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SCLEROTHERAPY USING OK-432 (PICIBANIL) IN TREATING HEAD AND NECK LYMPHANGIOMAS IN CHILDREN

Abstract

Head and neck lymphangiomas are congenital malformations which can be a challenge to treat surgically as they tend to defy surgical planes. Sclerotherapy is an alternative treatment. Intralesional OK-432 (Picibanil) induces an intense inflammatory reaction within the cystic space leading to its obliteration. We present our experience of using OK-432 sclerotherapy in treating Nepalese children with head and neck lymphangiomas.

Key words: scterohetapy, ok-432, lynphanglonas

INTRODUCTION

Head and neck lymphangiomas are congenital malformations generally seen in children less than 2 yrs. Majority of them involve the cervical and facial areas. Lymphagiomas can be very challenging to treat as they lack definite demarcation with the tendency to infiltrate vital neurovascular structure in spite of being benign[1]. Various treatment modalities have been tried. Some opt for watchful wait as spontaneous regression has been seen in 6%.[2] However, surgical excision remains the primary choice [2,3,4]. Sclerotherapy is also considered a good alternative[5,6]. Various agents like Bleomycin, hypertonic saline, alcoholic solution of Zein, Doxycline, OK-432 (Picibanil) have been used for sclerotherapy[7]. OK-432 (Picibanil, Chugai Pharmaceuticals Co, Tokyo) is a lyophilization of culture of low virulence Su strains of Group A Streptococus pyogens treated with Benzyl penicillin, initially used as immunotherapy for malignant tumors in Japan. It was first introduced by Ogita S et al [7] in 1987 for treatment of lymphangiomas. Since then used, it has been considered simple, safe and effective treatment modality for lymphagiomas.[1-6] We present our experience of using OK-432 in treating Nepalese children with head and neck lymphagiomas

MATERIALS AND METHODS

It was a prospective, longitudinal, analytical study carried out at Ganeshman Singh Memorial Academy of ENT- Head and Neck Studies, Tribhuvan University Teaching Hospital, Kathmandu, Nepal from 2011-2014. Children with clinical and ultra sonographic diagnosis of lymphangiomas in head and neck region were included in the study.No basic lab test carried out before treatment. The demographics of the patients, site and size of lesion were noted. Sclerotherapy using OK-432 was done as out-patient procedure with no sedation. With aseptic technique, an 18 G needle mounted on 20 cc syringe was used to aspirate straw colored fluid from the most fluctuant area of the lymphagioma. Equal amount of diluted OK-432 in the concentration of 0.01 mg/ml OK-432 (0.1 mg of OK-432 per 10 ml of NS) as per Ogita et al[7] was infiltrated without exceeding 20 ml in each sitting. All patients were observed for few hours and were sent home with an advice to take paracetamol/ibuprofen for pain relief and to report to hospital if any complications were noted. Patients were followed up on 6 to 8 weekly basis. In each visit, the approximate size of the lesion was measured. Any obvious remaining swelling was aspirated. However, no infiltration was done in absence of an aspirate. The outcome of the sclerotherapy was measured as complete response if there was no obvious swelling, partial if more than 50 % decrease in size of swelling without aspirate and no change if the size of the swelling remained the same. Complications if any were noted.

RESULT

A total of 41 children with the age range of 9 days to 16 years (mean age 6 year) received the treatment. However, the outcome of only 35 patients could be measured as 6 were lost for follow up. Out of the 35 patients, 23 were male and 12 were females. The sites of involvement were submandibular region in 11, cervical region in 10, submental/ submandibular region in 4 along with floor of mouth in 4,2 cases each of lesion involving parotid, cheek and neck extending to axilla/scapula. (Fig 1)

