

Research Progress on Clinical Treatment of Hemangioma and Vascular Malformation in Children

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Abstract: Childhood hemangioma is a common benign tumor composed of vascular endothelial cells that occurs mostly in children, with a high incidence rate, generally 4–10%. The incidence rate is as high as 75% within a few weeks after birth, especially in the skin and subcutaneous tissue. Hemangioma can be invasive, growing rapidly, and may lead to spontaneous ulceration. It can also regress on its own. When it affects multiple areas on the head and face, it can create a significant mental and psychological burden for both children and parents. Treatment methods for hemangiomas have become more mature, with expert consensus and clinical practice guidelines available. Understanding of how these treatments work has also improved. It is important to review the available treatment options to assist both healthcare providers and parents in choosing the most suitable treatment for children with hemangiomas. This helps in making informed decisions about treatment methods.

Keywords: Children hemangioma; Vascular malformation; Clinical treatment; Progress

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1. Introduction

The implementation of China's two-child policy has resulted in an increased number of newborns. Consequently, there has been a year-on-year increase in cases of hemangiomas in children ^[1]. Hemangioma is a common benign tumor composed of vascular endothelial cells that mostly occurs in children, with an incidence of 4–10% ^[2,3]. The incidence rate is as high as 75% within a few weeks after birth. Hemangioma is usually visible in various parts of the human body, especially the skin and subcutaneous tissue. Hemangioma can be invasive, growing rapidly, and may lead to spontaneous ulceration. Multiple hemangiomas can also occur at

different areas of the face. Therefore, it brings great mental and psychological burden to children and parents, especially in the proliferative period. Hemangiomas can potentially lead to damage to muscle or skin blood vessels, secondary infections, and, in severe cases, ulceration. These complications can result in significant issues such as damage to one's appearance and even vision loss ^[4]. Treatment methods for hemangiomas have become more mature, with expert consensus and clinical practice guidelines available. Understanding of how these treatments work has also improved. It is important to review the available treatment options to assist both healthcare providers and parents in choosing the most suitable treatment for children with hemangiomas. This helps in making informed decisions about treatment methods.

2. Interventional therapy

Interventional therapy entails introducing an embolic agent into the blood supply and return site of the hemangioma through a catheter. This changes the hemodynamics of blood flow within the hemangioma. Subsequently, a sclerosing agent is percutaneously injected under ultrasound guidance. The sterile inflammatory reaction triggered by the hardening foam promotes the occlusion of the hemangioma, ultimately achieving the desired therapeutic outcome ^[1,5-8]. For different hemangiomas and vascular malformations, a combination of different sclerosing agents such as lauromacrogol or polidocanol injection ^[9] has been proven effective. Interventional therapy is widely employed in clinical practice for treating pediatric hemangiomas due to its advantages like minimal trauma, notable efficacy, strong repeatability, and its non-interference with subsequent treatments. It is generally well-received by parents, making it the primary approach for pediatric hemangioma treatment in clinical practice.

3. Drug treatment

In clinical practice, commonly used drugs for treating infantile hemangioma include propranolol, bleomycin, pingyangmycin, and others ^[10]. Propranolol is primarily administered orally, while bleomycin and pingyangmycin are mainly applied externally or subcutaneously ^[11].

