A SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY STUDY OF THE THERAPY OF INTRAVASCULAR LOW INTENSITY LASER IRRADIATION ON BLOOD FOR BRAIN INFARCTION

Xuechang Xiaoa , Jiazheng Donga, Xiaofan Chua, Jian-Ling Jiaob,
Shaowei Jiaa, Xiyuan Zhenga, Cixiong Zhoua, Timon Cheng-Yi Liucd, Song-Hao Liub

[a] Department of Neurology, Shenzhen People's Hospital (the Second Affiliated Hospital of Medical Faculty, Ji-nan University), Shenzhen, GD 518020 , China. [b] Quantum Electronics Institute, South China Normal University, Guangzhou, GD 510631, China. [c] Laboratory of Light Transmission Optics, South China Normal University, Guangzhou, GD 510631, China. [d] The Key Laboratory of Biomedical Photonics of Ministry of Education of China, Huazhong University of Science and Technology, Wuhan, HB 430074, China

We used single photon emission computed tomography (SPECT) in brain perfusion imaging to study the changes of regional cerebral blood flow (rCBF) and cerebral function in brain infarction patients treated with intravascular low intensity laser irradiation of blood (ILIB). Seventeen of 35 patients with brain infarction were admitted to be treated by ILIB on the base of standard drug therapy, and SPECT brain perfusion imaging was performed before and after ILIB therapy with self-comparison. The results were analyzed using the brain blood flow function change rate (BFCR%) model. The effect of ILIB during the therapy process in the other 18 patients was also observed. In the 18 patients, SPECT indicated an improvement of rCBF (both in focus and in total brain) and cerebral function after a 30 min-ILIB therapy. And the 17 patients showed an enhancement of total brain rCBF and cerebral function after ILIB therapy in comparison with that before, especially for the focus side of the brain. The enhancement for the focal area itself was extremely obvious with a higher significant difference ($P<0.0001$). The mirror regions had no significant change ($P>0.05$). BFCR% of foci was prominently higher than that of mirror regions ($P<0.0001$). In conclusion, the ILIB therapy can improve rCBF and cerebral function and activate brain cells of patients with brain infarction. The results denote new evidence of ILIB therapy for those patients with cerebral ischemia.

Key Words: brain infarction, cerebral function, low intensity laser, regional cerebral blood flow (rCBF), single photon emission computed tomography (SPECT)

Introduction

Intravascular low intensity laser irradiation on blood (ILIB) was developed in the 1980s in the former Soviet Union (1,2). There are reports of general effects on the immune system, including decreased blood viscosity, improvement of microcirculation, detoxification and oxygenation, normalization of haemostasis, and activation of immune and proliferative processes. Indications reported in the literature include occlusive vascular diseases of the extremities, unstable angina, acute myocardial infarction, diabetic angiopathies, acute pneumonia, lung abscess, bronchial obstructive diseases of the lungs, drug resistant forms of schizophrenia, rheumatoid arthritis, acute calculous pyelonephritis, ischemic heart disease, circulatory encephalopathy, haemorrhagic shock, Tourette's syndrome, etc.

Systematic research on ILIB and its clinic applications was not done in China until the 1990s. It has been shown that ILIB has obvious therapeutic effects for cerebral ischemia (4). In order to discuss its possible mechanisms, we used single photon emission computed tomography (SPECT) brain perfusion imaging to investigate the effects of the intravascular low intensity He-Ne laser irradiation (HN-ILIB) regional cerebral blood flow (rCBF) and cerebral function in patients with brain infarction in shis study.

Subjects and Methods

Thirty-five patients with brain infarction were admitted into the study. They were diagnosed according to the criteria of the fourth Chinese cerebrovascular disease conference(5). Among them were 19 male and 16 female patients, aged 18 to 80 (avrage age = 60 years), with 8 cases less than one week, 18 cases from one week to one month, and 9 cases longer than one month in duration of illness. All the patients had been examined by CT or MRI, and showed the following infarction sites: 13 cases in the basal ganlia, 6 in the internal capsule, 5 in the cortex, and 11 with multiple sites. Many had complications: 10 cases with hypertension, 8 with diabetes mellitus, 6 with Parkinson's syndrome, 2 with coronary heart disease and 1 with chorea.

