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Original Research Article

Long-Terms Adverse Effects of Using Permanent Fillers in Facial Soft Tissue Augmentation

Alaa Hussein Al-Farhan* Bahir Sabah Allawi
College of Medicine, University of Babylon, Hilla, IRAQ

*E-mail:alaasurg2003@yahoo.com

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Abstract

Soft tissue augmentation of the face using different types of fillers has been increased tremendously in the last years. Many adverse effects has been reported after the use of the permanent type of fillers. Most of these adverse effects are permanent and can cause medical and psychological impact on the patients.

The aim of this study is to evaluate the long term adverse effects and influencing Factors of the permanent fillers injected in the face and the possible ways used to treat them. it is a prospective study of 42 patients who presented with delayed-onset adverse effects after injection of polyacrylamide hydrogel (PAAG) or Boldenone Undecylenate as a permanent fillers in the face.

Many adverse effects would appear long after the injection of the permanent fillers in the face. Some of the adverse effects are permanent and can cause severe psychological disturbances. Only little can be done to treat such complications. The adverse effects were grouped into four groups, Four patients presented with severe inflammatory reactions. Twenty seven patients had multiple nodules. Five patients had asymmetry in their faces. other patients were suffering from hard masses in their checks. Aspiration was done for some of the hard masses. Drainage was done for the inflammatory cases. Removal of the nodules was done for two cases and some were injected with triminicilone acetate. Temporary fillers were used to correct the patients with asymmetries, Fat injection was not successful to treat the asymmetries. The use of threads , fillers and PRP act as a trigger to the inflammatory reaction in some of these patients.

Key Words: Soft tissue augmentation, adverse effects, polyacrylamide hydrogel (PAAG), Boldenone Undecylenate.

الاثار الجانبية البعيدة المدى لاستخدام المواد المالئة والمستخدمة في زياده الأنسجة الرخوة للوجه

الخلاصة

هنالك تزايد كبير في السنين الاخيرة في استخدام المواد المالئة المستخدمة في زياده الأنسجة الرخوة في الوجه. وقد سجلت العديد من الاثار السلبية للمواد المالئة الدائمية. ومعظم هذه الاثار السلبيه هي اثار دائمية وممكن ان تترك اثر طبي ونفسي لدى المرضى . والهدف من هذه الدراسة هو تقدير الاثار السلبية البعيدة المدى والعوامل المساهمة في ظهور هذه المضاعفات للمواد والتي استخدمت في الوجوه . وهي دراسه مرتقبه ل ٤٢ مريض عانوا من اثار جانبيه وبعيده المدى لاستخدام المواد المالئه (الفلر) من نوع البولي اكيل امايد الهايدراجلوالبولدينون اندي سيلينيت في الوجه. استخدام المواد المالئه الدائمية قد يعقبها مضاعفات مستقبليه وهي مضاعفات قد تكون دائمي هو تسبب اثر نفسي شديد والقليل من الحلول موجوده وقد تساعد بشكل طفيف في مثل هذه الحالات. وقد قسمت الاثار الجانبية الى اربع مجاميع، اربعة من المرضى كانوا يعانون من التهاب شديد متكرر. سبعه وعشرون منهم كانوا يعانون من عقد متعدده تحت الجلد . خمسه منهم كان لديهم عدم تناظر في الوجه . والباقون كانوا يعانون من كتل صلبه . وقد تم اجراء سحب لقسم من الكتل الصلبه واجراء تصريف للحالات الشديدة الالتهاب. وتم ازاله بعض العقد جراحيا او حقنها بماده الترايميسيلينون . وتم استخدام ماده الفلر الوقتيه لتعديل بعض الاختلالات في الوجه . في بعض الحالات استخدام البلازما الغنية بالصفيحات الدمويه والخيوط او الفلر كان احد العوامل المحفزة للألتهابات الشديدة.

الكلمات المفتاحية: تضخيم الانسجة الرخوة ، الاعراض الجانبية ، جل البولي اكريل اميد ، بول دينون اندي سايللينيت.

Introduction

In the recent years, injectable fillers are commonly used as non-surgical cosmetic procedure. It is used for skin defects, facial wrinkles and folds, depressed scars and for aesthetic purposes [1]. Soft tissue fillers can categorized into three types: temporary, semi-permanent, and permanent fillers[2].

