SCLEROTHERAPY AS TREATMENT MODALITY FOR ORAL PYOGENIC GRANULOMA (RANDOMIZED CONTROLLED CLINICAL TRIAL)

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ABSTRACT

INTRODUCTION: Pyogenic granuloma (PG) is a type of reactive hyperplasia that results in the enlargement of soft tissues. Oral PG is traditionally treated by surgical excision with a scalpel in addition to removal of the irritant or trauma source. Surgical removal of a pyogenic granuloma is associated with bleeding and pain. A high rate of recurrence is very common which might be due to incomplete removal. Sclerotherapy would be a good treatment choice for large- sized lesions.
OBJECTIVE: To evaluate postoperative pain and recurrence using sclerotherapy versus conventional surgical excision in treating oral pyogenic granuloma.
Materials and methods: 20 patients with pyogenic granuloma were enrolled in this randomized controlled clinical trial, divided equally into two groups. Group-I (test group) treated by Ethanolamine Oleate injection as a sclerosing agent. Group- II (control group) treated by surgical excision. Patients were evaluated in terms of pain at the 2nd and 7th day postoperatively and monthly for recurrence up to 6 months.
RESULTS: The evaluated parameters demonstrated improvement by the end of the study in comparison to baseline, in terms of postoperative pain. None of the patients in test group reported recurrence at 6 months follow- up. On contrary 2 patients reported recurrence in the control group. However, there was no statistical significance between the two groups.
CONCLUSION: Sclerotherapy is simple, inexpensive technique that showed no recurrence for treatment of oral PG.
KEYWORDS: Pyogenic granuloma, Sclerotherapy, Surgical excision, Ethanolamine Oleate
RUNNING TITLE: Sclerotherapy treatment for oral pyogenic granuloma

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INTRODUCTION

Pyogenic granuloma (PG) is a relatively common non-cancerous tumour- like growth. It can occur in the skin and oral cavity (1,2). The two Frenchmen Poncet and Dor (3) were the first to describe pyogenic granuloma in French literature in 1897. It can appear at any age, more commonly in young adults with female predilection (1). Clinically defined by a nodular soft mass that may exhibit a smooth or lobulated surface, with sessile or pedunculated base (4). The lesion's color varies from reddish-purple to pink. They are painless and hemorrhage may occur as a result of the tissue's high vascularity (1). The differential diagnosis of PG includes inflammatory gingival hyperplasia, peripheral giant cell granuloma, heamangioma and peripheral ossifying fibroma. Histopathological examination confirms the final diagnosis. (5,6).

The exact etiopathogenesis is still unknown, and several factors appeared to be related to their formation. It is believed to be reactive lesion that develops in response to different factors as trauma (1), chronic irritation, hormonal factors (7) or certain drugs (8).

Surgical excision of PGs is considered the treatment of choice. The procedure is followed by curettage of the underlying tissue. To reduce the probability of recurrence, excision with a margin of 2 mm around the clinical periphery and to the periosteum should be performed besides the elimination of any foreign body, calculus, or faulty restoration (9,10). Pyogenic granuloma recurs at a relatively high rate following simple excision (9). complications such as scarring and bleeding are frequently observed following surgical excision (11).

Sclerotherapy has been proposed as an effective method of treatment for pyogenic granuloma. Their mechanism of action is endothelial injury, inflammation, thrombosis, fibrosis, and final lesion destruction (12). The total number of applications, the lesion's response, and the treatment's success all vary and are dependent on a variety of variables, including the protocol used and the lesion's vascular flow (13).

Among these commonly used chemical agents for sclerotherapy are sodium tetradecyl sulphate, ethanolamine oleate and absolute ethanol injection.

Ethanolamine oleate (EO) acts by an intra- and extravascular inflammatory response and fibrosis in the endothelium. Coagulation is triggered by oleic acid, while fibrin clot suppression is coordinated by ethanolamine. To avoid future blood loss, the vascular lesion is replaced by fibrosis (14).

