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Original Article

Sclerotherapy in the treatment of pyogenic granuloma

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Abstract

Backgound Pyogenic granuloma would be defined as the benign growth composed of clusters of hyperplastic capillaries divided into lobules by fibromyxoid stroma. The limited therapeutic effect and the high recurrence rates associated with traditional treatment modalities, in addition to large size and occurrence of some lesions in surgically difficult areas necessitate the seek for an alternative therapeutic approach. Sclerotherapy is not routinely reported as an option for treating pyogenic granuloma.

Objective To assess the tolerability and efficiency of sclerotherapy (polidocanol solution 3%) in pyogenic granuloma treatment.

Methods An open-labeled, interventional therapeutic trial conducted from December 2020 to September 2021. Patients who were diagnosed clinically with PG were enrolled in the study and treated by intralesional injections of polidocanol solution 3%.

Results There was significant reduction in the mean of lesion sizes during the second visit when put head-to-head with the first visit, the reduction was also present in the third visit when compared to the first two (P value <0.05). Moreover, nearly 62.5% of patients showed complete resolution during the second visit and the remaining 37.5% resolved completely during the third visit. A significant moderate negative correlation was detected between duration of the lesions and resolution. Other factors, like age, gender, site and sizes of the lesions, didn't have significant impact on response to treatment.

Conclusion Sclerotherapy with polidocanol solution 3% is a safe and effective treatment for pyogenic granuloma.

Key words
Pyogenic granuloma; Sclerotherapy; Polidocanol.

Introduction

Pyogenic granuloma (PG) are considered common and benign vascular lesions that can occur on the skin or mucous membranes[1] and even intravascularly.[2] It can occur at any age with no sex predilection for the cutaneous lesions and female predominance for the mucosal ones.[3] It may arise spontaneously, in sites of injury, or within area of capillary malformation.[1] Certain medications like OCP, retinoids, gefitinib, capecitabine, vemurafenib and rituximab were reported to induce PG.[4-6] The hormonal effect of pregnancy (second and third trimester)[7] and burns especially with hot liquids have also been linked to the development of PG.[8]

Usually PG are diagnosed based on their clinical appearance with painless glistening red papule that bleeds spontaneously or following

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irritation.[9] However dermoscopy may aid in the diagnosis as PG appear with the combination of structures such as red homogenous area, white collarette, white rail lines, ulceration and vascular structures.[10] Histopathology is rarely required for the diagnosis where it reveals a well-circumscribed proliferation of small capillaries embedded in edematous fibromyxoid interstitial stroma and arranged into lobules by intervening thick bands of dense fibrous tissue.[11]

PG is classically treated by curettage or shave excision, combined with base destruction by cauterization (electrical or chemical) or diathermy coagulation.[12] However many other modalities were documented with different rates of success like cryotherapy,[13] laser (PDL, CO_2, Nd:YAG and diod),[14] topical beta blockers[15] and oral beta blockers.[16]

Sclerotherapy is defined as the selective destruction and transformation of a blood vessels into a fibrous cord by injecting a sclerosing agent into its lumen.[17]

Sclerosing agents are categorized into three groups based on their mechanisms of inducing endothelial injury.[11] Hyperosmotic agents, like hypertonic saline, hypertonic saline–dextrose, and non-chromated glycerin, endothelial cells dehydration can be acted. Chemical irritants, like chromated glycerin (glycerin plus potassium chromate) and polyiodide iodide, are corrosives having cauterizing effect. And lastly detergent sclerosants, like sodium tetradecyl sulfate, polidocanol, and sodium morrhuate, which alter the surface tension around endothelial cells.

Polidocanol is a detergent sclerosant that is a synthetic fatty alcohol consisting of[(18)]:

1. Hydroxypolyethoxydodecane (95%): the active component which is a urethane local anesthetic lacking an aromatic ring.[18]
2. Ethyl alcohol (5%): added as a preservative.[18]

A liquid which is considered viscous at the room temperature with the below specifications:

(1) 15-21^{o}C: melting point, (2) has water miscibility capabilities, (3) 6-8 pH, (4) 0.97 g/cm^3 density at room temperature which extremely resembles water.[19]

Polidocanol is available in different concentrations (0.25%, 0.5%, 1%, 2%, 3%) and may be used directly as a liquid or assembled into a foam before being used according to the indications which include spider veins, reticular veins, varices and hemorrhoidal disease (1st and 2nd degree).[20] Its maximum dose is 2 mg/Kg.[21]

This study will focus on to assessing both the tolerability and efficiency of sclerotherapy (polidocanol solution 3%) in pyogenic granuloma treatment.

