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STUDY ON TOPICAL TIMOLOL AS TREATMENT MODALITY OF CUTANEOUS PYOGENIC GRANULOMAS

Medical Science

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ABSTRACT

AIM-To study topical timolol as treatment modality and Its efficacy in cutaneous pyogenic granuloma (PG)
METHOD- In this study, patients with cutaneous pyogenic granuloma between august 2020 to feb 2021 were given timolol maleate 0.5% gel/ointment thrice a day and followed up for 12 weeks every 4th week. Outcome and side effects were evaluated.No other systemic or topical treatment was given
RESULTS- total 11 patients with cutaneous PGs were treated with 0.5% timolol maleate gel/ointment in age group from 6 to 60yrs with 6patients less than 30yrs old. Four patients completely responded to treatment with complete resolution of lesion within 7-30days,with no reoccurrence at 3months of follow up. Three patients partial response to treatment. Two patient showed no response ,rest two patient were lost during follow up. No major local or systemic side effects were observed except for slight local erythema in 1 patient
CONCLUSIONS: Timolol may be effective preferable non-invasive alternative treatment modality for fresh particularly small pyogenic granulomas in young patients, though response of PGs seems variable.

KEYWORDS

INTRODUCTION

Pyogenic Granuloma (PG) also called lobular capillary hemangioma. Pyogenic granuloma, sometimes known as granuloma pyogenicum, refers to a common, acquired, benign, vascular tumor that arises in tissues such as the skin and mucous membranes.[1] The scientifically accurate term for this entity is the lobular capillary hemangioma. [2]

The term PG is misnomer. Earlier pyogenic granulomas were thought to be an exaggerated granulomatous reaction to an infectious or pyogenic etiology, that is why termed as 'pyogenic granuloma' and 'granuloma pyogenicum.'

When it occurs in the intraoral mucosa in the setting of pregnancy, notably on the gingiva, it is referred to as granuloma gravidarum, granuloma of pregnancy, or epulis gravidarum, usually in the second or third trimester.

Clinicaly presents as a solitary, red, pedunculated papule that is very friable and may ulcerate sometimes or may bleed on handling. Less common presentation as a sessile plaque. Often seen on cutaneous or mucosal surfaces.

Different treatments modalities have variable degrees of success and variable rates of recurrence. No matter the treatment, the patient should be counseled about the risk of recurrence.

Here are many treatment options for cutaneous PG including topical steroids, imiquimod, silver nitrate, cryotherapy, electrocautery, laser ablation, or surgical excision.[3]

In non-visible areas, complete excision is the preferred method of lesion removal because of lower rates of recurrence and an excellent specimen for histopathologic characterization. The excision is performed under local anesthesia.

For small and fresh cases of cutaneous PGs topical timolol can be better option to avoid invasive procedure specially in young patients.

METHODS-

11 patients with cutaneous PG of recent onset (<6weeks) and smaller size were reviewed. All patients were prescribed 0.5% timolol maleate gel thrice daily. The data analyzed included the following parameters: age, sex, duration of symptoms, location of PG, previous treatment received, duration of treatment, outcome, size after at least one week after treatment initiation, followed every 4 weeks thereafter and size at final visit which was at least 6 weeks after treatment cessation. Complete resolution of the granuloma at 6 weeks was considered as treatment success. If after 6 weeks of topical therapy, incomplete resolution of the lesion was not observed, it seems that any further treatment would not lead to any improvement – treatment was stopped, and was surgically excised . Exclusion criteria included recurrent PG at presentation/follow-up, any concurrent systemic/topical medication for pg in last 2-3 months and Pregnant women and lesion older than 6weeks were excluded.

All measurements/findings were taken during opd (out patient department) hours in all patients and all patients were photographed at every visit after obtaining written consent.

RESULTS

Study participants-Seven(7/11; 63.3%) patients were males. The age of the patients ranged from 6 years to 60years with a mean age of 31.1 years. In 6patients, the finger tips/upperlimb was affected; the cause of the PG was attributable to trauma ;The mean duration of symptoms prior to presentation was 4.7 weeks (range: 2 to 12 weeks). Morphologically 10 (90.9%) of the lesions were sessile and only one patient had a pedunculated mass. Four (36.3%) patients had previously received imiquimod/topical medication (not timolol) in past(but not in last 6weeks) with minimal improvement noted prior to presentation.

