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Treatment of infantile hemangioma by intralesional injection of propranolol combined with compound betamethasone

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Abstract. – OBJECTIVE: To explore the effective and convenient methods of infantile hemangioma treatment.

PATIENTS AND METHODS: From October 2010 to June 2014, 31 infantile hemangioma patients admitted to our hospital, were administered propranolol combined with betamethasone injection treatment of lesions.

RESULTS: All patients were followed for 6 months-2 years. In treated patients, 24 patients with tumor had complete or nearly complete remission while 6 patients showed partial regression. In 1 patient the tumor had no evident change. Adverse reactions of the therapy included local tissue atrophy, ulcer and anorexia, mild diarrhea in the early treatment. Ulcer wound healed after dressing change.

CONCLUSIONS: Treatment of infantile hemangioma lesions with an injection of propranolol combined with betamethasone showed good efficacy. The method is safe and reliable with clear curative effect, convenient, less complicated, and especially suitable for patients with a small area infantile hemangioma.

Key Words:
Propranolol, Compound betamethasone, Intralesional injection, Infantile hemangioma.

Introduction

Infantile hemangioma is one of the most common benign tumors in children, shortly after birth, and these tumors are self-limiting. But in proliferating hemangioma, ulcer and necrosis may also occur. Hemangioma located in the head and face or exposed parts or in important organs has a clear effect on the appearance and cause potential organ dysfunction. So there is a need for active treatment. Use of propranolol in the treatment of serious and complex infantile hemangioma has shown a strong advantage[1-3]. Its therapeutic effect is rapid with mild side effects, but cannot make complete involution of the tumor or prevent recurrence after stopping drug. Often there is the need for laser treatment, operation, and other clinical interventions. At our department from October 2010 to June 2014, we applied propranolol combined with betamethasone as an injection for the treatment of lesions in 31 cases of infantile hemangioma[4,5], with satisfactory curative effect, as reported here.

Patients and Methods

Patients

All the studies were approved by the Institutional Ethics Committee at our hospital. There are 31 little patients in this group, age 4-20 months. Tumor growth site: 16 cases of head and face, 9 cases of limbs and 6 cases of trunk. The tumor area ranged from 1.0 cm × 2.6 cm to 2.1 cm × 5.3 cm. Children with bronchitis, pneumonia, tracheal, bronchial asthma, sinus bradycardia, atrioventricular block and acute heart failure were excluded from the study. Informed consent was obtained from the parents prior to the study.

Treatment Method

Compound betamethasone injection: preoperative tumor area was estimated, to determine betamethasone dosage, which is generally 0.05 ml/cm^2, at a total dose of not more than 0.3 ml. The injection process: With the appropriate pressure around the tumor, No. 4.5 needle was inserted into the tumor peripheral normal skin in tumor direction, and after pumping back with blood, the drug was injected. Attention was paid to multipoint injections from different directions and to the depth of tumor body, so that the medicine can be evenly distributed to the tumor. Injection to the surface of mucosa or skin caused paleness and slight swelling. After injection, pressure was

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applied around tumor for 5 min, and spillover of drugs prevented by hemostasis. It is important to not to use a needle in hemangiomas surface, which can lead to the eye of needle bleeding, extravasation of drugs, thus reducing the efficacy. One injection was given every 4-6 weeks, with a total of 4 to 5 for one course of treatment, and treatment interval of one month. The injection was repeated until the disappearance of the tumor. During the injection treatment, oral propranolol use was strictly according to the indications and contraindications. The patient inspection was improved before the treatment (for monitoring blood pressure, heart rate, electrocardiogram, ultrasound Beckoning diagram and glucose), with ECG monitoring and once drugs began to be used, blood glucose was measured after 1h, 2h, and also heart rate, respiration, and blood pressure were recorded. The starting dose of propranolol was at 1.0 mg/kg·d[2], twice, 12 h interval administration. After 2 days the dose was increased to 1.5 to 2.0 mg/kg·d, twice, 12 h interval administration. Patients were evaluated once every 4 weeks, with inspection of vital signs, heart rate, body weight and blood glucose, and based on these results oral dosage adjustment was made. After 8 weeks of drug treatment, the drug was discontinued; the average treatment time was 5 to 6 months. Regular hospital visit follow-up or telephone follow-up was made for each patient.

The evaluation of curative effect of the treatment is divided into 4 levels[6-8]: Level I — ineffective, the tumor showed no shrinking and stayed the same or increased continuously; Level II — improved, the tumor shrank significantly or but less than 2nd/3rd, the treatment needs to be continued; Level III — effective, tumors shrank significantly after treatment in [3]80% patients, with the skin color close to normal or slight pigmentation, no dysfunction, but the appearance has not been fully restored to normal, with continued treatment; Level IV — excellent, after treatment tumor disappeared completely, skin surface with normal color, no dysfunction, no recurrence and follow-up needed.

