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Effectiveness of oral propranolol for infantile hemangiomas started after 5 months of age.

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Dear editor,

Cutaneous vascular anomalies are a group of disorders that can be classified as vascular malformations or vascular tumors, depending on their biological behavior and pathogenesis.

Infantile hemangiomas (IHs) are the most common benign vascular tumors in infancy, with a reported incidence of approximately 5%. IHs occur more frequently in female infants; prematurity, low birth weight and placental anomalies appear to be the most significant risk factors with a 40% increase in risk for every 500 gram decrease in birth weight.[1]

Their pathogenesis remains unknown. At present, there are three main hypotheses: the theory of tissue hypoxia, the theory of embolization of placental endothelial cells, and the theory of increased angiogenic and vasculogenic activity.

His, composed of multipotent stem cells, immature endothelial cells, pericytes and mesenchimal cells, are characterized by the abnormal growth of blood vessels in the early proliferative phase, followed by the gradual spontaneous regression of the lesion in the involuting phase.[1]

The majority of IHs are small and they regress spontaneously without any need for intervention. However same IHs can cause serious complications and require treatment. Therapeutic options include pharmacologic, topical or systemic, surgical or laser interventions. Systemic therapy is reserved for larger IHs, in particular those with more aggressive growth characteristics or hight risk of functional impairment.[2]

Propranolol is a nonselective beta-adrenergic receptor blocker that has a long history of use in pediatric cardiac disease for treatment of hypertension, hypertrophic cardiomyopathy and other cardiac conditions at doses of up to 6-8 mg/kg/day.[3] Since the serendipitous discovery of the benefit of propranolol for IHs in 2008,[4] this medication has been rapidly adopted as the first line treatment for complicated lesions. The recommended starting dose is 1 mg/kg/day divided into two separate doses of 0.5 mg/kg to achieve later a therapeutic dose of up to 2-3 mg/kg/day.

Systemic propranolol is clearly efficacious, with rare side effects. These include symptomatic hypoglycemia, hypotension, bronchial hyper-reactivity, seizure and restless sleep.[3]

We report the case of a 18 month old female child who was born at 37 weeks, with a weight of 2,700 kg, from cesarean cut for placenta previa.

She came to our Dermatology Department for the presence of a nodular lesion of red violet color, soft in consistency, located at left scapula appeared a few days after birth (Figure 1a). No sign of ulceration was evident. Familial history was negative for hemangiomas. The ultrasound examination showed intense vascularization. The patient was then diagnosed with an infantile hemangioma by clinical and ultrasound features.

We performed a cardiological examination with electrocardiogram and blood pressure measurement that resulted within the standards. A pediatric hematochemical examination to evaluate the liver and kidney function was also performed providing results within the standard.

We decided, in collaboration with pediatric specialists, to start treatment with propranolol beginning with a minimum dose of 1 mg/kg/day in order to get to the final dose of 2-3 mg/Kg/day in 2 doses a day. No adverse effects were reported.

Monthly clinical evaluation was performed, with measurement of heart rate and blood pressure; acquisition of new pictures of the lesion and adjustment of drug dose. After 6 months, we noticed a remarkable improvement in the lesion both in consistency and color. The lesion appeared to be much more soft, flat and pink (Figure 1b). The end of the therapy was established considering the results obtained in terms of the lesion reduction.

The majority of IHs have little impact on infants' and children's health, but a few of them, especially those that are located on the head, face and neck and develop rapidly, can interfere with normal function and appearance.

The goal of the therapy is to minimize or eliminate long term sequelae. New modalities, such as oral propranolol, led to fewer surgical interventions and they had fewer side effects compared to other oral therapies. Oral propranolol has been repeatedly demonstrated as the first-choice drug for IH and, at present, is available in several countries with a specific indication for pediatric patients.[3]

The treatment is highly effective (up to 96-98% of response after 6 months) and has an optimal safety profile, with a low incidence of adverse events.

According to the international consensus recommendations and to the drug's summary of product characteristics (SmPC), oral propranolol should be administered in infants between 5 weeks and 5 months of age, for a duration shorter than 6 months.[3]

The aim of this case report is to evaluate the efficacy and safety of propranolol treatment for IHs in patients whose first administration occurred at a higher age than the one prescribed in the technical sheet (between 5 weeks and 5 months).

The effect appeared quickly in the first few days and was sustained during the following weeks leading to a remarkable shortening of the natural course of the lesion.

Based on our observations, we would suggest the use of propranolol, also in patients with hemangioma above 5 months age, in order to reduce related complications, which may be severe and irreversible.

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Figure 1 (a). Infantile hemangiomas pre-treatment.

Figure 1 (b). Infantile hemangiomas post-treatment. The lesion appeared to be much more soft, flat and pink.