm, output 9.55 mW). Blood flow in the facial artery was measured before and after irradiation to determine changes (**Fig. 1**). PP-LILI was applied once a week four times on average. During the course of the therapy, oral diabetes medications were continued.

Blood samples (3 cc) were collected from the cubital vein before and after PP-LILI and immediately centrifuged (1200 G for 5 minutes) to analyze blood glucose, hemoglobin A1c, HDL-C, LDL-C, and stress hormone (ACTH and cortisol) levels. ACTH was quantified by a chemiluminescence immunoassay; cortisol, by an electrochemiluminescence immunoassay; and blood glucose, by the enzymatic method. To ensure consistency, blood samples were collected at the same time of the day in consideration of the impact of measurement time and circadian rhythm on test values.

Changes in blood flow to the facial artery were assessed using a laser Doppler flow meter (Advance ALF21) that quantified blood flow in the facial artery (one of the branches of the total carotid artery that carries blood to the brain) for 15 minutes each - once during the resting period, and a second time after completion of PP-LILI.

Ethical consideration

This study was conducted after review and approval (2304) by the Ethics Committee of Ryotokuji University. Written informed consent was obtained from each patient after a full explanation of the nature and aims of the study.

Statistical evaluation of the data was performed using the sign test and paired t-test, with p-values of less than 0.05 considered to be significant.

Results

Changes in Blood Glucose, Insulin, TC, HDL-C, and LDL-C Levels

PP-LILI led to a significant decrease in blood glucose levels from 173.5 ± 57.0 mg/dl before therapy to 132.4 ± 42.4 mg/dl after therapy ($P < 0.01$; **Fig. 2**). Moreover, insulin and TC levels also showed a significant decrease: insulin levels decreased from 15.3 ± 11.8 μ U/dl to 10.7 ± 7.9 μ U/dl ($P < 0.05$; **Fig. 3**), and TC levels decreased from 214.5 ± 48.1 mg/dl to 198.0 ± 55.7 mg/dl ($P < 0.01$; **Fig. 4**). HDL-C levels decreased from 51.9 ± 9.5 mg/dl to 49.4 ± 9.8 mg/dl, but the decrease was not statistically significant (**Fig. 5**). On the other hand, LDL-C levels significantly increased from 119.7 ± 34.9 mg/dl before therapy to 129.4 ± 37.9 mg/dl after therapy ($P < 0.05$; **Fig. 6**). Thus, such a decrease in LDL-C levels, unlike HDL-C levels, was proportional to a significant

Fig. 1: Stress-free Therapy® device (Controlled Medical Device Approval No. 224AFBZX00075000: probe 20 mm in diameter, far infrared wavelength 9000-12000 nm, output 9.55 mW) (left) and the measurement portion of the blood flow (right). The facial artery is a branch of the total carotid artery which supplies blood to the brain.

decrease in blood glucose, insulin, and TC levels.

Changes in Stress Hormone (Cortisol and ACTH) Levels

Both cortisol and ACTH levels were significantly lower after PP-LILI than before therapy. Cortisol levels decreased from 10.7 ± 5.4 $\mu\text{g/dl}$ to 8.0 ± 3.7 $\mu\text{g/dl}$ ($P < 0.01$; **Fig. 7**), and ACTH levels decreased from 20.5 ± 11.4 pg/ml to 14.6 ± 7.4 pg/ml ($P < 0.05$; **Fig. 8**).

Changes in Blood Flow to the Facial artery

The mean blood flow to the facial artery significantly increased from 3.0 ± 2.1 ml/min/100g tissue before PP-LILI to 8.1 ± 4.7 ml/min/100g tissue after PP-LILI (both measured for 15 minutes) ($P < 0.001$; **Fig. 9**). As shown in **Table 1**, 7 cases (case No.: 3, 4, 8, 11, 12, 13, 14) displayed the 3-fold increases of blood flow after PP-LILI.