Outcomes-

Four 4/11(36.3%) patients had complete resolution of the PGs after a mean duration of treatment of 4.4 weeks (range: 3-6 weeks). Three (3/11) 27% patients showed partial response with decrease in size but not completely resolved, Of the 11 patients who had received previous topical timolol, 2 patients had a persistent PG, which showed suboptimal resolution at 6 weeks of treatment and it was surgicaly excised, it was noticed that the bleeding during handling and surgical excision was significantly reduced as compared to patients who didn't apply topical timolol before surgery. Two(2/11) were lost during follow up with one patient showed up for 2 follow ups with partial response after 4 weeks. The mass was excised, and the histopathological examination was consistent with a PG. The mean duration of treatment that resulted in total resolution of the PG in those who had not received any previous treatment was significantly less at 3.8 weeks as opposed to 5.67 weeks in the three patients who had received topical therapy (p = 0.01),with no recurrence at 3months follow up.No significant local or systemic side effects were reported.

Although slight erythema was observed in one patient after 6 weeks of treatment.

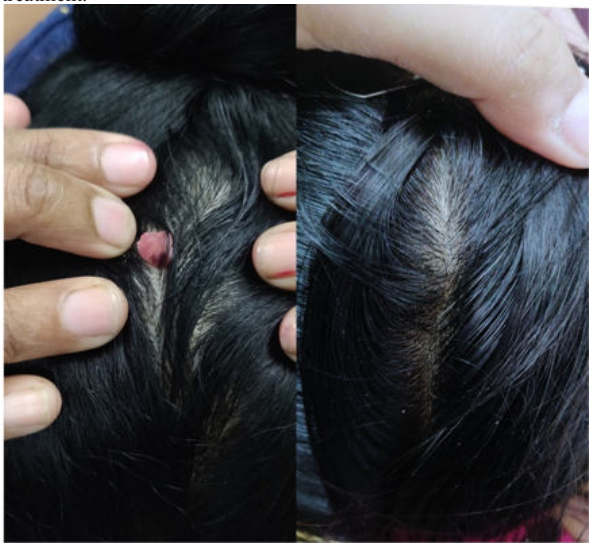

figure1: A 19years-old female who presented with a sessile pyogenic granuloma on scalp (left) received topical timolol 0.5% for 4 weeks resulting in complete resolution (right)

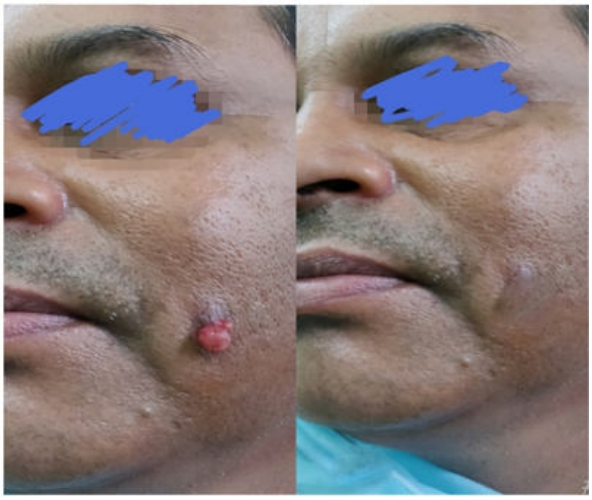

figure2: A 42-years-old male with a pyogenic granuloma on left cheek(left), which resolved completely following 6 weeks of topical timolol (right).