Table 1. Changes in Brain Perfusion and Brain Blood Flow in 18 Brain Infarction Patients after 30 minutes ILIB Therapy

Site	Ratio of Regional and Total Brain Perfusion		BFCR%
	Before Therapy	After Therapy	
Focus Side	9.63±2.09	12.05±2.37	27.50±20.33
Mirror Side	12.52±1.86	12.77±1.89	3.13±7.61

Table 2. Changes of Brain Perfusioni and Brain Blood Flow in 17 Brain Infarction Patients after ILIB Therapy.

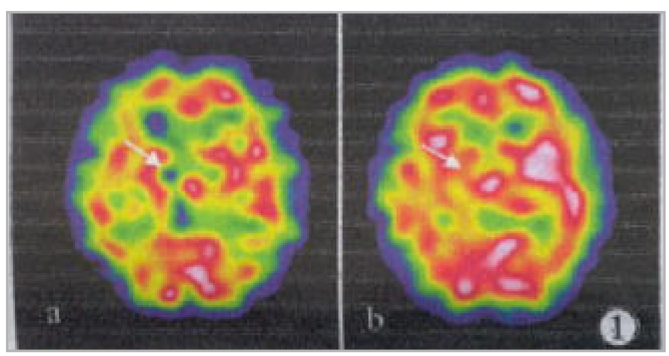
Site	Ratio of Regional and Total Brain Perfusion		BFCR%
	Before Therapy	After Therapy	
Focus Side	8.11±2.27	10.30±3.65	30.70±30.01
Mirror Side	11.18±2.45	11.94±3.13	9.85±19.70

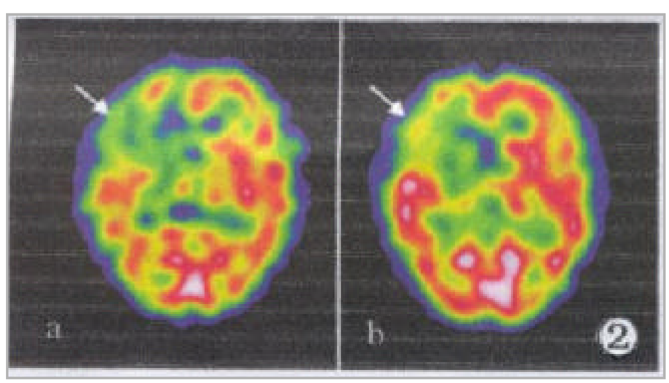
Seventeen patients were treated with HN-ILIB therapy in addition to 7- 10 days' routine drug therapy. The output power 1.5~2.5mW of He-Ne laser (?=632.8nm, model ZJC480A) was regulated by a diaphragm-mediated system, and measured using a power meter (China Institute of Metrology, model MP2). Basilic vein or median basilic vein in the paralyzed arm was the spot irradiated.. A course of treatment took 10 days, once a day, 60 min each time. Each patient was examined with SPECT (Siemens DIACAM/ICON SPECT System, with general low power probe) brain perfusion imaging twice-before and after the HN-ILIB therapy course-in order to make a self-comparison. The remaining 18 patients received SPECT first next treat them, treatment with HN-ILIB for 30 min, followed by SPECT again. The developer was 99mTc-ECD. The data-collecting condition was: 128 ×128 matrix, 360° rotation, 5.6/ gate.15 sec. The imaging-managing condition located: previous data management was done by Butterworth low-pass filtration function, and then Ramp reverse projection was used to reconstruct images, Chang's is method was used to complete the attenuation adjustment. The layer thickness was 6mm. Brain blood flow function change rate (BFCR%) mathematical model was used to grantify and compare the affected corresponding manufacted areas. T-tests were used for statistical analysis.