Figure 2: Changes in Blood Glucose

Figure 3: Changes in Insulin

Figure 4: Changes in Total Cholesterol

Figure 5: Changes in HDL Cholesterol

Figure 6: Changes in LDL Cholesterol

Figure 7: Changes in Cortisol

Figure 8: Changes in ACTH

Figure 9: Changes in blood flow to the facial artery

Table 1: The changes in blood flow of the facial artery

Case	Sex	Age	Blood flow (ml/min/100g tissue; before the treatment)	Blood flow (ml/min/100g tissue; after the treatment)
1	Female	64	1.8382	4.8927
2	Female	60	2.2788	6.0511
3	Male	69	1.4403	5.0540
4	Male	62	1.6554	5.1752
5	Male	74	2.4357	5.3784
6	Male	66	3.4252	7.4445
7	Female	66	2.6650	7.7034
8	Female	50	2.1269	6.9604
9	Male	54	3.4819	9.3156
10	Male	47	4.2082	7.8473
11	Male	61	2.8971	9.7831
12	Male	68	1.1030	4.7177
13	Male	62	3.1497	9.6122
14	Female	67	2.1148	7.9232
15	Female	60	9.9197	24.030
AVE		62.0	3.0	8.1
SD		7.2	2.1	4.7

Discussion

Recent epidemiological and clinical studies have shown that the incidences of co-morbid vascular dementia and Alzheimer's disease are higher among patients with diabetes compared with non-diabetic population.⁶⁻⁸⁾ The following mechanism for this co-morbidity has been proposed: insulin resistance and hyperinsulinemia, which are observed in metabolic syndrome and diabetes mellitus, evoke a low-insulin state in the central nervous system that consequently causes decreased cerebral blood flow and accumulation of amyloid in the brain, ultimately leading to a development of AD.⁹⁾ Insulin also regulates glucose and energy metabolism in the brain. In hyperglycemia, the decreased transport of insulin to the brain causes decreased insulin action, attenuating the neuroprotective effects of insulin. Importantly, insulin receptors are densely localized in the hypothalamus and the hippocampus, important areas for memory.¹³⁾

We have previously reported that PP-LILI significantly decreases stress markers (ACTH and cortisol)

released from the hypothalamus, significantly improves insulin resistance in type 2 diabetes, and increases blood flow in the facial artery.⁹⁻¹²⁾ A novel finding of this study is that PP-LILI in patients with type 2 diabetes helped increase blood flow to the facial artery, thereby normalizing insulin resistance and metabolism (i.e., blood glucose levels). The facial artery is a branch of the total carotid artery which supplies blood to the brain. In healthy adults, the blood flow in the facial artery is usually regulated at the level around 7 to 11 ml/min.^{14, 15)} We would like to put special emphasis on the concept that the average flow in the patients in the present study was outside of the normal range (3.0 ± 2.1 ml/min) before the treatment but it improved to be within the normal range (8.1 ± 4.7 ml/min/100g tissue) after the treatment.

This may contribute to the prevention of dementia (e.g., VD and AD) associated with diabetes mellitus. Specifically, we suggest that decreased ACTH and cortisol levels (stress markers released from the adrenal cortex) and increased blood flow may help enhance neural activity and prevent accumulation of β amyloid

in the brain.

In regard to wavelength of the light, we have chosen mid-infrared wavelength incident light because water easily adsorbs such light, moreover we have irradiated bilaterally to enforce the therapeutic effect.

In the elderly, high HDL-C levels have been reported to be effective not only in reducing the risk of developing AD, but also for preventing cognitive decline and the development of VD.¹⁶⁻¹⁹⁾ In our present study, LDL-C levels, along with blood glucose and insulin levels, were significantly decreased, though HDL-C levels remained unchanged. This indicates that PP-LILI could be effective for preventing dementia.

Administration of insulin, combined with an adequate amount of glucose, enhances memory and inhibits the accumulation of β amyloid in brain cells in both healthy persons and patients with AD.¹⁶⁾ We pre-

viously reported that memory is also improved following PP-LILI.¹²⁾ Taken together, these results suggest that PP-LILI might be helpful for preventing the development of VD and AD, known as the causes of dementia, by normalizing insulin activity in the brain, increasing blood flow to the facial artery, and enhancing neural activity in the hippocampus and other areas to improve memory.

Conclusion

Our study revealed that PP-LILI significantly increased blood flow to the facial artery and normalized insulin and stress hormone metabolism. Our findings may help to develop new therapeutic strategies that could prevent the development of VD and AD.

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