The use of propranolol in the treatment of infantile hemangioma began in 2008 and demonstrated significant efficacy from its initial application ^[12]. Clinical practice also proved the efficacy of propranolol in the treatment of infantile hemangioma. The main drug in the treatment of hemangioma. As a synthetic non-selective β -adrenergic receptor blocker, it can block β_1 and β_2 receptors, causing a decrease in heart rate and blood pressure ^[13]. The mechanism of action of propranolol in the treatment of hemangioma has not been fully understood. It is generally believed that in the early stages, propranolol reduces the release of nitric oxide within 1–3 days after treatment initiation, leading to vasoconstriction. In the middle stage, it inhibits angiogenesis by blocking pro-angiogenic signals and induces apoptosis of endothelial cells, resulting in a long-term therapeutic effect ^[14]. Propranolol may also induce apoptosis of various types of cells including endothelial cells *in vitro* by blocking β_2 receptors ^[15]. Therefore, induction of apoptosis may be another mechanism of therapeutic effect of propranolol on hemangiomas. Propranolol is effective as a first-line oral treatment of hemangiomas, but it also has side effects. Its main side effects are bronchospasm, hypotension, hypoglycemia, bradycardia, etc ^[12,13]. After being approved for marketing, it was discovered that propranolol might lead to adverse reactions, including agranulocytosis, hallucinations, purpura, and psoriasis-like dermatitis. Additionally, its efficacy in treating larger hemangiomas is not satisfactory. Therefore, the combination of drugs is mostly used to treat superficial hemangiomas with a small range of involvement.

4. Surgical treatment

Surgical treatment can be considered for deep or mixed hemangiomas that do not respond to medical therapy, pose life-threatening or function-threatening risks (e.g., airway obstruction), or do not improve with local therapy due to contraindications or treatment failure. This option is particularly relevant when the hemangioma is located on the scalp or trunk, and when it is situated in a concealed or deep area, possibly in conjunction with vascular malformation ^[2,16]. Surgical intervention is more effective than medications, but it comes with certain risks and complications ^[17]. For example, it may cause postoperative incision scars, skin color and skin texture inconsistencies in the affected area, etc., which may impact the child's mental health or future opportunities. This ensures that parents have a complete understanding and can carefully weigh the pros and cons of surgery. Typically, surgical intervention is not the primary treatment option for hemangiomas due to the potential for varying degrees of scarring.

5. Laser treatment

Multiple laser options are available for hemangioma treatment, including dot matrix CO₂ laser, pulsed dye laser, frequency-doubled Nd-doped yttrium aluminum garnet (Nd:YAG) laser, and photodynamic therapy, among others ^[17,18]. Different laser therapy devices have different working principle, therapeutic effects, and functions. For example, when frequency-doubling Nd-doped YAG laser irradiates hemangioma lesions, melanin particles in the epidermis can be competitively absorbed due to poor laser penetration ^[19]. Pulsed dye laser is designed according to the "selective photothermal effect theory," which has better curative effect and fewer side effects, but there are still adverse reactions such as purpura, skin texture changes, temporary pigment changes, and atrophic scars after use. The advantages of photodynamic therapy are high tissue selectivity, definite curative effect, and small systemic adverse reactions. However, due to the use of photosensitizers, postoperative light protection is required ^[21]. Due to its strong penetrating power, photodynamic therapy is currently mostly used for the elimination of postoperative scars.

6. Other treatments

In addition to the above-mentioned treatment methods for hemangiomas that are widely used at present, there are other methods such as hormone therapy, interferon therapy, cryotherapy, and radionuclide therapy for hemangiomas. However, it is not easy to control the dosage of drugs, hormones, and interferon used. These drugs might have a greater impact on the body in the later stages of life. Besides, the radiation produced in these therapies might cause hypopigmentation spots, bone growth inhibition, and scars at the treatment site. These methods are rarely used clinically at present ^[16,17,21].

For all infantile hemangioma patients, the selection of treatment measures should depend on the following three aspects, in order of importance: the location of the tumor, the age of the child at the time of treatment, and the size of the tumor ^[22]. The above treatment methods have their own indications and side effects in different degrees. In order to achieve a better therapeutic effect in the clinical treatment of hemangioma, a combination of multiple treatment methods is often used. The main goal of treating hemangiomas is not to eliminate all lesions but to alleviate the symptoms and control the progression of disease ^[9]. Therefore, it is very important to find a balance in the treatment, which includes aspects like safety, bodily functions, and especially aesthetics or appearance. It is important not to bring extra burden to the patients and their families due to excessive treatment.

Disclosure statement

The authors declare no conflict of interest.

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