Patients and methods

The following open labeled, interventional therapeutic trial was obtained and taken place at the medical city of Baghdad, dermatology and venereology center in Iraq and within the period between January 2020 and September 2021. The researchers had obtained all the ethical approvals from the Scientific Council of Dermatology and Venereology of the Iraqi Board for Medical Specializations.

Inclusion criteria This study has included any patient who was clinically diagnosed with pyogenic granuloma, regardless of the lesion's site and size or the patient's age and gender.

Exclusion criteria:

- Pregnant ladies.
- Lesions that carried diagnosis uncertainty were removed by excisional

biopsy and sent for histopathological examination.

- Patients taking drugs which are documented to induce pyogenic granuloma.

Thirty-five patients with clinically diagnosed PG were examined, diagnosed and treated in the study. Only 32 patients completed the study and 3 had defaulted for unknown reason.

All patients were informed about the nature of their disease, the available therapeutic options and the nature and mode of action of the sclerosant used. Patients who preferred to have their lesions treated by electrosurgery or surgical excision were not included. Only patients who gave an informed consent were included.

A brief history was taken from each patient including information about patient's name, age, gender, residency, duration of PG (in weeks), any provoking factor, previous treatments for the lesion and response to them and any concomitant medical conditions or medications along with the patient's contact information.

On examination, the lesion site and size were documented and the largest diameter of each lesion was measured in millimeters using a digital vernier caliper on all of the three visits.

Prior to administration of the treatment, the site of the lesion was sterilized using 70% ethanol alcohol spray, and then, polidocanol solution in a percentage of 3% (Aethoxysclerol® 3%, Kreussler pharma. Wiesbaden, Germany) was injected intralesionally using a 1 milliliter syringe with 30-gauge needle. The needle was inserted into the lateral side of lesion till its tip reached the center of the lesion then the solution was injected slowly. The injection was stopped when there was a leak of the injected solution, purple discoloration or blanching of the lesion. In addition to that, the amount of the injected solution was roughly tailored according to the site and size of the lesion ranging from 0.2 ml to 1ml. for example, lesions on the face were injected with small amount of polidocanol solution even if they were large.

After injecting polidocanol solution pressure with a gauze swab was applied to the lesion for about two minutes. The patient then was discharged without the need for dressing and told to come back after two weeks for follow up. On the second visit, the lesion was assessed for change in size and injected for a second time if it was not completely resolved and the patient would come back two weeks later for the last assessment. Photographs were taken on the first and each subsequent visits using Nokia 6.1 plus mobile camera 16 MP.

The results were categorized as no response (when there was worsening or no decrease in lesion size), partial response (when there was a decrease in lesion size) and complete resolution. As well as that, any side effects were reported including dyspigmentation, scarring and necrosis.

It is extremely essential to confirm the fact that the current study had not been, in any means, sponsored, funded or granted any financial support from any of public, private or non-profitable organizations.

Statistical analysis All the data that were obtained in this study were analyzed by using the 26th version of the SPSS which stands for Statistical Packages for Social Sciences. Most of the data that were presented, took the form of standard deviation, mean and/or ranges. Furthermore, the percentages and frequencies were the forms for presenting all the categorical data. The comparisons between lesion size during the three visits were conducted by using

the paired t-test. In addition, the assessment of the duration of lesion and resolution correlation was made by the Pearson's correlation test (r). Any value that is less than a 0.05 at the level of P was considered a significant one.

Results

32 patients were considered in this study as mentioned before. They were all diagnosed with pyogenic granuloma and treated by sclerotherapy.

Age and gender The range of patients' age in this study was between 5 to 68 year. The median age was 28.3 years with ±17 years as a standard deviation (SD). The focus was on the below 18 years patients with a percentage of 40.6% to the total number of them.

In another hand, the males were higher in proportion comparing to females as of 65.6% for the former and 34.4% for the latter and as of a ration of almost 1.9:1 male to female.