Oral pyogenic granuloma shows high recurrent rate (15). It is suggested to be caused by insufficient excision, inability to eradicate the causative component, or re-injury of the area (16).

According to the aforementioned this study is held to determine the efficacy of using a sclerosant agent for treatment of oral pyogenic granuloma regarding postoperative pain and recurrence rate.

The null hypothesis of this research is that there will not be a difference between sclerotherapy and conventional surgical excision in treating oral pyogenic granuloma regarding postoperative pain and recurrence.

MATERIALS AND METHODS

A. Materials

The study was accepted by the Research Ethics Committee of the faculty of Dentistry Alexandria university (IRB NO:00010556 - IORG 0008839) Registration of the study was done at U.S National Institutes of Health Clinical Trials Registry (NCT05099081). It also followed the principles of modified Helsinki code for human clinical studies (2013) (17) and CONSORT 2010 guidelines for reporting randomized clinical trials (18).

Sample size

This study was a randomized controlled clinical trial conducted between December 2020 and September 2021 in the Oral Medicine Department, Faculty of Dentistry, Alexandria University. Twenty patients with oral pyogenic granuloma were included in the study (number of groups=2). All subjects approved to participate in the clinical trial and a written consent was obtained. Sample size was estimated based on a previous study aimed to evaluate efficacy of sclerotherapy in the treatment of oral pyogenic granuloma (19). The minimum sample size was calculated to be 9 patients per group which was increased to 10 patients per group to make up for possible loss to follow up. The total sample size = number of groups × number per group= 2 X 10= 20 patients. Sample size was based on Rosner's method (20) calculated by Gpower 3.0.10.

Study design

Twenty Patients diagnosed to have oral pyogenic granuloma after taking medical history, performing clinical examination and incisional biopsy to confirm the diagnosis, were included in this study. Group I (test group): ten patients were treated with injection of ethanolamine oleate. Group II (control group): ten patients were treated with conventional surgical excision. Inclusion criteria included patients of both genders diagnosed clinically and confirmed histologically with oral pyogenic granuloma. Size of the lesion was not less than 5mm. Patients were having gingival pyogenic granuloma. Age ranged from 19 to 50 years old. Exclusion criteria included patients with uncontrolled diabetes, renal disease, coagulation disorders, allergic to any of the sclerosing drug constituents. Immuno-compromised patients. Pregnant and lactating women.

Methods

Prior to initiating treatment, patients in both groups provided a complete medical and dental history. Phase I therapy was undertaken. Patients were encouraged to maintain proper oral hygiene.

Biopsy: Under local anaesthetic, an incisional biopsy was performed to confirm the nature of the lesion. The removed samples were fixed in neutral formalin at a concentration of 10%.

Group I (test group)

The surgical area was anaesthetised with local anaesthetic agents (2 percent lidocaine and 1/100,000 epinephrine). Ethanolamine oleate® 5% Amp (EPICO, Egypt) was diluted to 2.5 percent EO in distilled water (21), A solution ranging in volume from 1.5 to 3 ml was gently injected into the lesion depending on its size (19). A 23-gauge needle was used to slowly inject the fluid into the lesion until it oozed out from the lesion surface. For five minutes, the lesion was squeezed (21). Figure (1)

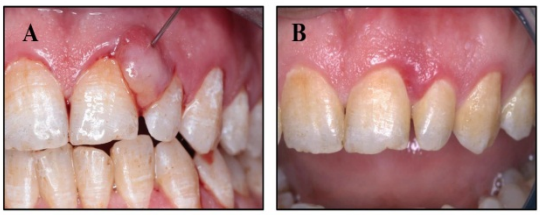

Figure (1): Treatment of Pyogenic granuloma by sclerotherapy A) injection of ethanolamine oleate B) Follow up

Group II (control group)

