OK-432 therapy for lymphangioma in children

Bs Nguyễn Trung Nhân
Bs Nguyễn Thị Ngọc Ngà

- Lymphangiomas are benign abnormal collections of lymphatic vessels
- 5.6% of all benign lesions
- 65% apparent at birth, 90% appeared second year
- Treatment: surgery, bleomycin, OK-432, Ethibloc…

OK-432

- OK-432 is a lyophilized mixture of a low-virulence Su strain of Streptococcus pyogenes of human origin incubated with penicillin G
- WBC induced and activated by OK-432, and the cytokines (including TNF) produced by these cells increased the endothelial permeability, and thus the accelerated lymph drainage and increased lymph flow let to shrinkage of the cystic spaces

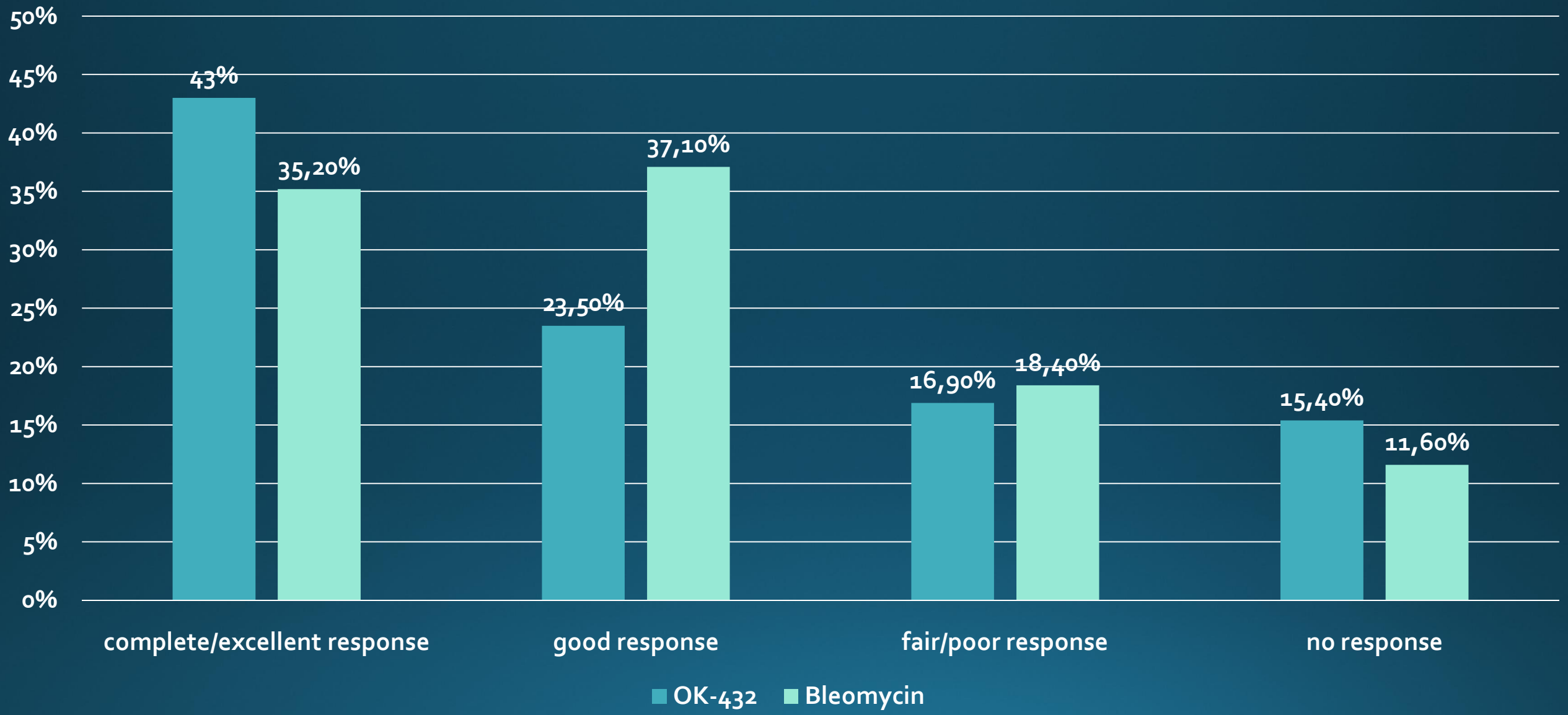
Figure 1 - Patient suffering from macrocystic lymphangioma before treatment with OK-432

