

## **Combinational effect of pulsed dye laser and propranolol on treatment of superficial hemangioma.**

Xuejian Liu<sup>1\*</sup>, Wenchuan Yang<sup>1</sup>, Maozhong Tai<sup>2</sup>, Yuhua Li<sup>1</sup>, Xia Wu<sup>1</sup>, Xiangli Chen<sup>1</sup>

<sup>1</sup>Department of Oncology, Linyi No.3 People's Hospital, Linyi, Shandong, PR China

<sup>2</sup>Department of Head and Neck Surgery, Linyi Tumor Hospital, Linyi, Shandong, PR China

### **Abstract**

**Objective:** To analyse combinational effect of pulsed dye laser and propranolol on treatment of Superficial Hemangioma (SH).

**Methods:** From June 2016 to June 2017, we collected 110 children with SH enrolled in Linyi No.3 People's Hospital. All patients were divided randomly and evenly into two groups (control group and study group). The patients in control group were treated with pulsed dye laser, while patient in study group were treated with pulsed dye laser and propranolol. The efficacies of those two different treatment methods were analysed and compared.

**Results:** The heart rate of the control group is  $143.29 \pm 5.96$  times/min, but that of the study group is  $120.03 \pm 2.36$  times/min. Moreover, the efficacy rate in the study group was 98.18% (54/55), which is higher than 74.55% (41/55) in the control group. Meanwhile, the adverse reaction rate in the study group is 3.64% (2/55), which is lower than 20.00% (11/55) in the control group.

**Conclusion:** Combination of pulsed dye laser and propranolol is effective in the treatment of superficial hemangioma.

**Keywords:** Pulsed dye laser, Drug, Treatment, Hemangioma.

*Accepted on October 25, 2017*

### **Introduction**

Superficial Hemangioma (SH) mainly appears in the head, face and neck of babies and some other parts like limbs. Some SH take up larger area than else. Generally, the SH in the patients' children at the age of 6 months grow fastest, if without timely treatment, the latter part of the treatment will be relatively difficult, as for the serious cases there are defects or functional dysfunction on their face [1]. Some scholars put forward that the Pulsed Dye Laser (PDL) combined with drug for treatment of superficial hemangioma is very effective. Therefore, to analyse its effect, this hospital treated SH with PDL and drug, detailed reports are as followings.

### **Materials and Methods**

#### **General materials**

From June 2016 to June 2017, we collected 110 children with SH enrolled in Linyi No.3 People's Hospital. All patients were divided randomly and evenly into two groups (control group and study group). The control group includes 20 males and 35 females aging from 29 days to 9 months with average age of  $3.26 \pm 1.19$  months. The study group includes 18 males and 37 females aging from 28 d to 8 months with average age of  $3.11 \pm 1.04$  months.

### **Methods**

Researchers treated the two groups with PDL, monitored seriously the body condition of children, did routine ECG, cardiac ultrasound, blood glucose, blood routine and blood biochemical tests; all of the machine used in the process of treatment are US SYNOSURE V-star PDL machine, the wavelength is 585 nm; The pulse width is 2 ms; diameter spot is 7 mm, the overlap parts between the spots is 10% to 20%, we adjusted the specific energy intensity according to the color of erythema and local reaction after irradiation, it is the most proper situation when some parts appeared purple, the pulse width is set to 2ms and the energy is set to 7.00 to 11.00 J/cm<sup>2</sup>. Patients usually accept treatment for 4-6 times, during which is an interval of 4 weeks. The patients in the study group were treated with pulsed dye laser and propranolol, and treated with propranolol at the same time of making PDL treatment. After meals, the patients took a dose of 0.25 mg•kg<sup>-1</sup>•d<sup>-1</sup> on the 1st day; 0.50 mg•kg<sup>-1</sup>•d<sup>-1</sup> on the second day; 1.00 mg•kg<sup>-1</sup>•d<sup>-1</sup> on the third day; 2.00 mg•kg<sup>-1</sup>•d<sup>-1</sup> after the fourth day. With the lesions disappeared, patients should take less or stop taking medicine in accordance with rules while the control group did not take medication.

### Observation of the indicators and assessment

Analysed the efficacy of the two groups and observed their color sink, color reduction, ulcers and other adverse reactions; recorded the changes of heart rate of children under treatment; the efficacy depends on the grading standards of Achauer [2,3], the disease proved to be cured when the tumor area reduced to a range of 76%-100%; the efficacy proved to be marked when the tumor area reduced to a range of 51%-75%; the efficacy proved to be effective when the tumor area reduced to a range of 26%-50%; the efficacy proved to be invalid when the tumor area reduced to a range within 25%; total efficacy=cured+marked+effective.

### Statistical analysis

All data were analysed with statistical software SPSS 22.0. The measurement data was expressed as mean  $\pm$  standard deviation and tested by t-test. The counting data was expressed as numbers and percentage and test by Chi-square test.  $P < 0.05$  suggests that the difference is statistically significant.

## Results

### Heart rate changes in control group and study group

The heart rate of the study group was lower than that of the control group after treatment. At the 4th day after treatment, the heart rate of the control group is  $143.29 \pm 5.96$  times/min, but that of the study group is  $120.03 \pm 2.36$  times/min (Table 1).