Local anaesthetic drugs (2 percent lidocaine and 1/100,000 epinephrine) were used to sedate the operative area. Pyogenic granuloma was excised by incisions made with a number 15C surgical blade and traction provided with mosquito forceps. Bleeding was managed with the application of a pressure dressing. Suturing the wound edges

continuously was used to control the bleeding. The lesion was excised with 2-3mm safety margin with curettage of the periodontium to prevent recurrence. Figure (2)

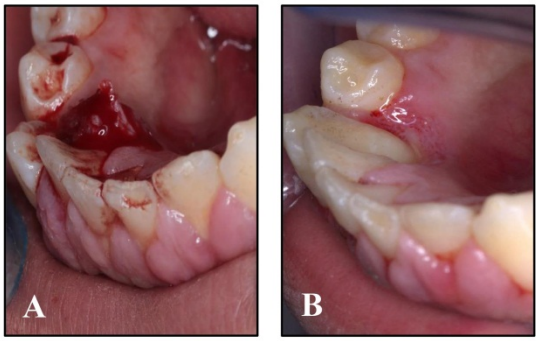

Figure (2): Surgical excision of pyogenic granuloma A) surgical excision B) Follow up

Clinical Evaluation

Pain: Postoperative pain was evaluated on the 2nd and 7th days using a numeric rating scale (NRS) (22) which is a segmented numeric version of the visual analog scale (VAS) in which a respondent selects a whole number (0 –10 integers) as follows: NRS= 0 (no pain), NRS =1-3 (mild pain), NRS =4-6 (moderate pain), and NRS =7-10 (severe pain).

Recurrence: Patients were recalled monthly for 6 months after the end of treatment.

Statistical analysis

Categorical data were presented as frequency and percentage values and were analyzed using Fisher's exact test. Ordinal data were presented as mean and standard deviation values and were analyzed using Mann-Whitney test for intergroup comparisons and Wilcoxon signed rank test for intragroup comparisons. The significance level was set at $p<0.05$ within all tests. Statistical analysis was performed with R statistical analysis software version 4.1.2 for Windows (23) (R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.).

RESULTS

Regarding biopsy performed all histological sections revealed a mass of granulation tissue surrounded by ulcerated stratified squamous epithelium. Numerous capillaries proliferated within the bulk, which was heavily infiltrated by chronic inflammatory cells.

Results of inter and intragroup comparisons of post-operative pain presented in table (1) and in figure (3), showed control group to have a significantly higher postoperative pain score than the test group in both intervals ($p<0.05$). In both groups, there was a significant reduction in pain score after 7 days ($p<0.05$).

Results of inter and intragroup comparisons of post-operative recurrence presented in table (2) and in figure (4), showed that 2(20%) cases had recurrence after 3 months in the control group while all the cases in the test group were free and the difference between both groups was not statistically significant (p=0.474).

Table (1): Inter and intragroup comparisons of post-operative pain.

Time	Post-operative pain (Mean±SD)		P-value
	Sclerotherapy	*Surgery*	
2nd day	1.70±2.58	5.86±0.69	0.004*
7th day	0.00±0.00	3.71±1.11	<0.001*
p-value	0.066	0.011*	

* Significant ($p<0.05$)

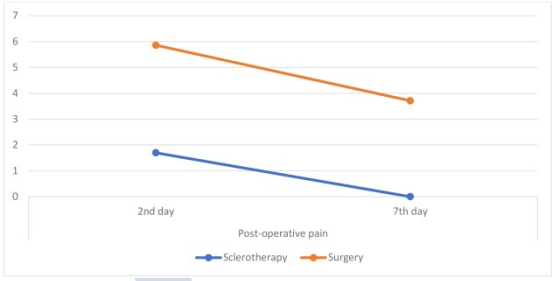

Figure (3): Line chart showing average post-operative pain.

Table (2): Inter and intragroup comparisons of pot-operative recurrence.

