Initial Experiences with Propranolol Treatment of Infantile Hemangiomas: Report of Three Cases

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Infantile hemangiomas (IH) are common benign tumors in infancy, affecting 5–10% of all infants and they can still cause disfigurement and serious complications depending on their location and size, which can be associated with ulcerations and haemorrhage. Since 2008, propranolol has become the first choice of therapy for complicated IH, compared to conventional approach with systemic corticosteroid therapy as first-line treatment and then interferon or vincristine as second- or third-line therapeutic agents. We report three cases of hemangioma, successfully treated with propranolol. Oral propranolol was given for a period of 6 months with monthly follow up. All cases showed dramatic response after stopping the treatment. Propranolol is novel and safe medication for treatment of infantile hemangioma. **Key words:** Hemangioma – propranolol – infancy

1. INTRODUCTION

Infantile hemangiomas (IH) are common benign tumors in infancy, affecting 5–10% of all infants, and up to 30% of premature newborns and chorionic villus sampling exposed infants (1, 2). Although 85–90% of all IH eventually undergo spontaneous involution, they can still cause disfigurement and serious complications depending on their location (obstruction of airways and vision), size (cardiac insufficiency, hypothyroidism), and speed of regression, which can be associated with painful ulcerations and haemorrhage (3). At birth, IH may not be apparent or may appear as flat circumscribed lesions with telangiectatic vessels on the surface. Within the first weeks of life, IH enter a phase of rapid growth on the surface. Within the first weeks of life, IH enter a phase of rapid growth on the surface. Within the first weeks of life, IH enter a phase of rapid growth on the surface. Within the first weeks of life, IH enter a phase of rapid growth on the surface. 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administering full dose, the lesion decreased considerably. At the end of 6 months, reduction of 90% in size and coloration of perianal hemangioma and total regression of periorbital hemangioma were observed (Figure 2).

Case 2: A 11 month old female infant presented with a large hemangioma on neck, measured 6x5 cm, confirmed by MRI (Figure 3). Bulge on the neck started to be noticeable at 3th month of life. The patient was investigated as in case 1, and the same dose regimen for propranolol was followed (2 mg/kg/day in three divided doses). Within 10 days of giving this dose, the swelling decreased to half of original size. After 6 month of treatment there was near total regression of hemangioma (Figure 4).

Case 3: A 3-month-old male infant presented with a hemangioma of nose with progressive growth from second month of life with left periorbital expansion. Propranolol therapy was introduced according to standard protocol to therapeutic dosage (2mg/kg/day in three doses). After 6 month of treatment there was near total regression of hemangioma (Figure 5).

In all three cases there weren’t any side effects of propranolol therapy. Thereafter, the dose was gradually tapered over 2 weeks and stopped. Regular monthly post-treatment follow up of both the patients did not show any rebound of hemangioma. Parents of all patients were overall satisfied with treatment.

4. DISCUSSION

Although the majority of IH have little impact on childhood health, various problematic head and neck hemangiomas will develop rapidly and interfere with normal function and appearance (5). The proposed mechanism for the action of propranolol is that it induces vasoconstriction and capillary endothelial cell apoptosis (7). Potential explanations for the therapeutic effect of propranolol - a nonselective beta-blocker - on infantile capillary hemangiomas include vasoconstriction, which is immediately visible as a change in color, associated with a palpable softening of the hemangioma; decreased expression of VEGF and bFGF genes through the down-regulation of the RAF–mitogen-activated protein kinase pathway (which explains the progressive improvement of the hemangioma); and the triggering of apoptosis of capillary endothelial cells (8).

Nevertheless, several case studies have further provided evidence of the dramatic effect of propranolol on massive, proliferating, life threatening, and involuting lesions (5, 8, 10). Systemic corticoids, long considered as the therapy of choice for hemangioma of infancy, have hard to control insidious adverse effects, besides variable response (11). The use of alpha-interferon is described in the literature with good results, although with the inconvenience of being a prolonged intravenous treatment that has significant adverse effects (12). Due to the limited literature and research available on the impact of propranolol on hemangiomas and other vascular tumors, a precise protocol for its clinical use does not yet exist. Treatment protocol that is adopted in our institution is based on guidelines regarding the appropriate patients, follow-up and dosing adjustments to reduce unwanted cardiopulmonary or systemic effects of propranolol. Experience from other authors (9, 11, 12), including our, has shown good outcomes regarding lesion involution, with few adverse effects connected with the propranolol.

5. CONCLUSION

All mentioned above, stated that propranolol is novel and safe medication for treatment of infantile hemangioma. The cases described presented HI regression similar to that observed in other studies. It has a tolerable side-effect profile, and there have been no serious side effects reported in appropriately screened patients.
Complementary studies are necessary to understand the true role of propranolol in the physiopathology and treatment of hemangiomas of infancy. As it looks now, propranolol is best option for medical treatment of infantile hemangioma to date.