Clinical information The most common site was face with 15 patients (46.9%) had lesions on the face. Duration of lesion was ranging from 1-24 weeks with a mean of 6.68 weeks and SD of ±5.24 weeks. Half of patients had lesion for more than four weeks duration (50%). **Table 1** shows the study patients' distribution by certain clinical information.

Table 1 The distribution of patients by clinical information in this study.

Variable	*No. (n= 32)*	*Percentage*
Site		
Face	15	46.9
Upper limb	7	21.9
Head	6	18.8
Lower limb	1	3.1
Others	3	9.3
Duration of lesion (Weeks)		
≤ 4	16	50.0
> 4	16	50.0

Management outcome

Size of lesions The comparison in mean size of lesion before and after treatment is shown in **Table 2** which first showed the decrease in mean size of lesion of all patients when the first two visits compared. The third visit showed more decrease in mean size of lesion when compared to first two, only for the eleven patients whose lesions did not resolve completely from the first injection (i.e., in the 2nd visit). Means of size of lesions were significantly reduced dramatically thought the visits starting from the first ending with the third one ($P < 0.05$). The comparison in mean size of lesion before and after treatment according to certain characteristics is **Table 3**. Means of size of lesion were significantly reduced in the second visit when it is compared to first one according to different characteristics ($P < 0.05$).

Table 2 Comparison in mean size of lesion before and after treatment.

Visit	*n*	*Size of lesion (mm) Mean±SD*	*P-Value*
Visit no. 1 (Pre)	32	9.43 ± 3.7	0.001
Visit no. 2 (Post)	32	2.93 ± 4.7	
Visit no. 1 (Pre)	11	11.54 ± 4.0	0.001
Visit no. 3 (Post)	11	0 ± 0	
Visit no. 2 (Post)	11	8.27 ± 4.2	0.001
Visit no. 3 (Post)	11	± 0	

Table 3 Comparison in mean size of lesion before and after treatment according to certain characteristics.

Variable	*Size of lesion (mm)*		*P-Value*
	1st visit	*2nd visit*	
Age (Year)	*Mean ± SD*		
< 18	10.3 ± 4.2	2.92 ± 5.4	0.001
18 - 39	8.44 ± 2.8	2.33 ± 3.7	0.001
≥ 40	9.22 ± 4.0	3.55 ± 5.0	0.014
Gender			
Male	9.09 ± 3.2	2.71 ± 4.1	0.001
Female	10.2 ± 4.8	3.4 ± 6.1	0.001
Duration of lesion (Weeks)			
≤ 4	10.62 ± 4.2	5.18 ± 5.4	0.001
> 4	8.2 ± 2.8	0.53 ± 2.1	0.001

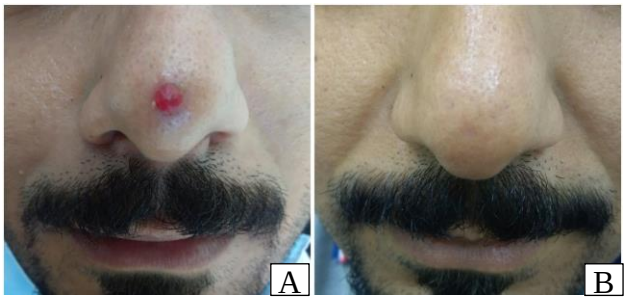

Figure 1 Pyogenic granuloma on the nose of 32 years old male; A: Before treatment; B: Complete resolution two weeks after treatment with intralesional injection of polidocanol solution 3%.

Figure 2 Pyogenic granuloma on the upper vermilion lip of a 7 years old female child. A: Before treatment; B: Complete resolution two weeks after treatment with intralesional injection of polidocanol solution 3% (Note the post inflammatory hypopigmentation).