Recurrence		Sclerotherapy	Surgery	P-value
Yes	**n**	0	2	**0.474**
	%	0.0%	20.0%	
No	**n**	10	8	

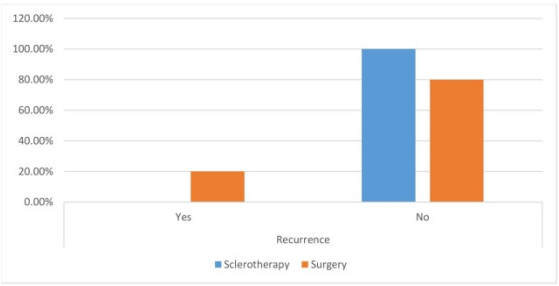

Figure (4): Bar chart showing post-operative recurrence.

DISCUSSION

The purpose of this study was to determine the efficacy of sclerotherapy in treating oral pyogenic granuloma versus conventional surgical excision.

The most frequently used treatment option for oral pyogenic granuloma is conservative surgical excision with elimination of the underlying irritant or cause of injury. (10). Scarring and bleeding are

frequently noticed as a result of surgical excision (9). Following simple excision, pyrogenic granuloma returns at a relatively high rate (11).

Sclerotherapy has been suggested that may be an effective treatment (24). Ethanolamine Oleate has been used successfully in treating oral pyogenic granuloma (12). When a large lesion develops in an inaccessible area for surgery, it might be an excellent option for therapy (25).

In this study we evaluated the use of ethanolamine oleate as a sclerosing agent in treating oral pyogenic granuloma in terms of postoperative pain and recurrence rate. The study enrolled 20 participants who had gingival oral pyogenic granuloma.

Postoperative pain was minimal in the majority of the test group's patients on the second day following injection with a statistical significance difference from the control group. A majority of patients (90 percent) reported no pain following injection in Fernandes et al. (2018), in accordance with our findings (26). However, three of the patients suffered postoperative pain following injection, which may be due either to the high pressure of the injection resulting in vascular leakage (27) or to the sclerosant solution penetrating the normal mucosa and leaking out (28).

Likewise. According to Da Silva Barros (2021), evaluating sclerotherapy for oral benign lesions. A number of variables had to be taken into consideration in order to avoid necrosis and ulceration while also reducing pain. These included the concentration dose, the timing of intravascular injection, and the amount of sclerosing agent to use (29). Pain that is referred from related dental pathology can be the source of discomfort (30).

In control group, the majority of cases had postoperative bleeding and pain. This can be explained by the fact that the use of sutures may exacerbate the bleeding and pain while eating. Additionally, suture removal from the mucosa can cause pain, as sutures may become embedded in the mucosa (31).

Following up with the patients after 6 months revealed that none of the patients in the test group had a recurrence, which can be related to the fact that sclerosing agents induce damage to the endothelium of the vessels, resulting in fibrosis (32). Khaitan et al. (33) reported that they were able to successfully cure 40 patients having pyogenic granuloma after administering 1–4 successive doses of sodium tetradecyl sulfate as a sclerosing agent at a weekly interval all the 40 patients showed complete regression of the lesion with no recurrence after 6 months follow up period. According to a subsequent study by Shah and Ranghani (34), on 15 clinically diagnosed cases having oral pyogenic granuloma (8 cases) and mucocele (7 cases), (90%) of cases showed complete regression with no recurrence.

In the control group, 2 patients reported recurrence in the 3rd month of follow- up. The recurrence seen may be due to the remnant lesion or an already present irritant (5). Patients not following oral hygiene instruction can also aid in the recurrence of the lesion (35-37).

Al-Noaman 2020 (38) found no evidence of recurrence in patients treated with modified excision with deep curettage. In comparison, individuals treated with simple excision and root planing experienced a recurrence of the lesion. This means that removing 2 mm of normal tissue and doing a deep curettage may help prevent illness recurrence (10). Sapp et al. (39) report that oral pyogenic granulomas return very frequently following simple excision.

CONCLUSION

In the present study, we concluded that sclerotherapy is an excellent treatment for oral pyogenic granuloma which is simple, less traumatic, reduces postoperative complications and with very low rate of recurrence.

Conflict of Interest

The authors declare that they have no conflict of interest.

Funding

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