Management of periorbital hemangioma by intralesional glucocorticoids and systemic propranolol: a single-center retrospective study

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Abstract: Periorbital hemangioma may lead to the vision impairment so effective treatment should be adopted in time. In this study, we made a retrospective analysis of intralesional glucocorticoids and systemic propranolol in the management of periorbital hemangioma. From Jan. 2006 to Dec. 2013, twenty-five children with periorbital hemangioma were enrolled into this study. Among them, sixteen children accepted intralesional injection of compound betamethasone preparation. Eight children accepted systemic propranolol. One child accepted both of the two treatments. The follow-up period ranged from 6 months to 60 months. The results showed that in the patients with intralesional compound betamethasone preparation, 13/16 patients' tumors involuted completely. 3/16 patients' tumors didn't involute completely at the end of follow-up. In the patients with systemic propranolol, 8/8 patients' tumors involuted almost completely. One patient didn’t respond to intralesional glucocorticoids, and so switched to systemic propranolol, which lead to the involution of tumor finally. The adverse effects in the patients with intralesional glucocorticoids included local soft tissue atrophy, local ulcer, and Cushing-like manifestations, which occurred in three patients respectively. In the patients with systemic propranolol, mild diarrhoea occurred in one child. According to our observation, both of intralesional glucocorticoids and systemic propranolol achieved good results in the management of periorbital hemangioma. Systemic propranolol showed superiority in efficacy and safety. We recommend systemic propranolol as the first-line therapy. However, for the children who can’t tolerate systemic propranolol, intralesional glucocorticoids still is a feasible choice.

Keywords: Periorbital hemangioma, intralesional glucocorticoids, systemic propranolol

Introduction

Infantile hemangioma (IH) is a common benign tumor in childhood, with the highest incidence in the head and face [1]. Periorbital hemangioma, including hemangiomas in the upper eyelid, lower eyelid, inner canthus, outer canthal and orbital septum, could oppress the eyeball, obstruct vision axis, affect visual development, and result in amblyopia finally. Therefore, early intervention is required to avoid above negative consequences [1, 2].

Glucocorticoid therapy had a history in the treatment of IH over 30 years [3, 4]. Studies [2, 5-8] showed that intralesional injection of glucocorticoids in periorbital hemangioma got good results with fewer side effects. And since the first report in 2008 [9], systemic propranolol has shown great advantages in severe hemangioma [10-12]. Several studies [13, 14] also showed the efficacy of systemic propranolol in periorbital hemangioma. Till now, there is not a randomized controlled trial to compare the two kinds of treatment in periorbital hemangioma.

Here we introduce a retrospective analysis of intralesional injection of compound betamethasone preparation (Trade name: Diprosan, Schering-Plough, New Jersey, USA) and systemic propranolol in the management of periorbital hemangioma in our clinic. Special attention was paid to the efficacy and safety of the two treatments. The results may be helpful for us to make an appropriate therapeutic choice for this common disease.
Management of periorbital hemangioma

Patients and methods

This research was approved by the Committee on Clinical Investigation of Jinling Hospital. Informed consent was provided for the patients' parents or guardian, according to the Declaration of Helsinki. The diagnosis of IH was consistent with that described in the literature [1]. From January 2006 to December 2013, 25 cases of periorbital IH were included in the study, including 17 females. Among the 25 patients, the lesions were located in upper eyelid in 12 cases, in inner canthus in 3 cases, in outer canthus in 3 cases and in lower eyelid in 7 cases. The initial treatment age ranged from 1 month to 7 months with an average age of 3.1 months.

Among them, sixteen children only accepted the intralesional injection of Diprosan. Diprosan 1 ml/ampoule contains betamethasone disodium phosphate 2 mg and betamethasone dipropionate 5 mg. Local anesthesia was adopted with 2% lidocaine solution. Then, the drug solution was injected directly into the lesion at multiple sites around the margin of the tumor. The dosage ranged from 0.5 ml to 1 ml according to the tumor size. Withdrawing before the injection was made to avoid the flow of liquid into the blood vessels. Slow injection was important to avoid high pressure, the back flow of liquid into the artery, and abnormal embolization. After the treatment, the patient was followed up every two month. If the tumor grew again, re-injection was performed.

From Jan. 2010, systemic propranolol was adopted to treat periorbital hemangioma in our clinic. Eight patients were treated until Dec. 2013. The dosage was 1 mg/kg/day initially, and increased to 2 mg/kg/day gradually in two week. The treatment was stopped at one year old. The potential complications, such as bradycardia, diarrhea, hypoglycemia or hyperkalemia, were monitored and managed when necessary.

One patient accepted the intralesional Diprosan firstly. The tumor showed no response to two times of injection. So he switched to the systemic propranolol treatment.

To evaluate the therapeutic effect, we rated the results as “Markedly effective”, “effective” or “invalid”. “Markedly effective” means the rapid shrinkage of the tumor after treatment and almost complete involution during follow-up. “Effective” means some shrinkage of the tumor

Figure 1. Case 1. A 2-month-old male child had a hemangioma in the left upper eyelid (A). Intralesional injection of Diprosan 0.8 ml was adopted. Two months later, the tumor shrank (B). At 1 year old, the tumor almost involuted with local telangiectasis (C). At 5 years old, the tumor completely involuted. The vision of left eye was normal (D). The results were ranked as “markedly effective”.

after treatment and incomplete involution during follow-up. “Invalid” means no obvious change of tumor after treatment and the alternative to other therapy. In the patients over three years old, eyesight was checked and recorded regularly.

