

Early Pyogenic Granulomas in Older Adults treated with Topical Timolol: A Case Series

Denise Ann Tsang, MBBS, MRCP, M Med*, Koh Wei Liang MBBS, MRCP, MRCPS, FAMS, FRCP and Lee Shan Xian, MBBS, MRCP

Department of Dermatology, Changi General Hospital, Singapore

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***Corresponding author:** Denise Ann Tsang, Department of Dermatology, Changi General Hospital, 2 Simei Street 3, 529889, Singapore

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ABSTRACT

Topical timolol has been employed to treat pyogenic granulomas (PG) in children and young adults with mixed results. To date, there are no studies examining the use of topical timolol in older adults (middle-aged and elderly age groups) with primary PG. We report a series of 5 patients (age range 42-87 years) with early PG who responded favourably to topical timolol.

Keywords: Pyogenic granuloma; Adult; Elderly; Topical timolol

Introduction

Topical timolol is a beta-adrenergic receptor antagonist that has been employed in the treatment of pyogenic granulomas (PG) due to its vasoconstrictive and anti-angiogenic properties. Patients who are not surgical candidates, or who have lesions over delicate areas – where invasive modalities are not desirable

– may benefit from topical timolol as a therapeutic option. Most studies examining the use of topical timolol in the treatment of PG have been undertaken amongst children and young adults. Results have been variable across these studies. We report a series of 5 adult patients (age range 42-87 years) with early PG (i.e. onset 1-4 weeks) who responded favourably to topical timolol (**Table 1**).

Table 1: Case series of 5 adults with pyogenic granulomas treated with topical timolol M: male, F: female

Case	Age/race/sex	Co-morbidities	Site	Duration of lesion	Size (mm)	Treatment	Result (at 4 weeks)
1	55/Chinese/M	None	Right middle finger	4 weeks	6x6	Topical timolol 0.5% 2 drops QDS	PR
2	68/Chinese/F	Hyperlipidaemia	Left ring finger	2 weeks	3x2	Topical timolol 0.5% 2 drops QDS	CR*
3	58/Chinese/F	Diabetes, hyperlipidaemia, fibroids	Umbilicus	1 week	7x8	Silver nitrate, followed by topical timolol 0.5% 2 drops BD	CR**
4	42/Indian/M	None	Left big toe	4 weeks	5x7	Cryotherapy, followed by topical timolol 0.5% 2 drops BD	PR***

5	87/Chinese/M	Hypertension, IHD, COPD/asthma BPH	Left wrist	1 week	6x6	Cryotherapy, followed by topical timolol 0.5% 2 drops QDS	CR
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CR: complete response – total disappearance of the lesion, PR: partial response – reduction in the number and/or size of the lesions/ decrease in bleeding tendency,

COPD: Chronic obstructive pulmonary disease, IHD: Ischaemic heart disease, BPH: Benign prostatic hyperplasia

*CR at 1 week

**CR at 3 weeks

***achieved CR at 11 weeks

Case 1

A 55-year-old Chinese male presented with a growth over his right middle finger that bled intermittently over 4 weeks. Examination showed a 6mm x 6mm friable vascular papule clinically consistent with PG (Figure 1a). He received treatment with topical timolol 0.5% 2 drops 4 times daily. A decrease in the size of the lesion and resolution of bleeding was noted 4 weeks later (Figure 1b).

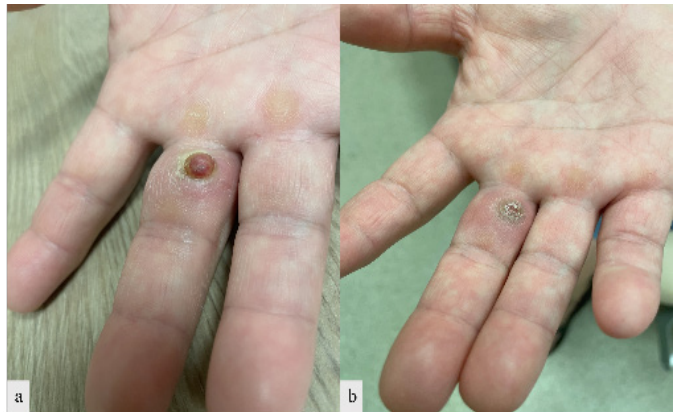


Figure 1a: Before timolol 1b: Decrease in size and resolution of bleeding after timolol.

Case 2

A 68-year-old Chinese female presented with a growth over her left ring finger after accidentally scraping it against a metal chair 2 weeks ago. The lesion bled intermittently on contact. Examination showed a 3mm x 2mm friable vascular papule clinically consistent with PG (Figure 2a). She received treatment with topical timolol 0.5% 2 drops 4 times daily. The lesion resolved within 1 week (Figure 2b).

bleeding tendency of the lesion was noted 4 weeks later (Figure 4b), and complete resolution was seen at 11 weeks (Figure 4c).



Figure 2a: Before timolol 2b: Resolution of lesion after timolol at 1 week.

Case 3

A 58-year-old Chinese female presented with a growth over the umbilicus with occasional bleeding over 1 week. Examination showed a 7mm x 8mm friable vascular papule clinically consistent with PG (Figure 3a). She received treatment with a single application of topical silver nitrate, followed by topical timolol 0.5% 2 drops twice daily. The lesion resolved in 3 weeks (Figure 3b).