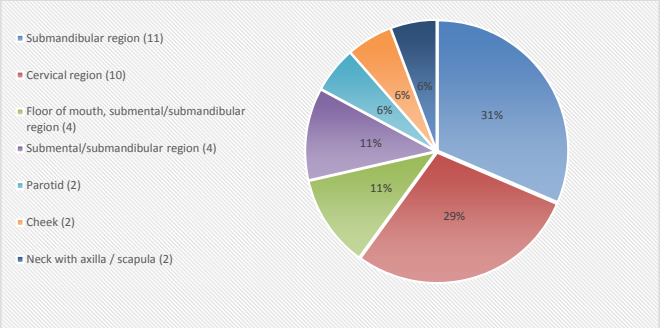
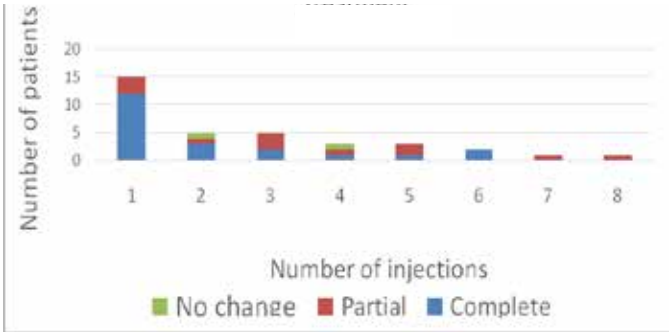


Fig.1 Number of patients according to sites.

The size of the lesion ranged from 2x2 cm to 15 x 15 cm. The follow up varied from 1 ½ month to 25 months with the average of 9.6 months.



Complete resolution was noted in 21/35 (60%) from 6 to 36 weeks,partial in12/35 (34.2%) in 6 to 48 weeks and no response in 2/35 (5.7%). The response to treatment had no relation to size of the swelling.

The average sclerotherapy session was 3 with a range from 1 to 8. Out of the 21 patients with complete recovery, cystic hygroma in 12 patients resolved with 1 injection, 3 patients needed 2 injections, 2 patients had 3 injections, 1 had 4 injections. Patients requiring 5 and 6 injections were 2 each. Amongst the partial response group, 3 patients required 1 injection, 1 required 2 injections, 3 required 3 injections, 1 required 4 injections, 2 required 5 injections, 1 each required 7 and 8 injections. No change was noted in one each patient after 2 and 4 injections. (Fig 2)

There were no complications noted. However, a 9 months old child with lymphangioma involving the floor of mouth was admitted for observation with regards to airway concerns. However, he did not require tracheostomy or any other airway intervention at any point. None of the patients returned with recurrence.

DISCUSSION:

Ok-432 causes inflammatory reaction leading to destruction of the epithelial lining and subsequent sclerosis and cicatrical contraction of the lesion [3]. It does not cause damage to adjacent structure unlike other sclerosants hence has no risk of scarring or adhesions and does not cause difficulty in surgical excision later.[5,10] Bleomycin has been used as sclerotherapy for cystic hygroma since 1977 as it was found to have antitumoral activity. It has shown good response in 88% cases. It however carries a risk of pulmonary fibrosis.[6] An alcoholic solution of Zein (Ethibloc) as sclerotherapy has shown good response in 60% cases but with a risk of scarring in weeks or months following the treatment. Pain is the main side effect noted with doxycycline.[6,10]

Surgical excision [6,10] although is a management option, complete resection is difficult leading to partial resection. Hence, the recurrence rate varies from 15-53%. The complication rate following primary surgery is 12-33%. Following salvage surgery, the risk of complications, morbidity and poor cosmetic results are also very high.

Ogita S et al[7] in 1987 introduced OK-432 as a new sclerosing therapy for treatment of cystic hygroma in children. Nine patients from 4 months to 14 years with lesions in the shoulder, neck, abdomen, face, retroperitoneum and ear received intracystic injection of equal amount of 0.1mg of OK-432 in 10 ml physiological saline after aspiration of intracysti cfluid. 4 patients required repeat injection in 3 - 4 weeks' time as the initial dose was considered inadequate. Favorable results were obtained in 6 months to 1 ½ year follow up with complete regression seen in 8/9 (88%), marked regression in 1/9 (11%) patient within 2 – 3 months. No serious side effect was noted except for fever in 2-3 days and local inflammatory reaction in 3-4 days post treatment. None of the patients had damage to the overlying skin hence none had scar formation. There was no recurrence noted either.