Results

In the patients with intralesional glucocorticoids, the tumors shrank in one week after the treatment. And the tumor color faded. One month after the injection, the tumor involuted obviously. The tumor became soft, flat and turned dark red. Two months after the injection, most of tumors continued to involute. A few of tumors grew at the edge and required treatment again. In our cases, eleven patients underwent the treatment once, three patients twice, and two patients thrice. At the end of follow-up, 13 patients’ tumors got almost complete involution, with local telangiectasia left in 6/13 patients. In 3 patients, the tumor shrank, but did not fully involuted. For effects evaluation, it was markedly effective in 13 cases, effective in 3 cases.

In the patients with systemic propranolol, the tumor became flatten in one to two week. About one month later, obvious shrinkage of the tumor was observed. During the period of treatment, the tumor continuously and slowly involuted. The treatment last for 4 to 9 months with an average of 6.5 months. At one year old, the
treatment was stopped. We didn’t observe the reoccurrence of the tumors in follow-up. At the end of follow-up, 8/8 patients’ tumors involuted almost completely. And they are still in follow-up currently. For effects evaluation, all patients were ranked as “markedly effective”.

In a 5-month-old male child with a proliferating IH in the right upper eyelid, injection therapy twice received no obvious improvement. At 7-month-old, he started oral propranolol treatment for five months. The tumor shrank slowly. At 3 years old, the tumor almost involuted. The effect of intralosomal glucocorticoids in this child was ranked as “invalid”. And the effect of systemic propranolol was ranked as “markedly effective”.

Adverse effects in our cases were mild. In the patients with intralosomal glucocorticoids, one patient had local soft tissue atrophy and returned normal 6 months later. One patient had local ulcer, which healed after several times of changing dressing. One patient presented Cushing-like manifestations which disappeared within three months. No other systemic or local complications, such as growth retardation, retinal artery embolization, pigmentation, eyelid skin necrosis, occurred in these patients. In the patients with systemic propranolol, mild diarrhea occurred in one child, which recovered in several days with oral montmorillonite powder. No other systemic or local complications were observed.

In this study, the vision of nine patients was evaluated between 3 and 5 years old. Only one patient had ipsilateral amblyopia. It was the case who didn’t respond to intralosomal glucocorticoids and switched to systemic propranolol. The other eight patients had normal vision.

Discussion

Infantile hemangioma is a common benign tumor in head and neck. Among them, periorbital hemangioma attracts special attention because of the potential danger of impairing the visual development. The cornea deformation and astigmatism caused by tumor oppression is the main cause of amblyopia [6]. Therefore, to control tumor growth, prompt tumor shrinkage, and release tumor oppression on the cornea as soon as possible are essential to avoid the occurrence of astigmatism and subsequent amblyopia.

Clinical study [5] has confirmed that local injection of corticosteroids achieved good results in small-size hemangioma. Local injection of glucocorticoids into periorbital hemangioma could promote tumor shrinkage and improve ipsilateral eye astigmatism rapidly [2, 6-8]. Early treatment of periorbital hemangioma can achieve better results. Most of our cases were treated below three months age. The tumors involuted rapidly. Diprospan we used is the combination of betamethasone disodium phosphate and betamethasone dipropionate. Soluble betamethasone disodium phosphate takes effects rapidly after injection. And betamethasone dipropionate becomes a reservoir for sustaining effect due to its slow absorption. The effect can last for 2 to 4 months or more.

Systemic propranolol treatment in severe hemangioma was firstly reported in Jun. 2008 [9, 10]. A large-sample retrospective analysis showed that only 0.9% (10/1130) patients’ hemangiomas didn’t respond to systemic propranolol [15]. Several studies [13, 14] also
Management of periorbital hemangioma

report the satisfying effect of systemic propranolol in periorbital hemangioma. In this study, 8/8 patients with systemic propranolol had a quick and persistent response. And another patient who was resistant to intralesional glucocorticoid also responded to systemic propranolol. This suggested that systemic propranolol had superiority in the comparison of efficacy with intralesional glucocorticoid. Although several studies [16, 17] reported the rebound of tumor after the stop of propranolol treatment, we didn’t observe recurrence in our cases after one year old.

The adverse effects in our patients are mild on the whole. In the patients with intralesional glucocorticoids, local soft tissue atrophy, local ulcer, and Cushing-like manifestations occurred in three patients respectively. All of these complications recovered in several days with appropriate management. In our study, 1/9 patients with vision evaluation developed ipsilateral amblyopia. This child failed respond to glucocorticoid treatment. Although systemic propranolol was employed subsequently, and lead to the continuous involution of the tumor, ipsilateral amblyopia still occurred due to the long-time tumor oppression on the eyeball.

In summary, according to our observation and the results of previous studies [2, 6-8, 13, 14], both of intralesional glucocorticoids and systemic propranolol can achieve good results in the management of periorbital hemangioma. Systemic propranolol showed superiority in the efficacy and safety. We recommend systemic propranolol as the first-line therapy for periorbital hemangioma. Nevertheless, for the children who can’t tolerate propranolol treatment due to the side effects [18], and the children who are contraindicated to propranolol treatment because of bronchitis, asthma, or heart defect, intralesional glucocorticoid still is a feasible choice.

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Disclosure of conflict of interest

None.

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Management of periorbital hemangioma


