

The Clinical Observation of Photodynamic Therapy with Operation on Intracranial Malignant Tumor

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Abstract Objective To observe the effect of photodynamic therapy with operation on intracranial malignant tumor. **Methods** 20 patients (from 2000 to 2004) were treated by photodynamic therapy during the operation. The photosensitizer (HMME, 10mg) was infused into the vein of the patient at 24h before operation. The He-Ne laser irradiated the tumor's cavity for killing these survival tumor's cells after resecting the tumor under the microscopy. The patients were followed up. **Results** The rate of melioration of post-operative KPS score was 80%, the skin phototoxic reaction can not to be observed. **Conclusion** The results indicate photodynamic therapy is an effective assistant approach for treating intracranial malignant tumor. It is necessary for improve surgical outcome and patient's life quality.

Key Words Photodynamic therapy; HMME; Intracranial malignant tumor

Photodynamic therapy (PHD) is the new developing investigation domain of the therapy on the intracranial malignant tumor, it has had great achievement since 1970s. Compared to the operation, radiotherapy and chemotherapy, PHD can eliminate local tumor selectivity. It has the synergistic action when practicing with the radiotherapy and chemotherapy. This new method will decrease the operation size and improve the postoperative outcome. This test chooses 20 patients with PHD to confirm the effect of photodynamic therapy with operation on intracranial malignant tumor.

MATERIALS AND METHODS

Patients

20 patients with photodynamic therapy were included, with age from 28 to 55 (median 38) years old. There were 13 males and 7 females, and 16 patients with supratentorial tumors (9 cases in frontal lobe, 7 cases in temporal lobe), 4 patients with infratentorial tumors. The first clinic symptom was high intracranial pressure (ICP), and 2 cases with epilepsy, 2 cases with limbs dyskinesia, 1 case with orientation and calculation descent. The pathological results were that 17 cases was astrocytic tumor, among them, 12 case with grade II, and 5 cases with grade III, 2 cases had lung cancer

metastasis, 1 case was Ependymoma. To evaluate Karnofsky Score that 17 cases were above 60, 3 cases were below 60. Simple operation group was 18 cases, with 8 males and 10 females, and age from 19 to 66 years old, 13 patients with supratentorial tumors, 5 patients with infratentorial tumors. 10 cases were Astrocytic tumor grade II, 8 cases were grade III. The results of Karnofsky Score evaluation were that 16 cases were above 60, 2 cases were below 60. All patients had been confirmed with MR images and pathology.

Materials

HN -600 model laser therapy machine (Changchun Zhongji Instrument Ltd.), laser wave-length is 632.8nm (He-Ne Laser). The Maximum laser power is 600mW. The output style is mono-core optical fiber output. The output style is suitable to have a therapy with body surface and intraluminal pattern. Photosensitizer (HMME, 10mg/ml) is supplied by the Second military medical university drug-chemistry institute.

Methods

According to the history, symptom, physical sign and MR image data, we first give the final diagnosis of malignant tumor. Then 20 ml HMME were used with intravenous drip in the experimental group before operation, and after 24 hs the experi-

mental group have the operation therapy. The tumors were total resected by microscope. Then we utilize the HN-600 model laser therapy machine (dosage 300 J/cm²) to process the laser exposure. There are 1 cm between the optical fiber head and the neoplasia bed, and washing the neoplasia cavum intermission with saline to reduce the temperature and prevent infection. Postoperative the group should keep away the light 3 days to observe the symptom remission and variety state. All patients have the routine radiotherapy after discharge. Every 3 months we have the follow-up by telephone and record the existence time, symptom variation and Karnofsky Score. Every patient has the MR scan when return visit.

RESULTS

Earlier effect of the PHD therapy group is satisfied. The clinical symptom of all patients had improved or disappeared, and no new loss of nerve function occur. The wounds heale well while the patients were discharged from hospital. There are no cerebrospinal fluid leak. Each case has no skin photosensitivity reactions and visual acuity descent. Total amelioration rate is 80%(16/20), and in simple operation group it is 77.8%(14/18). The complete result was showed in Fig.1 and table 1. sur-

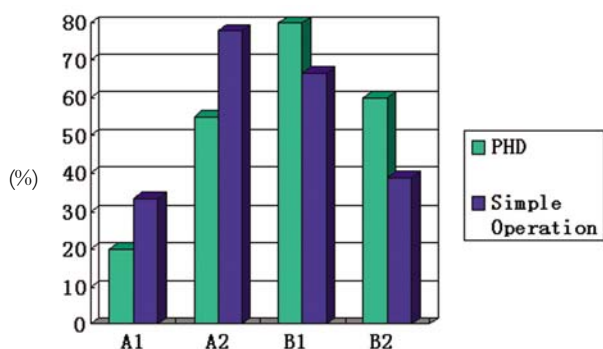


Fig.1 A1 means 1 year recurrence rate; A2 means 2 year recurrence rate; B1 means 1 year survival rate; B2 means 2 year survival rate

vival rate of the patients in experimental group is obviously higher, and the recurrence rate is more lower ($P<0.01$) than that in the other one ($P<0.05$). The results show that the PHD therapy can improve the clinical symptom. This experiment evaluation is according to the Karnofsky score and the postoperation MR image.