Ogita S et al[9] included further more patients in their subsequent study. Forty-six patients received OK-432 sclerotherapy as primary therapy (group A) out of which 23 (52%) noted total shrinkage of the lesion without serious complications, 8 (17%) had marked shrinkage, 12 (26%) had slight shrinkage while 3 (6%) had no response.There were 24 cystic lesions of which 22 showed significant shrinkage, 22 were of cavernous type of which 9 showed shrinkage. In groups B consisting of 14 patients (treatment following incomplete surgical removal) and group C consisting of 4 patients (failed Bleomycin treatment) there was significant

clinical improvement seen in 5 and 2 respectively. No recurrence was noted during follow-up period of 6 to 87 months

Some other studies also showed promising results ranging from 55%-71%[1,5,10,11] which was comparable to our result of 60% complete resolution seen over a period of 6 to 36 weeks and partial response in 34.2% over 6 to 48 weeks.Everaldo R et al[5] found total shrinkage in 12/19 (63%) and partial shrinkage in 7/19 (36%) children in the age range from 1 month to 11 years, who were followed up between 2 to 40 months. Except for fever, no major complication was noted. There was no recurrence. They concluded having good response regardless of size and location of the lesion and OK-432 being better than bleomycin. Sung et al[1] in 2001 assessed the response in 21 patients of which 71% had complete to nearly complete shrinkage in weeks, with an average 2 injections. They recommended OK-432 as the first line treatment and surgery as the second modality only if the response to sclerotherapy was not satisfactory.

Giguere CM et al[11] carried out a prospective multi-institutional trial in 2002 which included 13 US tertiary care referral centres. There were 30 patients aged 6 months to 18 years, out of which 29 patients had head and neck lymphangiomas. The patients were divided into two groups, the first group received 4 doses of OK-432 in 6 to 8 weeks apart under general anesthesia. The cyst was localized by palpation, transillumination, ultrasound guided or fluoroscopy guided. The second or delayed treatment group were observed for 6 months for spontaneous resolution. OK-432 was ultimately given if there was no regression seen. The outcome was noted as complete if size reduced by more than 90%, substantial if more than 60% on CT or MRI at 6 months, 1 and 2 years post treatment. There was 66% overall good outcome with 86% being macrocystic. The total lesion volume was not predictive of successful response.

Various factors have been studied related to outcome of OK-432 sclerothapy.[8] Good outcome has been seen in macrocystic type as compared to microcystic and also with no previous surgery as there is better communication between cysts and hence better diffusion.[3,10] Complete aspiration of cystic contenth as a better result and so does if inflammation related symptoms occurs. However, the exact explanation of the latter is not known. There is no significant relation of the injected dose and success rate once adequate dose has been reached.[11]

The follow up varies from 2 months to as long as 87 months in different literature.[5,9]In our study, the follow up ranged from 6 weeks to 48 weeks.

Minor complications such as fever in 2-4 days, erythema, swelling and discomfort in 5 to 6 days post treatment is common.[7,9,11] Major complications like cervical cellulitis 4 to 5 weeks after first injection, stridor requiring tracheostomy for massive lymphangioma of the left neck extending intrathoracically and left sided proptosis secondary to spontaneous intracystic hemorrhage 4 weeks post OK-432 injection of lymphangioma adjacent to the left orbit have been noted in the literature.[11] There does lie the risk of airway obstruction especially in lesion involving parapharyngeal space, floor of mouth, hypopharynx which may require tracheostomy and care under intensive care team.[3] None of our patients had any complications.

There were a few limitations in our study. The type of lesion based on the size of the cyst was not classified, hence the outcome of the sclerotherapy could not be assessed accordingly. The site of injection was on the most fluctuant part of the cyst based on clinical examination. This probably would have been more effective had it been under ultrasonographic guidance.

CONCLUSION

OK-432 has been found to be safe and effective non-surgical treatment of lymphangiomas.

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