All patients were followed up monthly, 1 visit monthly. The drug dosage was adjusted according to body mass, curative effect and side effects. Vascular tumor size, texture and color change were recorded and tumor pictures were recorded. Blood chemistry, biochemical parameters (liver and kidney function, blood glucose and blood lipid) and electrolytes were measured and any adverse reactions were taken into account, and symptomatic treatment was considered at all times.

Results

In this group of children treated by combined use of drugs, 19 cases showed excellent results, and 6 effective, 5 improved, and 1 ineffective cases were observed. The overall effective rate was 96.8%. With the extension of combined medication time, tumor further narrowed, patchy fading, skin color became shallow, and blood of the tumor body surface gradually disappeared. Adverse reactions: (1) Heart rate slow down: after medication, heart rate slowed down in 4 cases, without obvious discomfort and no special treatment was needed. (2) Sleep changes: 5 cases showed excitement, sleeplessness, after taking

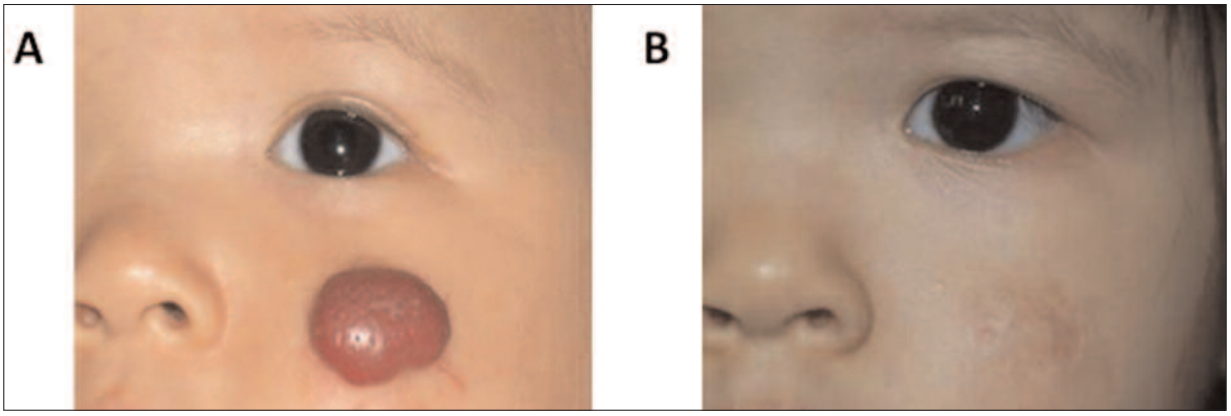

Figure 1. ***A,*** 6 months baby boy, suffering from hemangioma; ***B,*** 8 months after combined therapy.

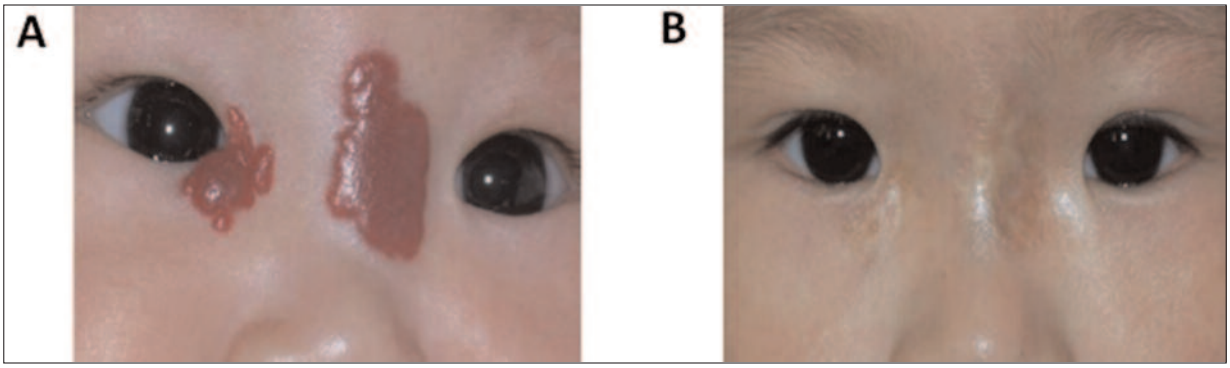

Figure 2. ***A,*** 5.5 months baby girl, suffering from hemangioma; ***B,*** 10 months after combined therapy.

treatment for about 1 month, and patients recovered. (3) Effect on digestive system: 4 cases showed nausea, diarrhea, abdominal discomfort, abdominal distension, constipation or other symptoms and usually these symptoms disappeared in 1 week. (4) Body weight: growth delay in 1 case (chest hemangioma of one of the twins); however, after 3 months, body weight increase was recovered. For typical cases, see picture 1A, 1B, 2A, 2B, 3A and 3B.