DISCUSSION

The treatment problem of the brain malignant tumor has always been the difficult point in the neurosurgery domain. And the surgical operation is a generally accepted treatment method. The effective treatment specificity of PHD is very high. The basic principle is that the photosensitizer (HMME) can pass through blood-brain barrier (BBB) destroyed by malignant tumor. The HMME can be stored with the higher density in the brain tumor, and it is very lower in the normal brain. Then we can use the particular wave-length laser expose the tumor. And the HMME will have chemical reaction to yield the single state. This oxygen can induce apoptosis of tumor cell by action with the biomacromolecules in the tumor. However the brain malignant tumor can be resected completely, the neoplasia bed still remains the tumor cells. On the other hand cut the brain tissue excessively will bring back the neurologic defect. The He-Ne laser has more penetration power that can eliminate remain cell. So PHD can be utilized in the glioma, glioblastoma, and recurred tumor, especially for the tumor located in the important function region.

The clinic observation demonstrated, that PHD therapy has a fine effect, which can improve the survival quality, and don't increase side reaction and complicationses. The PHD is a comprehensive treatment of the glioma, and often combining with the surgical operation. In order to eliminate the remaining tumor cell selectively after the operation can rise the survival rate and prolong the patient's life. Preoperation we should have photosensitizer injected within certain time(decided by photosensitizer metabolism property), and the tumor was re-

Table 1 the follow up outcome

Group	Nubers	Amelioration rate of Karnofsky Score(%)	1 year recurrence rate (%)	2 years recurrence rate (%)	1 year survival rate (%)	2 years survival rate (%)
PHD+Operation	20	80	20	55	80	60
Simple Operation	18	77.8	33.3	77.8	66.7	38.9

sected completely as much as possible. The certain wave-length laser is used in the operation. Then postoperation it should avoid the light sometime (decided by the style of photosensitizer). The PHD therapy has the more clinical applicated foundation.

1. The malignant brain tumor often relapses in the original tumor location, and the PHD action is just the local cell-toxicity effect which is decided by the quantity.

2. The depth of light penetration of the malignant tumor is about 2.9 mm, and the normal only 1 mm. The necrosis depth of the malignant tumor tissue can be 3~5 times more than the light penetration depth actually. This is related to the microvascular inflammatory reaction, lesion and emphraxis surrounding the tumor tissue.

The PHD is mainly used as an operate assistance approach in neurosurgery. Perria (Italy) had reported the PHD therapy (PDT) in intracranial tumor. Then some scholar had processed the correlated research. Kaye et al. reported 120 cases with PDT, including the glioblastoma and low level glioma. The average survival time of 38 patients is 24 months. Compared to the contrast group the average survival time prolonged relatively. Linfeng has processed 17 cases intracranial tumor with PHD founded at the animal experiment. The short-term effect was well. Now, many scholars have realized the effectiveness of PDT, and make some series innovation such as expanding sacculus, divided exposure, multi-fiberoptic exposure and local photosensitizer injection etc.

Problem and Future

1. The PDT causes the brain tissue edema and necrosis. Once reported that the edema induced by PHD therapy lead to cerebral hernia. But our experiment did not take place the similar condition.

We think the cause of cerebral hernia is that the smaller excise range and larger exposure dosage.

2. The exposure skin and retina may have the exfoliative dermatitis and sight descent. But if we have light avoided strictly after the operation, such symptom will not appear.

3. Some reports show that the function of liver and kidney has a little lesion. So after operation we should have the function tested conventionality. Along with the provement of photosensitizer, smaller toxicity and lighter photosensitivity reactions will be solved.

4. The better exposure effect will base on the technique development of light source and fiberoptic. And it will make smaller exposure time and more penetration.

REFERENCE

1. van den Bergh H. Photodynamic therapy of age-related macular degeneration: History and principles. *Semin Ophthalmol*, 2001 Dec, 16(4):181-200.
2. Zimcik P, Miletin M. Photodynamic therapy as a new prospective method for cancer treatment. I. History, basic principles. *Ceska Slov Farm*, 2004 Sep, 53(5): 219-224.
3. Kathrin Scherer. Structure-activity relationships of three differently substituted 2, 7, 12, 17-tetrakis-(beta-methoxyethyl) porphycene derivatives in vitro. *Arch Dermatol Res*, 2004 May, 295(12): 535-541.
4. John Webber, Mark Herman. Photodynamic treatment of neoplastic lesions of the gastrointestinal tract. Recent advances in techniques and results. *Langenbecks Arch Surg*, 2000 Jul, 385(4): 299-304.
5. Terzis AJ, Dietze A, Bjerkvig R, et al. Effects of photodynamic therapy on glioma spheroids. *Br J Neurosurg*, 1997 Jun, 11(3): 196-205.
6. Rodriguez E, Baas P, Friedberg JS. Innovative therapies: photodynamic therapy. *Thorac Surg Clin*, 2004 Nov; 14(4):557-566.