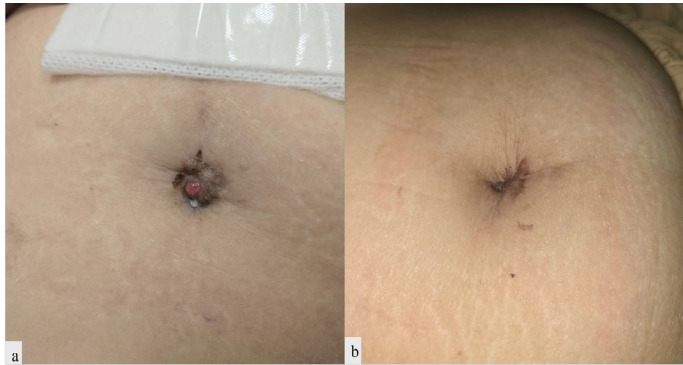


Figure 3a: Before timolol 3b: Resolution of lesion after timolol at 3 weeks.

Case 4

A 42-year-old Indian male presented with a growth over the left big toe that bled intermittently over 4 weeks. Examination showed a 5mm x 7mm friable vascular papule with contact bleeding, clinically consistent with PG (Figure 4a). He received treatment with a single cryotherapy session, followed by topical timolol 0.5% 2 drops twice daily. A reduction in the size and



Figure 4a: Before timolol 4b: Reduction in the size and bleeding tendency after timolol at 4 weeks 4c: Resolution of the lesion after timolol at 11 weeks.

Case 5

An 87-year-old Chinese male presented with a growth over his left wrist that bled intermittently over 1 week. Examination showed a 6mm x 6mm friable vascular papule clinically consistent with PG (**Figure 5a**). He received treatment with a single cryotherapy session, followed by topical timolol 0.5% 2 drops 4 times daily. The lesion resolved in 4 weeks (**Figure 5b**).



Figure 5a: Before timolol **5b:** Resolution of lesion after timolol at 4 weeks.

Discussion

The lack of uniform clinical response to topical timolol has been thought to be due to the expression of only 50% of beta-adrenergic receptors in PG¹. Amongst various factors influencing clinical response, a younger age was the only factor

found to predict a more favorable outcome². The affinity of beta-adrenergic receptors to their ligands decreases as a person ages, with subsequent reduction in their binding sensitivity. Theoretically, beta-blockers would be of less value in treating PG in older patients³.

Topical timolol in the treatment of PG in children is well-described in existing literature. Among adults, most studies to date have been performed in the younger age group (**Table 2**).

There have been few studies examining the use of topical timolol in older adults – these were conducted in patients with paronychia and/or pyogenic granuloma-like lesions secondary to epidermal growth factor receptor inhibitor therapy, rather than isolated primary PG lesions⁴⁻⁶.

Our study supplements current literature by looking specifically at the response amongst older adults who fall into the middle-aged (40-59 years) and elderly (≥ 60 years) age groups. We report 2 women and 3 men (age range: 42-87 years, mean: 62 years) who received treatment with topical timolol for PG. All patients responded to topical timolol by the 4 week mark. Complete response was seen in 3 patients within 1 to 3 weeks. These results are surprisingly favourable, considering previous studies which have suggested that topical beta-blockers would be less effective in older patients. We postulate that the encouraging response seen in our study may be due to the selection of patients with early PG (duration of lesions: 1-4 weeks). Early PG tend to have a greater vascular component, compared to later ones which consist of a larger fibrous component^{7,8}. Given that topical timolol exerts its therapeutic effects on the vascular component, it is logical that patients with early PG tend to respond better.

Table 2. Studies examining the use of topical timolol in adult patients with pyogenic granulomas.

Study, year	n	Age (mean)	Timolol (%)	Duration of treatment	Result	Remarks
Millsop J et al., 2014 [9]	1	39	0.5 solution once daily	3 months	CR	Topical timolol was combined with intralesional steroids and laser
Gupta D et al., 2016 [10]	10	24.9	0.5 solution four times a day	3-24 days	4 CR, 3 PR, 3 NR	The oldest patient was a 50-year-old male with multiple scalp PGs - CR for smaller lesions but NR for all other lesions.
El Taweel AEI et al., 2020 [2]	10	28.1	0.5 cream twice daily	2 months	2 CR	Among the studied variables, age was the only factor influencing clinical response. Younger patients responded better.
Williams N and Morrison B 2020 [11]	1	62	0.5 solution twice daily	10 weeks	CR	Topical timolol was combined with topical steroid/topical antifungal
Patra AC et al., 2022 [12]	22	28.6	0.5 solution twice daily	6 weeks	2 CR, 20 PR	Percentage size reduction: 40.9% with topical timolol versus 3.39% with placebo, $p = 0.002$
Manjeet et al., 2023 [13]	12	25	0.5 solution twice daily	4 weeks	2 CR, 5 PR, 5 NR	The oldest patient was a 50-year-old male with a right index finger PG who showed NR at 4 weeks.

CR: complete response – total disappearance of the lesion, PR: partial response – reduction in the number and/or size of the lesions/decrease in bleeding tendency, NR: no response – absence of clinical response

PG: pyogenic granuloma

This study is subject to certain limitations. All lesions were diagnosed clinically without histological confirmation. Two patients received cryotherapy and 1 patient received topical silver nitrate application in addition to topical timolol. Larger studies are needed to determine the efficacy of topical timolol as monotherapy in this population, and longer term follow-up will be useful to monitor for recurrence⁹⁻¹³.

Conclusions

Existing literature supports the use of topical timolol in the treatment of PG in children and young adults, and a younger age generally portends better outcomes. Our study adds that topical timolol could also be efficacious in older adults, if they have early PG. The age of the lesion may be as important a factor as the age of the patient in predicting treatment outcomes.

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