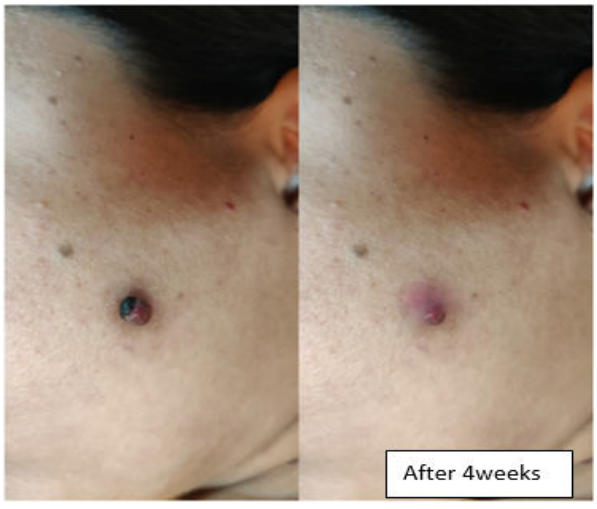

figure 3. A 23-year-old female with a pyogenic granuloma on left cheek (left), which did not resolve completely following 4weeks of topical timolol (right) but a significant reduction in size was present after 6.4weeks with slight erythema and hyperpigmentation around resolving lesion.

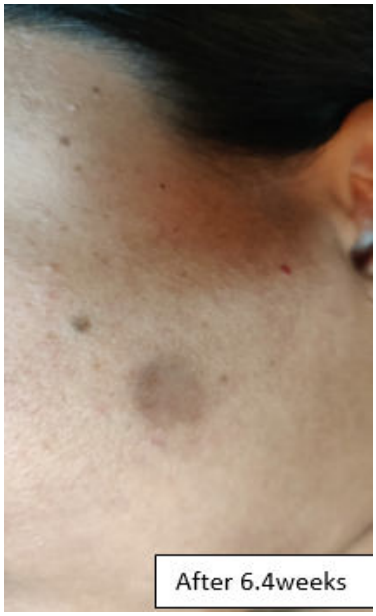

figure4 : Same 23-year-old female with a pyogenic granuloma on left cheek, which resolved completely following 6.4 weeks of topical timolol leaving behind hyperpigmentation at the lesion site.

figure5: A 14-year-old male with a persistent pyogenic granuloma (left) on finger tip, which did not resolve completely following 6 weeks of topical timolol (right) but did decrease in size slightly and was ultimately excised. Histopathology was consistent with a pyogenic granuloma

Figure 6 - Same14year-old male with a persistent pyogenic granuloma

on finger tip, which did not resolve completely following 6 weeks of topical timolol and was ultimately excised. Histopathology was consistent with a pyogenic granuloma, there was minimum bleeding during excision which made excision easier and faster.

DISCUSSION

PGs are also known as 'lobular capillary hemangiomas' and they represent benign, acquired, vascular tumors that are usually seen following an episode of inflammation such as surgery or trauma. PGs can occur at any age.[8] It is hypothesized that PGs occur secondary to local tissue hypoxia within the traumatized endothelial cells, which results in the expression of growth factors such as vascular endothelial growth factor and basic fibroblast growth factor, leading to aberrant healing and the eventual mass formation.

The response of PGs to β blockers(topical timolol) seems to be variable. Although topical timolol has the advantage of least adverse events, ease of administration, and better cosmetic outcomes, it's efficacy in PG may not be universal . Topical timolol may be a treatment option in young children, elderly, fresh and small size lesions and when invasive modalities are not desirable.Also its use in preoperative period for atleast 2 weeks reduces the bleeding which makes its surgical excision easier

The use of beta-blockers in the management of benign vascular lesions was first reported by Léauté-Labrèze *et al*.[4] This accidental discovery initiated interest of clinicians in using beta-blockers in the treatment of PGs as well. Throughout dermatology literature, multiple case reports have highlighted the anecdotal success of topical beta-blockers in the treatment of PGs on the skin.[5] The mechanism of action of beta-blockers in the treatment of hemangiomas is not completely well understood but it is hypothesized that beta-blockers cause vasoconstriction of capillaries supplying the hemangioma, inhibition of proangiogenic growth factors, and apoptosis of proliferating endothelial cells.[6] Beta-blockers also target angiogenic factors such as vascular endothelial growth factor and basic fibroblast growth factor, which are required for the growth and maintenance of PGs.[7]

Limitations of this study include the limited number of subjects,The size of study population is very small number and not all patients could complete the follow up course of 3months.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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