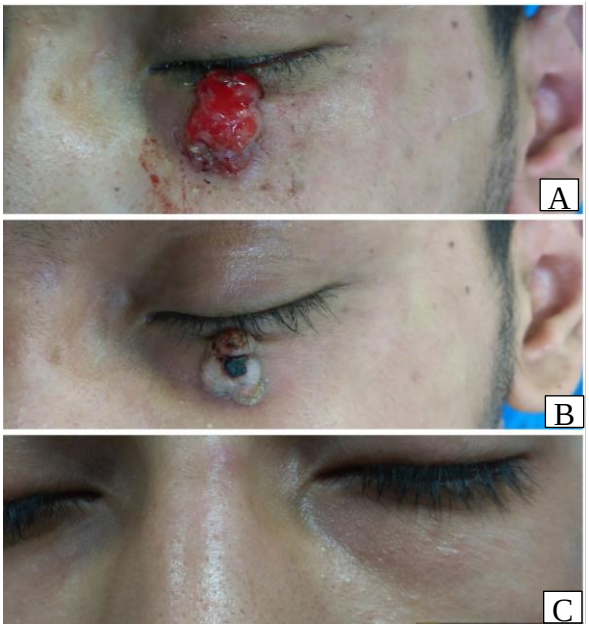

Figure 3 Pyogenic granuloma on the lower eyelid of a 16 years old male. A: Before treatment; B: Partial resolution two weeks after first intralesional injection of polidocanol solution 3%. C: Complete resolution two weeks after second intralesional injection of polidocanol solution 3%.

Complete resolution In this study, during 2nd visit, we noticed that 20 patients (62.5%) showed complete resolution and the rest of patients (37.5%) were resolved completely in the 3rd visit.

Complication Twenty-eight (87.5%) of study patients didn't suffer from any complication; while two (6.2%) of them developed depressed scar and one (3.1%) developed hypopigmentation and one (3.1%) developed necrosis.

Correlation between duration of lesion and resolution A detection of a moderate negative correlation was seen and considered statically significant between duration of lesion and resolution (r=-0.441, P=0.013).

Discussion

In the current study, 32 patients were enrolled, all of them were clinically diagnosed with PG and treated by sclerotherapy with polidocanol solution 3%.

The mean and the standard deviation of (SD) of age in this research was 28.31±17.0 years, (ranging from 5-68 years) with a highest proportion < 18 years (40.6%). The proportion of males was higher than females (65.6%) with a male to female ratio 1.9:1. The most common site was face (46.9%). Duration ranged from 1–24 weeks with a mean of 6.68 weeks and SD of ±5.24 weeks.

By comparison, 15 patients were recruited in the study of Bansal and colleagues in 2019. They reported a female to male ratio of 2:1. The mean age was 30.5 years. Most of lesions were on the

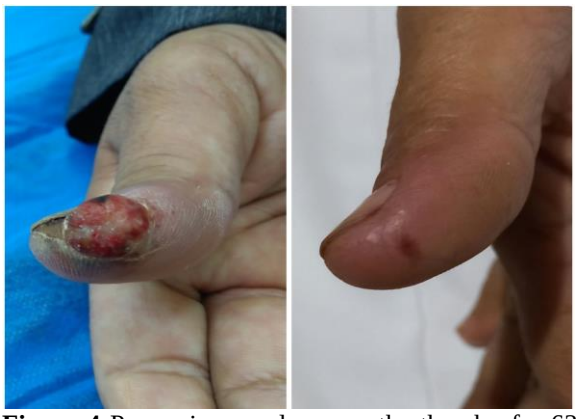

Figure 4 Pyogenic granuloma on the thumb of a 63 years old male. A: Before treatment; B: Complete resolution two weeks after treatment with intralesional injection of polidocanol solution 3%.

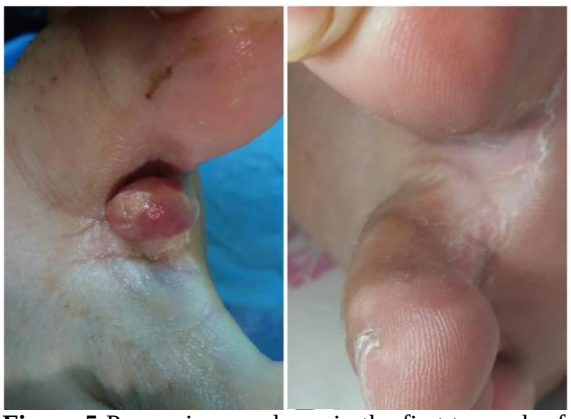

Figure 5 Pyogenic granuloma in the first toe web of 48 years old female. A: Before treatment; B: Complete resolution two weeks after treatment with intralesional injection of polidocanol solution 3%.

lips (40%), followed by face and scalp (20%) and one case each on finger, nose and neck (6.6%).[22]

