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# Efficacy and safety of intralesional corticosteroid application for hemangiomas

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**Background/aim:** There are different modalities for management of infantile hemangiomas (IHs). In this report, our aim is to evaluate whether intralesional corticosteroid treatment is associated with systemic side effects and whether this is an effective treatment modality for IH.

**Materials and methods:** Six children treated with intralesional corticosteroids for problematic hemangiomas were included in the study. Clinical characteristics, response to treatment, weight, height, blood pressure, morning serum cortisol, and adrenocorticotropic hormone levels were recorded.

**Results:** Each child received intralesional triamcinolone at a dose of 2 mg/kg for 2–5 injections at monthly intervals. Subjects were followed for 1 year. All patients had adrenal suppression following the second or third triamcinolone injections. Five patients demonstrated partial response and one demonstrated no response.

**Conclusion:** Intralesional steroid injection may effectively induce the resolution of hemangiomas, but all the patients in our group had adrenal suppression after treatment. The use of intralesional steroid therapy is not a superior treatment option for hemangiomas. It also has side effects comparable to systemic steroids.

**Key words:** Hemangioma, intralesional, corticosteroid, adrenal suppression

## 1. Introduction

Infantile hemangiomas (IHs), the most common benign tumor of infancy, occur in about 10% of infants. Although they occur in 8%–12% of newborns, this prevalence rate can reach 22% in premature babies. There is marked predominance of female cases. Classically, IHs appear shortly after birth as a light pink telangiectatic macule. They have a natural history of rapid growth during the first year of life, followed by a slow spontaneous regression phase after 12–18 months. Approximately 70% of hemangiomas regress completely by the age of 7. IHs that do not regress by the sixth year of life will develop residual abnormalities, the most common of which are telangiectasia, atrophic wrinkling, yellowish discoloration, redundant skin, scarring, and alopecia (1,2).

The goals in the management of the IH are to prevent or reverse complications like ulceration or scarring and permanent disfigurement and to minimize psychosocial stress for parents. Since incidence of spontaneous resolution in hemangiomas is very high, close clinical follow-up and observation are adequate in most cases (2).

There are different modalities for management of IHs. Systemic corticosteroids were the preferred treatment in severe cases until recently. Their principal effect is to stop the growth and induce regression of the lesion, possibly by inhibiting angiogenesis and inducing apoptosis. Steroids must be used with caution secondary to the risk of systemic side effects, such as growth disturbance and immune suppression. Since systemic steroids have potentially serious side effects, intralesional corticosteroid injection has been recommended by certain authors because of reported rapid onset of action and associated safety (3). Since Léauté-Labrèze et al. reported the incidental finding that IHs regress in children treated with propranolol, a nonselective beta-blocker for cardiac and renal conditions, this medication has been widely used to treat IHs (4). Nevertheless, there is still controversy regarding the effectiveness and adverse effects associated with this treatment. Use of propranolol is also difficult because of compliance and side effects in some cases (5,6).

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Here we report our experience with 6 patients with IHs treated with intralesional corticosteroid injection. We evaluated whether intralesional corticosteroid treatment is associated with systemic side effects and whether this is an effective treatment modality for IH.

## 2. Materials and methods

Six children treated with intralesional corticosteroid for hemangiomas at our pediatric oncology department were retrospectively evaluated. After physical examination, superficial and abdominal ultrasonography was performed in all patients for exclusion of other vascular malformations. Indications for intralesional corticosteroid injections were cosmetic disfigurement in 2 patients, bleeding in 3 patients, and ulceration in 1 patient. Prior to treatment with intralesional corticosteroids, response rate and compliance with oral propranolol were poor in all 6 patients. Propranolol had been initiated at the daily dose of 1 mg/kg in two divided doses and increased to 2 mg/kg on day 7 for 2 months. Propranolol was stopped in one child because of bronchial hyperreactivity and in two children because of the poor compliance of the parents. No significant changes in size or color were observed in the remaining patients after 2 months.

This study was approved by the hospital's ethics committee. Informed consent was obtained from the parents. All children received intralesional triamcinolone at a dose of 2 mg/kg for 2–5 injections at monthly intervals. The injections were given by a 22-gauge needle directly into the IH. Weight, height, blood pressure, morning serum cortisol, adrenocorticotropic hormone (ACTH), fasting serum glucose, and serum electrolytes were measured before each injection and at 4-week intervals thereafter to evaluate corticosteroid side effects. Patients with an early morning serum cortisol concentration of <5 ng/mL 4 weeks after injection were considered to have adrenal suppression. Patients were followed monthly for 1 year. The size of the IH was measured at each visit. Complete response was defined as a reduction of over 75% in size, consistency, or color of the lesion. Partial response was defined as a reduction of 50%–75% with respect to these same parameters and no response was defined as no change following treatment.

## 3. Results

We evaluated 6 girls with median age of 7 months (range: 5–18 months) treated with intralesional corticosteroid injections. Basal height and weight percentiles and serum ACTH and cortisol levels were within normal ranges in all patients. The hemangiomas were located on the trunk in 4 cases and on the head in 2 cases. The number of injections varied from 2 to 5 injections. One of the patients received 5, two received 4, one received 3, and two received 2 injections of intralesional triamcinolone. Pretreatment cortisol concentrations were normal in all 6 patients, indicating normal adrenal function, before steroid treatment. All patients had adrenal suppression following the second or third triamcinolone injections. Intralesional triamcinolone injections were discontinued when a patient developed abnormal serum cortisol. Patients' demographics, the location and size of the IH, treatment response, adrenal suppression, and recovery times are shown in Table 1. Five patients demonstrated partial response and one demonstrated no response.