Biodegradable filler like hyaluronic acid (HA) is a temporary filler which may last between 9-12 months according to its properties. It is safe and considered as a first line for facial soft tissue augmentation [2]. Semi-permanent fillers such as fat, Sculptraand Radiesse are partially biodegradable and last for 1 to 3 years[3]. No biodegradable (permanent) fillers with very long duration such as silicone oil and polyacrylamide hydrogel have been used for facial augmentation [4-6]. Polyacrylamide hydrogel (PAAG) which contains 2.5% polyacrylamide and 97.5% water is used for facial corrective surgery and breast augmentation for many years worldwide [6-8].

Boldenone (BOL) is an anabolic steroid. It is used mainly as undecylenate ester by bodybuilders. However, it is used as a growth promotor on farms for improving the growth and feed conversion of cattle[9]. It had been used by unauthorized persons as an injectable filler to human faces.

Although some studies have indicated PAAG as a well-tolerated product with desirable aesthetic results and a few complications [10,11], many studies have shown that numerous adverse events occur after using this permanent filler. These complications may be, transient, nonsignificant such as : pain, hematoma, infectious (abscess), host tissue reaction (foreign body granuloma, edema, inflammation, redness, sensitivity), and miscellaneous such as gel migration, lumpiness, and gel indurations [8, 12–14]. Late adverse effects are discussed in this study with possible appropriate treatments.

Materials and Methods

This is a prospective study of 42 patients who presented with late onset adverse effects after injection of permanent fillers in their faces. Bolden one (BOL) complications were included in this study. All the cases were referred to the author and none of the them were primarily his cases. Treatment and follow-up were done from 2013 to the end of 2015.

Total of 42 patients (41 female and 1 male) with the age range of 22-54 years(mean =34.5 y.) were seen during the period of this prospective study. All of the cases were injected in their faces. The distribution of the injection sites in the face is shown in table 1.

Table 1: The distribution of injection sites in the faces

Site of injection	*No. of patients*
cheek	23
lips	4
eyebrows	3
Nasolabial	3
Lower lid and tear trough	4
glabelle	2
Marionette line	3

From the history, 39 cases (92%) were injected with polyacrylamide filler and three cases(8%) were injected with Boldenone Undecylenate, an anabolic agent for veterinarian use only (figure 1). Thirty two patients (76%) have no idea about the type, nature, or the possible adverse effects of the fillers. Others have simple idea about the duration only of these fillers. The three patients with anabolic agent injection were injected by non-medical personnel, while others were injected by physicians. The onset of complaining from the adverse effects were ranged from 1-4 years from the time of injection as shown in table 2.

Table 2: Duration between the time of injection and the appearance of the adverse effects

Time of reporting the complications	***No. of patients***
<1 year	2
1-2 year	*5*
2-3 years	11
3-4 years	22
>4 years	2

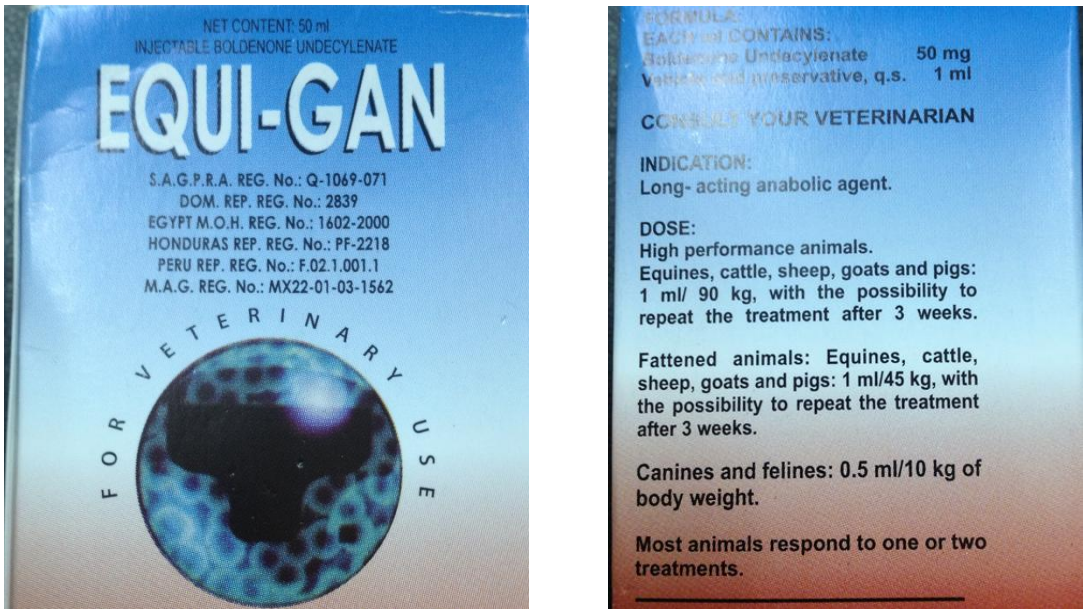

Figure 1: Boldenone (BOL) and its content

Results

The adverse effects were categorized into four groups according to their types. as shown in table 3. The Early complications were not included.