Figure 2 - Patient with macrocystic lymphangioma after treatment with OK-432

Before

After

- OBJECTIVE: Systematically review the published literature regarding the efficacy of nonsurgical therapies in the treatment of head and neck (H&N) lymphatic malformations (LM) in children.
- DATA SOURCE: MEDLINE.
- REVIEW METHODS: MEDLINE was searched for literature relating to nonsurgical treatments for H&N LM.
- RESULTS: The initial search returned 1876 articles, with 22 meeting criteria. The majority (20) were case series. All therapies were percutaneous, with OK-432 or bleomycin sclerotherapy being most common. Random-effects modeling revealed 43% (CI = 28.9%-57%) of patients undergoing OK-432 for LM achieved a complete/excellent response, 23.5% (CI = 5.8%-41.3%) achieved a good response, 16.9% (CI = 10.3%-23.4%) achieved a fair/poor response, and 15.4% (CI = 8.6%-22.2%) observed no response. In the bleomycin group, the results were: 35.2% (CI = 15.7%-54.6%) excellent, 37.1% (CI = 22%-52.3%) good, 18.4% (CI = 2.7%-34.2%) fair/poor, and 11.6% (CI = 3.5%-19.6%) no response. Seven major complications were noted out of the 289 patients in the series, including two mortalities.
- CONCLUSIONS: The literature indicates that sclerotherapy for H&N LM achieves excellent/good clinical response in a majority of patients, with few complications, and anecdotally does not complicate future surgery.
- *Otolaryngology–Head and Neck Surgery (2008) 138, 418-424. Nonsurgical therapies for lymphangiomas: A systematic review. Jason L. Acevedo, MD, Rahul K. Shah, MD, FAAP, and Scott E. Brietzke, MD, MPH,Washington, DC*


50%
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
43%
35,20%
23,50%
37,10%
16,90%
18,40%
15,40%
11,60%
complete/excellent response
good response
fair/poor response
no response
OK-432
Bleomycin

Objective: To describe and to determine the robustness of our study evaluating the efficacy of OK-432 (Picibanil) as a therapeutic modality for lymphangiomas.

Design and Setting: Prospective, randomized trial and parallel-case series at 13 US tertiary care referral centers.

Subjects: Thirty patients diagnosed as having lymphangioma. Ages in 25 ranged from 6 months to 18 years. Twenty-nine had lesions located in the head-and-neck area.

Intervention: Every patient received a 4-dose injection series of OK-432 scheduled 6 to 8 weeks apart unless a contraindication existed or a complete response was observed before completion of all injections. A control group was observed for 6 months.

Outcome Measures: Successful outcome of therapy was defined as a complete or a substantial (>60%) reduction in lymphangioma size as determined by calculated lesion volumes on computed tomographic or magnetic resonance imaging scans.

Results: Overall, 19 (86%) of the 22 patients with predominantly macrocystic lymphangiomas had a successful outcome.

Conclusions: OK-432 should be efficacious in the treatment of lymphangiomas. Our study design is well structured to clearly define the role of this treatment agent.

Arch Otolaryngol Head Neck Surg. 2002;128:1137-1144

Treatment of lymphangiomas with ok-432 (Picibanil) Sclerotherapy. A prospective Multi-institutional Trial. Iowa USA

- **Purpose**: The aim of this study is to investigate the optimal treatment for lymphangioma in children by analyzing the effectiveness and complications of treatment modalities.
- **Methods:**We reviewed 128 patients with lymphangioma treated at our institution between 1979 and 2005. Periods of treatment were divided arbitrarily into 2 groups: period I, from 1979 to 1988 (n = 53); and period II, from 1989 to 2005 (n = 75). According to radiological appearance, patients were grouped into 4 types: single cystic (SI; n = 23), macrocystic (MA; n = 11), microcystic (MI; n = 69), and cavernous (CA; n = 25).
- **Results:**Sclerotherapy as primary treatment was performed in only 2 patients (3.8%) in period I using bleomycin but increased significantly in period II to 48 patients (64.0%) using OK-432 (Pb.01). Nevertheless, primary surgical excision (69/78 patients, 88.5%) was significantly more successful than sclerotherapy (32/50, 64.0%) (Pb.01). The following are the locations and types of lesions: head/neck (n = 69; SI, 11; MA, 5; MI, 42; CA, 11), trunk (n = 34; SI, 6; MA, 6; MI, 15; CA, 7), and extremities/other (n = 25; SI, 6; MI, 12; CA, 7). The effectiveness of sclerotherapy in SI, MA, MI, and CA types was 90.9%, 100%, 68.0%, and 10.0%, respectively. Seventeen patients (SI, 1; MI, 8; CA, 8) who received primary sclerotherapy required surgical excision with good outcome. Complications after primary surgical excision were more serious compared with sclerotherapy.
- **Conclusion:**Sclerotherapy with OK-432 was not as effective as reported in the literature. We recommend OK-432 injection therapy alone for SI and MA types and surgical excision after pretreatment with OK-432 for MI and CA types.
- Journal of Pediatric Surgery (2007)42, 386 – 389**Treatment of lymphangioma in children: our experience of 128 cases.**Okazaki T[1], Iwatani S, Yanai T, Kobayashi H, Kato Y, Marusasa T, Lane GJ, Yamataka A.

