

The effect of bleomycin in case of congenital hemangiomas

Objective:

Despite various treatment utilised, vascular anomalies represent difficulty in many cases for physicians. Hemangioma is defined by an abnormal proliferation of blood vessels that can occur in any vascularized tissue. These vascular anomalies, considered by the most authors benign vascular tumors, have characteristic clinical manifestation: a proliferative phase, that starts neonatal and takes about 6-10 months, is responsible for rapid tumor growth, and an involutional phase, where the tumor size decrease, completely disappearing (according to some authors) around the age of 9 years.

The Bleomycin is a cytotoxic antitumoral antibiotic, that cause modifications of DNA. It has been also successfully used in intralesional injection treatment of cystic hygromas and haemangiomas, based specifically on a high sclerosing effect on vascular endothelium. We used this substance in the treatment of congenital hemangiomas and lymphangiomas, with different results. Indication of the treatment was given of hemangioma location (face region), namely infiltration of surrounding tissues, which made the complete surgical excision impossible.

We tried to develop an experimental model for a better understanding of the mechanism of action of this substance, and an explanation of the differences between results obtained in different groups of patients.

Method:

Between the first of October 2008 and January 2011, a prospective study was performed in Pediatric Surgery Clinic Târgu-Mureș, on a total of 59 patients, with intralesional injection of bleomycin. Bleomycin treatment was administered by percutaneous intralesional injection in each patient. Bleomycin powder (Bleocin 15mg) was reconstituted with 15 ml of normal saline (dilution 1 mg/ml). The maximum dose per injection did not exceed in any case 0,5-1 mg/kg. The injection was performed in general anesthesia, first we punctured the haemangioma, then with the needle left in place, the diluted solution was administered possible over the entire surface of the lesion.

To study the effect of bleomycin on angiogenesis, we used chicken embryo chorioallantoic membrane (CAM).

Results:

The evolution after injection was favorable, hemangioma disappeared completely or we noticed its gradual replacement by fibrous tissue, which stops its rapid growth and allows us the surgical excision. Number of sessions of bleomycin injection to achieve these results, was between 2 and 16, on average of 6- 8 injections, being directly related to size of tumoral formation and the age of patients. During this study we found that this treatment had better results if patients presented early after the appearance of hemangioma. No local or general adverse effects were noted.

Regarding the experimental part on the corioalantoid membrane, three days after bleomycin administration, we observed several histopathological changes: decreased stroma thickness and densification occurs, figurative elements tend to extravasated in stroma; large vessels that maintain the shape of blood vessels, but red blood cells are agglutinated with stasis, thrombosis, morphological the endothelium is no longer visible.

Conclusions:

This method allows as a treatment of choice for this lesions, without surgery, that is impossible in most cases, because of their location (face) and infiltration of vital tissue. Against to treatment with steroids and alpha-interferon, intralesional injection of bleomycin has a minimal risk of side effects (exulceration, pulmonary fibrosis). Analysis of the results shows that the frequency of vascular abnormalities is increasing and their early treatment brings a higher rate of complete resolution without scarring outstanding.

Histopathological changes observed on corioalantoid membrane treated with bleomycin, support our theory that this substance, besides sclerosing effect on vascular endothelium, also has an inhibitory effect on angiogenesis, which would explain the fact, that treatment is more effective in young patients. Through following experiments, we will try to study the histopathological changes in developed vessels in order to see the effects that we can get in older children with developed hemangioma. The corioalantoid membrane of the chicken egg seems to be a suitable model for following investigations of these vascular anomalies.

Keywords: congenital hemangiomas, Bleomicyne, vascular anomalies

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