### Comparison of efficacy between control group and study group

The number of cured cases in the study group was more than that of the control group. The efficacy rate in the study group was 98.18% (54/55), which is higher than 74.55% (41/55) in the control group (Table 2).

### Comparison of adverse reactions between control group and study group

There were more cases of color sink, ulcer in the control group than that of the study group. The adverse reaction rate in the study group is 3.64% (2/55), which is lower than 20.00% (11/55) in the control group (Table 3).

**Table 1.** Heart rate changes in control group and study group.

Groups	n	1 d after treatment	2 d after treatment	3 d after treatment	4 d after treatment
Control group	55	144.31 7.19	$\pm$ 142.39 6.34	$\pm$ 143.06 5.49	$\pm$ 143.29 5.96
Study group	55	140.30 6.13	$\pm$ 134.69 4.18	$\pm$ 129.60 3.52	$\pm$ 120.03 2.36
t		6.79	6.00	7.13	7.24

p	0.038	0.029	0.023	0.020
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**Table 2.** Comparison of efficacy between control group and study group.

Groups	n	Invalid	Effective	Marked	Cured	Total efficacy
Control group	55	14 (25.45)	12 (21.82)	16 (29.09)	13 (23.64)	41 (74.55)
Study group	55	2 (3.64)	15 (27.27)	20 (36.36)	19 (34.55)	54 (98.18)
$\chi^2$						9.05
P						0.015

**Table 3.** Comparison of adverse reactions between control group and study group.

Groups	n	Ulcer	Color sink	Color reduction	Adverse reaction
Control group	55	2 (3.64)	5 (9.09)	4 (7.27)	11 (20.00)
Study group	55	0 (0.00)	1 (1.82)	1 (1.82)	2 (3.64)
$\chi^2$					7.83
p					0.006

## Discussion

Hemangioma belongs to a kind of benign tumor in the vascular system, which often appears among infants and young children. According to Leaute-Labreze and other reports, the effect of the application of propranolol in infantile for treatment of hemangioma is quite remarkable, as a result, it has been widely spread in the international community [4-6]. Hence, to get a better treatment effect of SH, the hospital combined the drug propranolol with PDL when implemented treatment.

After employed propranolol on SH for 24 h to 48 h, the color of SH changed, the total area of the tumor began to reduce, and its texture gradually softened. Propranolol is a blocker for selective beta-type receptors that inhibits cardiac excitatory sympathetic nerves and stimulates blood vessels to contract [7-9]. The endothelial cells of SH showed as a monoclonal system, which will make the abnormal growth and proliferation of endothelial cells. In addition to, propranolol can promote angiogenesis through activating the pathway of ERK/MAPK by using VEGF (Vascular Endothelial Factor) and bFGF (fibroblast growth factor), which is highly expressed in serum and tumor when SH is in growth period. And in the subsided period, propranolol will show less or no expression to inhibit the expression of VEGF and bFGF in vascular tumor cells or endothelial cells, and then can inhibit the formation mouth of blood vessels and cell differentiation strongly [10-13]. And the main factor for the SH self-dissipation is the gradual declining of cells caused by apoptosis. Propranolol can bring about less activity of endothelial cells in blood vessels,

inhibit the growth of endothelial cells, and affect the activity of caspase and other proteins, induce the apoptosis of gastric cancer cells, pancreatic cancer cells and capillaries. But propranolol will make metabolism through the kidney, liver, which will cause the slowing of heart rate, the decreasing blood pressure, the reduction of platelets and other reactions. Therefore, more attention should be paid to dose in the process of treatment, take medicine in line with the instructions, and make appropriate adjustment according to the actual condition [14,15].

According to analysis to the study, the heart rate of the study group was slower than that of the control group after treatment. The heart rate of the control group was  $143.29 \pm 5.96$  times/min faster than that of the study group 4 d after treatment, and the study group was similar with that of Sun [4]. The number of cured patients in the study group was more than that in the control group, efficacy of the study group is 98.18% (54/55) higher than that of the control group, which is like the result in group of Wei [5]. The adverse reaction rate was 3.64% (2/55) in the study group lower than 20.00% (11/55) in the control group, which was similar with result of related study. The reason should be the combined using of propranolol and PDL in the degenerative phase, which can reduce the dose of propranolol, thus effectively shortening the treatment cycle and reducing the adverse reaction. The main mechanism of PDL for SH is that the wavelength of PDL gets close to the absorption peak of oxygenated hemoglobin. Blood capillary and hemoglobin are absorbed when the wavelength is at 585 nm, and the abnormal blood vessels are destroyed by their specificity. But it won't damage the adjacent skin tissue, the penetration depth is 2 mm, it can effectively promote the regression of hemangioma, enhance the overall effect. The complications of two groups require more clinical supplementary analysis.

In summary, the combinational effect of pulse dye laser and drug for treatment of SH is very good, which can promote the improvement of symptoms, and improve the efficacy while reducing adverse reactions.

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## \*Correspondence to

Xuejian Liu

Department of Oncology

Linyi No.3 People's Hospital

PR China