Table 3: Types of adverse effects of the permanent fillers

Group	Adverse effects	No. of patients	%
Group I	Severe inflammatory reaction	4	9.5
Group II	nodules	27	64.2
Group III	asymmetry	5	11.9
Group IV	Hard masses	6	14.2

In group I, five patients presented with severe recurrent inflammatory reaction in form of redness, swelling, fever, and pain. Three of them (7%) had recurrent discharge during the inflammatory period (figure 2). Two of them were with severe discharge that need to be drained under general anesthesia and one case was drained under local anesthesia and small gauze drain was put for few days until discharge subside. All of them , culture and sensitivity was done for the discharge and all were negative. Antibiotics was given empirically to all of the cases. The inflammation with discharge usually subsided in 1-3 weeks, while the inflammation without discharge usually subsided in one week. One patient gave a history of platelet rich plasma injection in her face followed by the inflammation. One patient mention tooth problem followed by inflammation. Another patient had thread lift followed by inflammation one week later.

Figure 2: Patient with recurrent inflammation after 2 years of injection of PAAG

In group II, 27 patients had multiple nodules in the cheeks and lips, presented as mobile nodules. The patients were worried about these nodules and enter in differential diagnosis of subcutaneous masses. Trial to dissolve the nodules was done by trimicinilone acetate intralesionally in three sessions for three cases only(11 %). Good response was observed in these cases. Two patients with nodule in their lips were surgically extracted. In two patients with nasolabial nodules had aspiration done by using 18G needle with 20cc syringe. Others were managed conservatively.

In group III, five cases (11.9 %) had deformity and asymmetry in their cheeks (figure 3). Four of them (9.5 %) had severe deformity as a result of either recurrent inflammation and discharge or because of attempt to evacuate of the filler. Two of them had underwent fat transplantation but without success. Temporary fillers were used many times to correct the asymmetry with moderate success. Fat injection was used to correct the deformities in two cases but with no success . Two other cases were exposed to the complications of the removal of too much soft tissue during removal of the permanent filler that lead to exposed cornea and keratitis, then full thickness skin graft was used to correct the eyelid problem. One of the patients had exposed to seven operations to correct the deformities of both cheeks and lower lids.

Figure 3: Patient with severe deformity after removal of PAAG from the check.

In group IV, six patients (14.2 %) were suffering from hard masses in their cheeks that lead them to feel unnatural texture. In addition these masses appeared to be descended downward in their cheeks and making unnatural Jowls. Trail to aspirate the filler was done in three cases but with little success. Temporary filler was used to correct some of the folds near the jowls with better results. The treatment that was used for the patients in this study can summarized in table 4.

Table 4: Management for the adverse effects

Group	No. of patients	
Group I	2	Evacuation of pus under GA+ antibiotics
	1	Frequent aspiration under LA+ antibiotics
	1	antibiotics
Group II	3	Triminicilone injection
	2	Excision of lip nodule
	2	Aspiration of nasolabial nodule
	20	conservative
Group III	2	Temporary fillers injection
	2	Fat injection+ filler
	1	conservative
Group IV	3	Trial of aspiration +filler
	3	conservative

Discussion

In Asian countries, there is a steady increase in the use of the permanent fillers such aspolyacrylamide hydrogel, with increase number of the associated complications that necessitating treatment [15]. Many types of adverse reactions have been reported in literatures post injection of the permanent fillers in the face. In this study, discussion of the late adverse effects that presented to the author were done. All the cases in this series were referred to the author with different types of adverse effects. None of them were initially injected by the author. forty two cases has been reported during two years. Hossein Kavoussi and Ali Ebrahimi reported in their study 20 cases of adverse

effects of polyacrylamide hydrogel during three years from 2008 to2011 in Iran [16]. In Japan, Ono et al treated 15 cases of polyacrylamide hydrogel from 2004 to 2007 [15]. Sajad Ahmad Salatiand Bandar al Aithan reported 9 cases of permanent filler adverse effects in Riyadh in Saudi Arabia in one center from 2009 to 2011 [17]. We think that These numbers are more than the reported of complications from use of such filler in Asia in comparison to Europe and United States. This could be due to limited or restricted use in the Western countries or because of overuse in eastern countries by bad trained or unauthorized personals.

