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Review Article

The Treatment of Lymphangioma by Intralesional Bleomycin Injection: A Review Article

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Abstract

Lymphatic system may give rise to lymphangioma and this entity is usually accepted as a benign tumor. The most common symptoms are tumescenses and enhancive disfigurement. As a sclerosing agent, bleomycin has been used in the management of patients with these lesions with successful outcomes. In this review the subject is overviewed and a concise literature regarding the treatment options with special emphasis to intralesional bleomycin injection is given. This treatment option creates achievement of noteworthy results in most of the children with lymphangioma without major undesirable side effects.

Keywords: Lymphangioma; Bleomycin; Intralesional sclerotherapy

Introduction

Lymphangiomas are congenital hamartomatous malformations of lymphatic system and consist of cystic spaces of varying size. The mostly involved sites in the body include head and neck and 75% of all cases present with head and neck lymphangiomas [1,2]. The incidence of lymphangioma is 1.5 to 2.8 per 1000 with equal sex disribution [3]. Of the patients with lymphangiomas, up to 65% present at birth and 80-90 % present at the end of 2nd year [1,4,5]. Surgical excision is the established management of lymphangioma. By preserving vital structures removal of involved tissue is the goal of surgical treatment. This objective cannot usually be obtained with surgical intervention alone. Besides surgical treatment involves complications including wound infection, hemorrhage, unsighty scar, postoperative fluid accumulations, various nerve palsies and lymphorrhea [6]. Due to above mentioned situations, intralesional sclerotherapy of lymphangiomas has been popularized recently. In this review article, intralesional sclerotherapy of lymphangiomas with special relevance to bleomycin usage is reviewed and discussed under the light of relevant literature.

Discussion

Management of lymphatic malformations using sclerotherapic injections of different agents into the lesions became a treatment option when it was noted that lymphangiomas spontaneously involuted when the became infected. Sodium morrhuate was the first agent used in the treatment of lymphangioma by intralesional sclerotherapy in 1933. Since then various sclerosing agents have been used with varying successes. These agents are OK 432, iodine, ethanolamine oleate boiling water, quinine, pingyangmycin, urethane, pure alcohol, sotradecaol, doxycycline, ethanol, sodium tetradecyl sulfate, acetic acid, hypertonic saline, ethibloc and bleomycin [3,7-10]. The first isolation of bleomycin was in 1966 by Umezawa as an anti-tumour, anti-viral and anti-bacterial agent [11]. The basic action of bleomycin is inhibition of DNA synthesis biochemically. Although the mechanism is not fully understood, it has been suggested that it causes fibrosis in the lesion in a non-inflammatory manner with a sclerosing effect on vascular endothelium [11,12]. Most of the studies reveal that the effectiveness of bleomycin is the most in macrcystic lesions [7,13]. But it has also been shown that after 6th dose of intralesional injection all variants of lymphangioma responded well [14]. Erythema, oedema, pigmentation of the skin, temporary hair loss and fever are the most common complications of intralesional bleomycin treatment [15,16]. It has been reported that these non-serious complications occured in 25-63 % of patients treated with intralesional bleomycin injection [3,16-22]. Induration and oedema may be life threatening if the lesions are close proximity to the upper airways especially in patients younger than 3 months of age so it has been suggested that children younger than 3 months of age should be admitted to hospital for 48 hours in order to avoid upper airway obstruction [14]. Mortality after injection of bleomycin is not commonly observed but it was reported in 3 cases out of 70 patients in a previous study [23]. Systemic absorption of bleomycin after intraparenchymal injection is another concern in intralesional bleomycin treatment of lymphangiomas and it has been suggested that OK-432 should be the first injection option if systemic absorption of the agent used is a matter [3]. In order to reduce discomfort for the patient postoperatively, it has been suggested that solution of bleomycin should be prepared by addition of lignocaine 2% along with normal saline with a ratio of 1:1 [24]. Pulmonary toxicity is the most unwanted side effect of bleomycin therapy in these patients. The risk depends on the dose of bleomycin used. Life threatening toxicity is rare in the total doses of below 150 mg or 450U. In oncology patients doses exceeding 30 mg/m2 of body surface area given intravenously are also considered to be harmless [3,25,26]. Death from pulmonary complications have been reported in two children after intralesional bleomycin therapy but an accurate relation to bleomycin use in these infants was not shown [4]. Reported series did not achieve a consensus on the dose of bleomycin usage in these patients. Doses of 0.3-1.8 IU/kg has been suggested [4,16,19,27-29]. It has been suggested that these injections should be given from 2-week-to 2 months intervals and accumulative amount of injected bleomycin has been reported to be maximal to 15 IU/kg or 50mg in total or 5mg/kg [5,7,28].

Conclusion

In conclusion, lymphangioma is a scarce but a significant disease.

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Bleomycin sclerotherapy is an effective treatment modality for the management of lymphangiomas and it should be first line modality before surgical treatment. The reason why the bleomycin is a favorable treatment choice is that it is easily applied and produces excellent cosmetic results. Accurate management of these children with bleomycin sclerotherapy is recommended. The clinicians interested with these patients should keep this treatment choice in mind. If there is a suspicion of lymphangioma case, the clinician should confer with a pediatric surgeon and the patient should be treated accordingly.

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