- **Objective:** To report the experience with OK-432 therapy for lymphangioma in children.
- **Methods:** Retrospective study of 19 children with lymphangioma treated with OK-432 in Ribeirão Preto, state of São Paulo, Brazil, between 1999 and 2003.
- **Results:** All patients presented response to OK-432, 12 had total shrinkage and seven had partial shrinkage varying from 50 to 80%. Patients had fever after injections of OK-432 for 2 to 10 days, no damage to the overlying skin was observed.
- **Conclusion:** OK-432 is safe, effective and can be used as primary choice of treatment of patients with lymphangiomas because of the excellent response. In these cases surgery should not be necessary. In patients with partial regression new injections of OK-432 must be used to shrink the lesion. Thereby safely surgery could be made.
- *J Pediatr (Rio J). 2004;80(2):154-8: Lymphangiomas, OK-432, children, sclerosing agents. OK-432 therapy for lymphangioma in children. Everaldo Ruiz Jr, Elvis T. Valera, Francisco Veríssimo, Luiz G. Tone*

- **INTRODUCTION:** Nonsurgical treatments, such as sclerotherapy have been attempted for head and neck lymphagiomas. Of the available sclerosing agents, picibanil has shown satisfactory shortterm treatment results in many studies, but no study has presented long-term treatment results. Accordingly, in the present study, the authors retrospectively reviewed the long-term treatment results of picibanil sclerotherapy.
- **MATERIALS AND METHODS:** Fifty-five lymphangioma patients who underwent picibanil sclerotherapy were enrolled. Data about initial and long-term response, recurrence, and excision rate were collected.
- **RESULTS:** Initial response rates were 83.5 percent and longterm response rates were 76.3 percent.
- **CONCLUSION:** Initial and the long-term response rate were equally good for lymphangioma.
- *Otolaryngology–Head and Neck Surgery (2009) 140, 120-123. OK-432 sclerotherapy in head and neck lymphangiomas: Long-term follow-up result. Jae Chul Yoo, MD, Youngjin Ahn, MD, Yune Syung Lim, MD, J. Hun Hah, MD, Tack-Kyun Kwon, MD, PhD, Myung-Whun Sung, MD, PhD,andKwang Hyun Kim, MD, PhD,Seoul, Korea*

- **BACKGROUND/PURPOSE:** Operating lymphatic malformation (LM) may lead to nerve damage with permanent cosmetic disturbance. Even sclerosants as ethanol and Sotradecol may sometimes harm more than cure. The purpose with this study was to evaluate the effect of a relatively new drug for intralesional injections, OK-432.
- **METHODS:** The diagnosis of LM was made clinically by means of ultrasound and MRT and/or CT. Thirty-two patients (28 children) with LM were consecutively enrolled in the study. Twenty-nine (27 children) had not been treated previously: 17 (15 children) had macrocysts (MAC), four microcysts (MIC) and eight had combined cysts (CC). Three patients (one child) had got previous treatment without any curative effect. All patients got intralesional injections with OK-432 at intervals according to a previously published protocol (Läkartidningen, 95 (1998) 2074).
- **RESULTS:** No serious adverse effects were seen. The results obtained were excellent in all with macrocysts but in one, who was pretreated with ethanol, where no LM-regression was seen. None of four with MIC-LM required further therapy; for two of them the results were excellent. Of 10 with CC, seven showed excellent results. Only one required surgery.
- **CONCLUSION:** OK-432 is effective and is proposed to be the first choice of treatment for LM.
- Int J Pediatr Otorhinolaryngol. 2002 Aug 1;65(1):1-6. **OK-432 therapy for lymphatic malformation in 32 patients (28 children).** Claesson G[1], Kuylenstierna R. Sweden

- **BACKGROUND:** Surgery has previously been the mainstay of treatment for lymphatic malformations but has attendant problems of marked scarring, high chance of recurrence and potential nerve damage. Alternative management for these lesions involves the intralesional injection of OK-432. The present paper reviews OK-432 use in lymphatic malformations in children.
- **METHODS:** A retrospective chart review was carried out of children undergoing intralesional OK-432 therapy from the Departments of Paediatric Surgery, Paediatric Otolaryngology and Plastic Surgery at Starship Children's Hospital, Auckland.
- **RESULTS:** Over the past 4 years, seven children under the age of 5 years underwent OK-432 therapy as day-case procedures requiring between one and seven procedures each. Four children had lesions involving the axilla/chest wall, two involved extra-mylohyoid tissues in the neck and one childhad lymphatic malformation involving tongue, floor of mouth and an extra-mylohyoid component. Spontaneous haemorrhage into a cystic space may be the cause of the observed partial resolution of the lymphangiomas in two. A predictor of a successful outcome was the ability to aspirate fluid prior to injection. Ultrasound guidance was useful to localize the lesions for aspiration and injection. Macrocystic lesions respond well to OK-432 therapy but the response of microcystic or cavernous lesions to OK-432 is disappointing and surgery remains the definitive treatment for these microcystic lesions.
- **CONCLUSION:** OK-432 appears to be a safe and effective treatment for the macrocystic component of lymphatic malformations.
- ANZ J Surg. 2004 Oct;74(10):855-8. **OK-432 and lymphatic malformations in children: the Starship Children's Hospital experience. New Zealand**