Fifty-two patients with PG were included in Zhao *et al.* study in 2019, in which a slight female predominance was observed (51.9%), female to male ratio was 1.08:1. Mean age at diagnosis was 26 years. Moreover, they reported a close results, as found that 51.61% of the cases (26 lesions) were found in the facial area, whereas, 22.58% of the cases (12 lesions) were found on the lip and oral cavity, six (9.68%) on the scalp, seven (12.90%) on extremity and one (3.23%) on trunk.[20]

Forty patients were enrolled in Khaitan *et al.* study in 2018. It was found that the average age of the patients was about 34.65 years old, and that females accounted for about 60% of the study population.[23]

The differences observed above can be related to different sample size, different type of trauma applied to different regions of body, in addition to different socioeconomic and environmental factors and educational factors that affect attendance to the clinics.

The study also revealed that means of lesion sizes were significantly reduced when comparing the three visits starting from the first one and on ($P<0.05$). Moreover, means of lesion sizes were significantly reduced in the 2nd visit compared to 1st visit according different characteristics ($P<0.05$). Finally, during 2nd visit, nearly 62.5% of patients showed complete resolution and the remaining 37.5% were resolved completely in the 3rd visit. On the other hand, a detection of a moderate negative correlation was seen between duration and resolution ($r=-0.441$, $P=0.013$)

Similar findings were observed by Khurana *et al.* study in 2021, in which 39 patients achieved complete resolution, with most (66.6%) lesions resolved after the first sitting.[24]

Zhao and colleagues reported that around (98.08%) of the 52 patients, received complete removal of the PG after one (43 (82.7%) patients) or two (8 patients) times of injection with polidocanol foam 1%.[20]

Moreover, a total of 15 clinically diagnosed patients of oral PG (8) and mucocele (7) were enrolled in Shah *et al.* study in 2018 received three consecutive injections with polidocanol

solution 3% at a weekly interval. Of the eight patients with PG, six (75%) (< 2 cm) required single injection to resolve, one (2-4 cm) required two injections and one (> 4 cm) required three injections to show complete resolution.[25]

In Carvalho *et al.* study, seven patients with PG were enrolled, the injection with Polidocanol solution 0.5% resulted in complete removal of six lesions, with inconspicuous scars (85.7%).[26]

The differences reported among above studies can be related to statistical factors in the form of study design and sample size, or to clinical factors in the form of the stage of the disease, location of lesion, duration, presence of infection or not, type of other intervention used, sclerosant used and its dose and frequency of intervention.

In the present work, majority of participants didn't suffer from any complication (87.5%); while 6.2% of them developed depressed scar, this percentage was higher than that published in Zhao *et al.* study, where only one of the 51 patients (1.92%) showed lesion recurrence and the rest have reached the standard of cure without exudation, pigmentation and scarring.[20]

In comparison to Khurana *et al.* study, complications noted were post-procedure pain (56.4%), prominent edema, purpuric staining around injection site (10.2%), thrombophlebitis, cyanotic discoloration, mild local pruritus, erythema, superficial ulceration, and paresthesia (5.1%).[24]

The results published in Shah *et al.* study, contradict the current one, as they reported that no post-sclerotherapy complications were observed except for local discomfort, and mild bleeding and swelling by few cases which resolved within an hour.[25]

The differences observed above can be attributed to the site of the lesions, size, duration, drug used, dose, experience of the person providing injection and the state of the tissue.

The advantages obtained from sclerotherapy are: patient discomfort was at its minimum levels, loss in blood was almost neglected, cumbersome was less by far, the needed surgical expertise is considered minimal, economically beneficial for patients. Furthermore, the local anesthesia, dressing for post-op or any additional medical care are not required at all and the patient can return to his daily routine immediately afterwards the operation. Sclerotherapy could be a validated alternative to conventional methods such as laser treatments, radio-frequency ablation, electrodessication and even conventional surgery. Moreover, it is considered simpler, easier, safer, more feasible and more affordable alternative with better success and less recurrences chances.[27]

Conclusion

Sclerotherapy with polidocanol solution 3% is a safe and effective approach in the treatment of pyogenic granuloma especially when occurred in a surgically difficult or cosmetically sensitive areas. It is cost effective, does not required pre operative anesthesia or post operative special care or dressing.

Patients of all ages and genders are amenable to treatment with sclerotherapy regardless of the lesion size and site.

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