Height and weight percentiles did not differ after the therapy. None of the patients developed growth delay or cushingoid phenotype. Blood glucose, blood pressure, and serum electrolytes were within normal ranges during the therapy. The time from first corticosteroid injection to adrenal recovery ranged from 4 to 9 months. Patients' serum ACTH and cortisol levels at diagnosis and follow-up are shown in Table 2.

**Table 1.** Patients' demographics, localization and size of the lesion, treatment response, adrenal suppression, and recovery times.

| Patient | Age at first injection (months) | Site and size of the lesion | Number of injections | Treatment response | Time of adrenal suppression (months) | Recovery time of adrenal suppression (months) |
|---|---|---|---|---|---|---|
| 1 | 5 | Anterior chest wall, 2.5 × 2.5 cm | 4 | Partial | 5 | 9 |
| 2 | 7 | Frontal area, 2 × 2.5 cm | 2 | Partial | 4 | 7 |
| 3 | 18 | Left shoulder, 3.5 × 3.5 cm | 3 | No | 6 | 9 |
| 4 | 17 | Anterior chest wall, 3.5 × 3.7 cm | 5 | Partial | 5 | 9 |
| 5 | 18 | Anterior chest wall, 3.8 × 4.8 cm | 4 | Partial | 3 | 9 |
| 6 | 5 | Nose, 3 × 2.5 cm | 2 | Partial | 2 | 4 |

**Table 2.** Patients' serum ACTH and cortisol levels at diagnosis and during follow-up.

| Patient | Cortisol, month 0 (ng/mL) | ACTH, month 0 (pg/mL) | Cortisol, month 3 (ng/mL) | ACTH, month 3 (pg/mL) | Cortisol, month 6 (ng/mL) | ACTH, month 6 (pg/mL) | Cortisol, month 9 (ng/mL) | ACTH, month 9 (pg/mL) |
|---|---|---|---|---|---|---|---|---|
| 1 | 5.7 | 10.1 | 5.2 | 11.2 | 3.4 | <1 | 6.1 | 9.2 |
| 2 | 7.1 | 9.3 | 5.3 | 8.1 | 3 | <1 | 6.2 | 8.2 |
| 3 | 18.7 | 12.3 | 6.3 | 10.2 | 1 | <1 | 5.9 | 8.1 |
| 4 | 5 | 7.8 | 1.2 | <1 | 3 | 7.1 | 8 | 10.1 |
| 5 | 5.6 | 8.1 | 3.8 | <1 | 2 | 5.4 | 7.9 | 9 |
| 6 | 5.5 | 9.8 | 4 | 2 | 5.2 | 8 | 5.6 | 9.1 |

Reference values for serum ACTH levels: 6.2–60 pg/mL.
Reference values for serum cortisol levels: 5–29 ng/mL.

## 4. Discussion

Although IHs are benign and self-limited lesions in children, the duration of the spontaneous regression cannot be estimated and this time period may result in psychosocial stress for parents. Different treatment modalities may be used for IH. Classical management strategy in IH is observation with regular follow-up. The decision to employ active therapy must be determined by the individual features of the IH, such as rapidity of growth and anatomical location (7).

The most commonly used therapy for hemangiomas was systemic corticosteroids until recent years. Many clinicians now hesitate due to their various potential side effects and the long duration of the treatment. Currently, propranolol has been shown to inhibit vascular proliferation of capillary hemangioma (4,8). It has been accepted as an effective treatment option for hemangiomas and used as first-line treatment (9–12).

On the other hand, various complications have been also reported with systemic propranolol treatment. Side effects profiles can include hypersomnolence, reflux, bronchospasm, hypotension, hypoglycemia, and hyperkalemia. In addition, response rate and proper oral use of propranolol can be poor in some children (13,14). When propranolol usage failed, we decided to use intralesional steroid in our cases.

Local steroid injection for treatment of hemangiomas was first described by Kushner in 1982 and has been used because of fewer side effects compared with systemic corticosteroids (15). Several authors reported successful treatment of hemangiomas with intralesional steroid therapy. Gangopadhyay et al. reported that overall response rate was 88.6% with administration of intralesional triamcinolone and no side effects occurred (16). Another two studies also showed response rates of up to 90% with intralesional corticosteroid treatment (17,18). Similarly, we demonstrated partial response in 83.3% of patients.

On the other hand, adrenal suppression and atrophic or depigmented skin changes have been reported to occur after intralesional corticosteroid injections (19). Morkane et al. reported that 13 of 15 infants had adrenal suppression 4 weeks after intralesional corticosteroid therapy. They also demonstrated a significant slowing in weight gain following intralesional steroid injections. The time from first injection to basal adrenal recovery was 4 to 65 weeks (20). Goyal et al. speculated that initial release of glucocorticoids into the circulation led to acute adrenal suppression (21). In our study all of the patients had adrenal suppression following the second or third corticosteroid injection and adrenal recovery took from 4 to 9 months from the first injection. However, a significant slowing in weight gain and cushingoid phenotype were not observed in our group. In addition, no patient developed atrophic or depigmented skin changes due to intralesional steroid application.

In conclusion, our study showed that intralesional steroid injection may be slightly effective for inducing the resolution of rapid growth of hemangiomas in children. However, all the patients in our group had adrenal suppression after intralesional steroid injections. The use of intralesional steroid therapy is not a superior treatment option for hemangiomas. It also has side effects like systemic steroids.

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