REFERENCES


IN MEMORIAM

Prof. dr Fuad Sisic
(1939 – 2011)

On June 6, 2011, after several years of serious illness, respected and esteemed professor Fuad Sisic died. Professor Šišić was born in 1939 in Sarajevo, where he finished Primary school, High school and the School of Medicine (1963) as excellent and prominent student. After graduation and completing the state exam, he worked as a general practitioner at the Health Centre Sarajevo in the period from 1966 to 1967. During the period from 1967 to 1992, he was employed at Military Hospital, and from 1992 to 2004 in Clinical Centre University of Sarajevo as general surgeon and vascular surgeon and Head of the Department of Vascular Surgery.

During 1971 he completed his residency in general surgery with great success at the Military Hospital in Belgrade. In the years 1972 and 1973 Prof Šišić completed education in the Clinic for Chest and Vascular Surgery – Rebrozgreh, and the Clinic for Cardiovascular Surgery in Ljubljana. The period from 1972 to 1974 is important for professional contributions of Professor Šišić: introduction of Seldinger angiography and splenopexy in Sarajevo Military Hospital, and vascular surgery in clinical practice in Bosnia and Herzegovina, as well as radical lymphadenectomy in malignancies of the urinary tract. At the same time professor Šišić enrolled postgraduate studies at the School of Medicine in Sarajevo, where he defended his master’s thesis in 1976. Doctoral dissertation on the topic “Importance of collateral circulation in evaluation of the indications for reconstructive interventions in the second stage of arterial insufficiency, atherosclerotic etiology of femoropopliteal localization”, Prof.Šišić defended in 1978. He showed talent and exceptional abilities in the field of vascular surgery. Although he didn’t work in the Clinical Hospital in 1979 he was elected titular professor at the Surgery at the School of Medicine in Sarajevo. On 1986 he was elected a Assistant professor of Surgery at the Military Hospital in Belgrade. In his work he showed extraordinary manual skills, as well as scientific, educational, pedagogical and organizational abilities. In 1990 he received honorary degree Primarius, in 1991 was elected Associate professor in the surgery in a Military Hospital in Belgrade. In 1993 he was elected as Associate professor at the School of Medicine in Sarajevo. He proved to be a good lecturer, good teacher, and a great vascular surgeon. Professor Šišić spent some time on education in renowned institutions - New York-Washington (1992), Paris (1997), Nijmegen (Netherlands) 1998, and Bonn (1998), Cairo (1999). At the beginning of the war, he established the Clinic for Vascular Surgery Clinical Center University of Sarajevo as an independent organization that successfully managed. Since 1994 he was elected a Director of the newly formed Institute for Scientific Research and Development Clinical Center University of Sarajevo for which development and organization, staffing and functional improvement Professor invested their creative, intellectual and leadership potential - where he stayed until retirement. Already at the beginning of 1992 Professor actively participated in the creation, establishment and implementation of war-surgical doctrine, and in 1996 initiated organization of the First Surgery Congress of Bosnia and Herzegovina with international participation as Chairman of the Organizing Committee. In 2001 Professor promoted bloodless treatment in Bosnia and Herzegovina; in 2002 he promoted the adoption and formulation of the doctrine of prevention of venous thromboembolism. He was our first surgeon who developed curriculum for focused specialization - Vascular Surgery, and in the postwar 1997 initiated and finalized the draft of “Guide for the residents” as editor in chief. In this guide residents received exceptional “guidelines” and a clear program of their future specialization. Thanks to the initiative and generous support of Professor Šišić the publication “Medical Journal”, which has regularly been published for 17 years, became respectable within physicians. He also initiated and edited the Information Bulletin Clinical Center University of Sarajevo and supported the development and publication of bibliographic databases, “Bibliography of works by the Clinical Center of 1985-2000.” By performing the duty of the Director of the Institute at the same time Professor was the Chairman of the Scientific Council of the Institute for Scientific Research and Development, and in that role wholeheartedly supported and skillfully guided postgraduates, doctoral students and researchers in the development and finalization of projects and scientific studies. Professor was a successful member of the Board of Director General in 1999 and supervisor of the Clinic for Heart Surgery Clinical Center in Sarajevo. During 2000 he was the Head of this Clinic. During many years of fruitful work Professor Šišić wrote and published many scientific works: 5 books as first author, 8 books as co-author, 11 books as editor, 69 scientific papers and investigator in five research projects. He was the first author in B&H who published a textbook of war surgery - “War surgery: for students of medicine and dentistry” in cooperation with co-authors, our outstanding surgeons. For his dedicated work Professor Šišić was honored by receiving a variety of social recognitions. Professor was lined with some specific traits - a keen sense of fairness, accuracy, precision, generosity, pride, and ambition. We lost a great man whose work and the results gave an important place in the “world” of medical science and profession in B&H

Prof Mirza Dilić, MD, PhD
Jelena Koprivica, MA
Prof Zivko Masic, MD, PhD