Results

In 18 patients SPECT revealed an obvious improvement in 30 regions of low rCBF and cerebral function following 30 min of HN-ILIB therapy, during acute, subacute and recovery stages of brain infarction (t=8.7249, P<0.0001); Figure 1~3. The result of quantified analysis -- that change was more prominent on the attached side. The improvement in the -- regions was not statisticaly significant (t=1.3043, P>0.05). BFCR% was much higher in the attached area than the corresponding unattached regions; Table (t=6.9127, P<0.0001).

The SPECT results in the 17 brain infarction patients showed 27 regions of low rCBF and cerebral function found before ILIB therapy had been miniaturized and improved to different degrees after the course of ILIB therapy; Figure 4. The quantification showed an enhancement of rCBF and cerebral function, especially for the affected side. (t=4.4052, P<0.0001). The enhancement of CBF for the --- regions was not significant (t=1.6995, P>0.05). Thus, BFCR% of the attached areas was higher than that of control regions; (Table 2;) (t=4.5278, P<0.0001). Four cases with the complication of Parkinson's Syndrome showed an improvements in the basal ganli, especially in the lenticular nucleus, Figure 4.

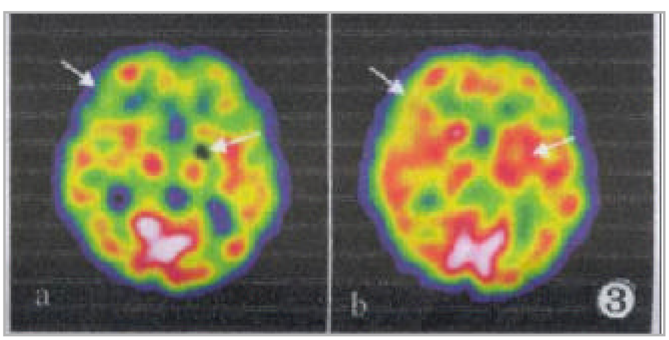


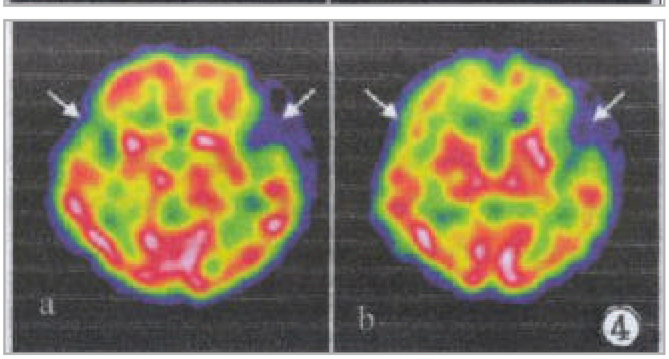


Discussion

SPECT is a functional imaging technology that has been used broadly in clinical work to detect blood flow, metabolic rate and function of organs in physical or pathological conditions. In this paper, we have assessed the local effects of ILIB on brain infarction. The SPECT of the patients showed reduction of blood flow, not only in the affected area but also in the surrounding regions. The immediate and after-treatment effects of HN-ILIB therapy were improvements in rCBF and cerebral function in the and mirror regions, especially in the infarct region.. In other words, HN-ILIB therapy can really increase rCBF, activate cerebral cytofunctional activities.

Duan et al(7) recently showed that ILIB effects may be due to signal transduction induced by low intensity laser irradiation. They probed signal transduction pathways of respiratory burst of bovine neutrophils induced by He-Ne laser irradiation at a dose of 300J/m^2 by using the protein tyrosine kinases (PTKs) inhibitor, genistein, the phospholipase C (PLC) inhibitor, U-73122, and the protein kinase C (PKC) inhibitor, calphostin C, respectively, they found that inhibitors of PTKs can completely inhibit the He-Ne laser-induced respiratory burst of neutrophils, and that PLC and PKC inhibitors can reduce but not inhibit this effect. These results suggest that PTKs play a key role in the He-Ne laser-induced respiratory burst of neutrophils and [PTK-PLC-PKC-NADPH oxidase] signal transduction pathways may be involved in this process. This experiment directly supported the biological information model for low intensity laser irradiation (BIML) (8). BIML has been used to explain the effects of laser biostimulation on red blood cells (9).