All the cases in this series were injected in their faces, while other reported many cases that had injection in their buttocks, hand, and penis with variant adverse effects [15]. This is because the patients in our society have more concern with their faces than other parts of the body. The most common site of facial adverse effects was the cheeks as in the study of Hossein Kavoussi and Ali Ebrahimi. The lip was the least area of complications in this study. While in other studies, the lip complication was in 23% in Hossein Kavoussi and Ali Ebrahimi study [16].

In this study, only 7% were injected with Boldenone Undecylenate. It has not been recorded by any other studies, because it is manufactured to veterinary use only, and Serious and permanent complications had occurred in this type of product when used in the human body.

Most of the cases (76%) had no idea about the type, duration, or the adverse effects of the injected fillers while Sajad Ahmad Salati mentioned 51% had no idea about the fillers nature [17]. This is because these cosmetic procedures are profitable and may be done by unscrupulous practitioners who are being reported globally to inject substandard and unauthorized products without detailing the patients about the nature of products.

Severe inflammatory reactions were reported in five cases, three of them gave history of tooth problem, use of thread lift sutures, or injection of hyaluronic acid filler. Jonathan Et al reported these complications after dental problem and platelet rich plasma (PRP) injection but not after HA fillers [19]. The reaction may be caused by irritation from these procedures or by infection. Christensen LH suggest the bacteria form a biofilm, which gives rise to a low-grade chronic infection that is resistant to antibiotics [7]. The culture for the drained pus was negative similar to the result of El-Shafey el aI [20]. He suggest that puncture of the polyacrylamide site may violate the tissue-implant barrier and causing inflammation or it may introduce bacteria that are not detected in the culture but may contribute to inflammation in the presence of that filler. The response to the course of antibiotics may support the bacterial cause.

In this paper there is twenty seven patients with nodules in their subcutaneous level, Kavoussi and Ebrahimi reported twenty patients with subcutaneous nodules after polyacrylamide injection and defined them as gel induration and did aspiration using 16G needle [16]. In this study, only two cases were treated with aspiration which was in the nasolabial fold causing asymmetry. These nodules are not serious and easily treated complication of PAAG probably induced by water exchange between filler and surrounding tissue with modest host immune reaction to the filler. The procedure was not accepted by many of the patients because of fear from the procedure and its results. Triminicilone injection intralesionally in the nodules was tried in three patients with good results, but it requires repeated injection. No side effects was reported. Amin et al also reported intralesional steroid with good success [8]. Resection of the nodules from the lips was done in two patients with better results as it is an easy and rapid way to manage the deformity.

Patients with severe deformity were four of the cases. The deformity developed after severe inflammation and trail to remove the filler. Trail of fat injection to correct the deformity failed as in the report of Manafiet al [14], and that is because there is no healthy tissue to host the fat. Trail of hyaluronic acid (HA) filler was successful in two patient after 8-10 times of sessions

to correct the deformity, but failed in others because of the severity of the deformity that need large volume of HA. and noncompliance of the patient because of the high cost of the HA fillers. No previous reports of injection of HA to correct the deformity found in the literatures.

Four of the patients had hardness in their cheeks, Christensen reported five cases of unreactive tissue and biopsy was taken from that tissue and reveal modest or no host reaction [7]. In this study , only two attempts of aspiration with large pore needle with little success, while in the others two, no treatment was used because the patients refused the aspiration method. Aspiration with 18 G needle may be good option only to the gel indurated masses in these type of patients. attempts to remove the hard masses may cause severe deformity in some of the cases as in figure 3.

Conclusion

Trials to treat the Unwanted long term side effects and deformities of facial permanent fillers injection is very difficult. Fat injection is not useful. Using temporary filler may help to correct some of these deformities. Intralesional steroid may be used for the nodular deformity. Avoidance of the permanent fillers is the primary consideration together with careful selection the authorized persons to inject the facial fillers. Further studies are required to elucidate the risks involved in this type of fillers. attempts to remove the hard masses surgically may cause severe deformity in severe cases, so surgical removal might not be advisable in such case.

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