Discussion

Hemangioma is the most common pediatric neoplasm that subsides slowly. However, some of the hemangiomas grow in the face, neck and other special parts or grow particularly rapidly, which can affect the normal organ function or cause ulcers, bleeding and pain and other complications[9,10]. Therefore, active and effective intervention is necessary.

Propranolol, the commonly used beta blocker, is also widely used in the treatment of rapid arrhythmia, angina, hypertension, and diseases such as pheochromocytoma. Léauté-Labrèze et al[7] discovered a new approach for the treatment of infantile hemangioma with propranolol. Oral propranolol in the treatment of refractory hemangioma has good short-term efficacy, mild adverse reactions, and can be used to control the disease and rapid growth of hemangiomas[11,12]. But the hemangioma cannot be completely dissipated, and propranolol needs to be combined with other treatment.

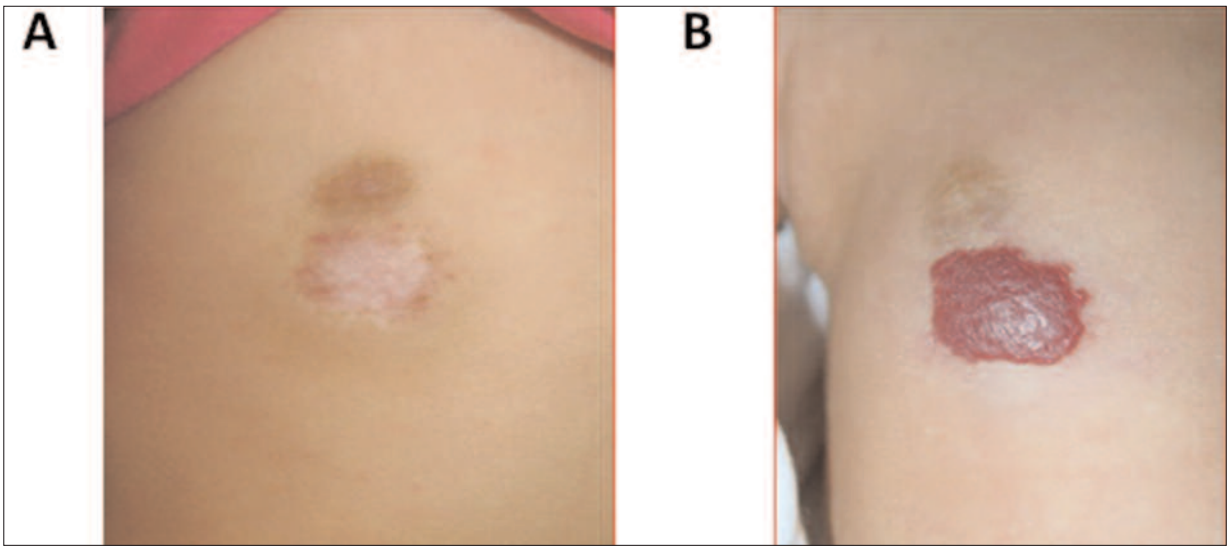

Figure 3. ***A,*** 7 months baby boy, suffering from hemangioma; ***B,*** 11 months after combined therapy.

Corticosteroid use for the treatment of hemangioma has a history of over 30 years[13-15], with good effect in the treatment of infantile hemangioma, with fewer side effects[16-18]. We applied betamethasone by local injection in the treatment of infantile hemangioma. The purpose of injection is to control rapid tumor growth and promote tumor shrinking. Betamethasone dipropionate mainly acts by increasing the number of mast cells in tumor so as to promote the apoptosis of vascular endothelial cells. Betamethasone injection used in this study is a combined compound preparation of short-acting drug betamethasone sodium phosphate and long-acting drug betamethasone dipropionate. After injection, soluble betamethasone sodium phosphate soon exerts its effects, but betamethasone dipropionate is slowly absorbed, forming a drug storage in local area with long-term effect. After Betamethasone Injection, the effect can be maintained for 2-4 months. Compared with laser, freezing, isotope application and sclerosing agent injection and other methods, hormone treatment has the advantages of no local redness, swelling in the early inflammatory manifestations. After the late hemangioma subsides, there is no residual scar and no pigmentation, which is quite similar to hemangioma regression process.

Conclusions

The combined application of Compound Betamethasone Injection and propranolol in the treatment of hemangioma, can produce synergy, improve efficacy, and reduce tissue reaction to ensure the tumor drug safety.

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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