According to BIML, at the dose level used in this study, laser irradiation can elevate the cAMP level in blood cells, decrease the viscosity of whole blood, improve the rheological property of blood and microcirculation, reduce free radical level and enhance cellular immunity. Other factors, e.g; carbon monoxide(10) and endothelin(11), may participate in blood flow regulation and brain perfusion induced by ILIB. Recent report also show futher studies are needed to elucidate the mechamisms involved nerve-endocrine-immune net due to ILIB (2,11,12,13,14).

Acknowledgement

This work was supported by the Project of National Natural Science Foundation of China (60178003), the Key Project of Guangdong Natural Science Foundation of Guangdong Province (011480), the Team Project of Guangdong Provincial Department of Science and Technology (20003061).

Correspondence to

Xiao XC, Department of Neurology,
Shenzhen People's Hospital,
Shenzhen 518020,
P.R. China
and Liu TCY (liutcy@scnu.edu.cn).

References

1. Samoilova KA, Kukui LM (1996): Photochemotherapy in clinical and veterinary medicine: therapeutic effects and mechanisms. Laser Therapy, 8: 62.
2. Tunér J and Hode L (1999): Low Level Laser Therapy. Graengesberg: Prima Books in Sweden AB.
3. Liu SH, Liu TCY and Gao YQ (1998): Mechanism on the Intravascular He-Ne Laser Irradiation on Blood and Its Clinic Applications. SPIE, 3344: 171-178.
4. Chen YH, Liu TCY and Li YL (2001): Cerebral Infarction Therapy Mechanism of the Intravascular Low-Intensity He-Ne Laser Irradiation on Blood. Laser JournL, 22(6) : 76-78.
5. Li Wen-Hui (1996): Diagnostic main points of cerebrovascular diseases. China Neurology Journal, 29: 379-380. [Chinese]
6. Brown DR, Hunter R, Wyper DJ, Patterson J, Kelly RC, Montaldi D, McCullouch J (1996): Longitudinal changes in cognitive function and regional cerebral function in Alzheimer's disease: a SPECT blood flow study. J Psychiatr Res, 30(2):109-126.
7. Duan R, Liu TCY, Li Y, Guo H, and Yao LB (2001): Signal transduction pathway involved in low intensity He-Ne laser-induced respiratory burst in bovine neutrophils: a potential mechanism of low intensity laser

biostimulation. Lasers Surg. Med. 29(2): 174-178.

8. Liu TCY, Duan R, Yin PJ, Li Y and Li SL (2000): Membrane mechanism of low intensity laser Biostimulation on a cell. SPIE, 4224: 186-192.
9. Liu TCY, Chen YH, Li Y and Duan R (2000): Information biology on low intensity laser irradiation effects on red blood cells. SPIE, 4224: 193-195.
10. Borisenco GG, Osipov AN, Kazarinov KD, et al (1997): Photochemical reactions of nitrosyl hemoglobin during exposure to low-power laser irradiation. Biochemistry Mosc, 62: 661-666.
11. Pan Xing-Wang, Xu Fu-Sheng, Wu Zong-Yao (2000): Effects of He-Ne laser intravascular irradiation on testosterone, endorphin and endothelin in heroin dependent people. China Physiotherapy Journal, 23: 73-75. [Chinese]
12. Xu Song-Lin (1998): Laser medicine. China Medical Journal, 77: 935-936. [Chinese]
13. Shi Fu-Ming, Wu Qi-Zhuan (1999): Effects of He-Ne laser on brain monoamine transmitter in mice. China Physiotherapy Journal, 22: 169-170. [Chinese]
14. Xiao Xue-Chang, Chu Xiao-Fan, Ni Jia-He, et al (2000): Effects of traditional Chinese medicine and intravadcular laser irradiation therapy in patients with senile deficiency of the kidney and brain infarction. Chinese Journal of Conjugation of Taditional Chinese and Western Medicine, 20: 264-266. [Chinese]