Complications after treatment with hyaluronic acid fillers — review

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ABSTRACT
In the event of complications caused by hyaluronic acid filler, they are usually mild or reversible. The most important complication to recognise and to treat as soon as possible is the vascular occlusion since skin necrosis or blindness can occur.

Keywords: hyaluronic acid, fillers, facial aesthetic medicine, anti-aging, complications, hyaluronidase.

Introduction
The last couple of years facial aesthetics is part of the development in the aesthetic business. And according to reports it will keep expanding the next couple of years [1].

STRESZCZENIE
W przypadku powikłań po wypełniaczu jakim jest kwas hialuronowy są one najczęściej łagodne lub odwracalne. Najważniejszym powikłaniem wymagającym jak najszybszego rozpoznania i leczenia jest niedrożność naczyń, ponieważ może wystąpić martwica skóry lub ślepota.

Słowa kluczowe: kwas hialuronowy, wypełniacze, medycyna estetyczna twarzy, przeciwstarzeniowe, powikłania, hialuronidaza.

Wprowadzenie
W ciągu ostatnich kilku lat zabiegi estetyki twarzy wpisują się w rozwój branży estetycznej. Według doniesień branża ta będzie się rozwijała w ciągu kolejnych kilku lat [1].
Thus the more aesthetic treatments the more likely an increase in complications.

It is very important to know how to perform procedures, but is every physician prepared enough to recognise and treat complications? Because of the composition of the hyaluronic acid fillers and their compatibility with the human body each treatment can be reversed by using hyaluronidase. If complications occur they are mostly mild or reversible. However we must not forget critical complications such as blindness and skin necrosis.

But what about countries were beauticians and other professions are still injecting faces with hyaluronic acid without knowing the anatomy and lacking the right background and study?

Hyaluronic acid fillers

Hyaluronic acid fillers are used to increase loss of volume and revitalize the skin.

During the last couple of years there has been an increase in different types of products on the market. Each hyaluronic acid filler can be classified according to cross-linking, gel consistency and hyaluronic acid concentration but also the manufacturing process by the company is often different as well [2].

Procedures with hyaluronic acid fillers are considered safe and after often performed for augmentation of the cheek and chin, volumization of the midface, correction of the tear trough, reshaping of the nose and lip enhancement [3].

Complications

Complications can be devided into early complications (minutes to days after the procedure) and late complications (weeks to years after the procedure) [4–6] (Table 1).

The most important complication to recognise and to treat as soon as possible is the vascular occlusion since skin necrosis or blindness can occur. Depending on the onset of complaints we can devise signs of vascular occlusion [7] (Table 2).

Blindness

From all the areas treated with dermal fillers the glabellar complex has the highest reported rate of blindness with 35%, followed by the nose with 24% [8].
The central area of the face is connected by the ophthalmic arteries, the facial arteries, their branches and anastomoses, and with that a potential vascular occlusion in the forehead, glabellar region, nose and naso-labial fold can cause blindness [9].

**Needle vs. Cannula**

There are 2 ways of injecting a filler at the desired place, either a needle or a cannula. Whereas the needle has a high precision of product placement, the sharp tip and the multiple pokes increase the chance of bleeding and bruising. Because of the sharp tip it is also easier to penetrate a vessel and thus a higher risk of vascular occlusion.

When using the cannula only one poke is needed to insert the cannula and treat a large

| **Early complications** | **Clinical Findings** | **Timing** |
|-------------------------|-----------------------|------------|
| Direct reactions after injection / Bezpośrednie reakcje po wstrzyknięciu: | Can be present / może być obecny | Minutes to days / od kilku minut do kilku dni |
| — Pain, erythema, edema, ecchymosis, itchiness / bó, rumień, obćęp, wybroczyny, świąd | Paller / błądność | Seconds to days / od sekundy do dni |
| Infection / Infekcje: | Reddish pattern / czerwony wzór | Minutes to hours / od minuty do godzin |
| — Bacterial(cellulitis/abcess), viral (Herpes) / bakteryjne (zapalenie tkanki łącznej/repien), wirusowe (opryszczka) | Bruise-like appearance / wyglądem przypomina siniak | Minutes to hours / od minuty do godzin |
| Nodules. / Guzki: | Pimpled appearance / krościankowata | Hours to days / od godziny do dni |
| — Palpable and visible / wyczuwalny i widoczny | Skin demarcation / demarkacja skóry | Days to weeks / od dni do tygodni |
| Tyndall effect. / Efekt Tyndalla: | | |
| — Bluish hue that is visible when a filler is placed too superficial / niebieskawy odcień, który jest widoczny, gdy wypełniacz jest umieszczony zbyt powierzchnie | Neocrosis / martwica | |
| Allergic / Hypersensitivity reaction: | Necrosis, ulceration / martwica, owrzodzenie | |
| — Anaphylaxis / anafilakcja | | |
| Vascular occlusion: / Niedrożność naczyń: | | |
| — Necrosis / martwica | | |
| Blindness / ślepota | | |

**Table 1. Komplikacje po iniekcji wypełniacza skórnego**

The central area of the face is connected by the ophthalmic arteries, the facial arteries, their branches and anastomoses, and with that a potential vascular occlusion in the forehead, glabellar region, nose and naso-labial fold can cause blindness [9].

**Table 2. First signs of vascular occlusion**

| **Symptoms** | **Clinical Findings** | **Timing** |
|-------------|-----------------------|------------|
| Pain / bół | Can be present / może być obecny | Minutes to days / od kilku minut do kilku dni |
| Blanching / zbielenie skóry | Paller / błądność | Seconds to days / od sekundy do dni |
| Livedo / siność siateczkowata | Reddish pattern / czerwony wzór | Minutes to hours / od minuty do godzin |
| Blue-ish discolouration / niebieskie zabarwienie | Bruise-like appearance / wyglądem przypomina siniak | Minutes to hours / od minuty do godzin |
| Pustules / krościanki | Pimpled appearance / krościankowata | Hours to days / od godziny do dni |
| Skin demarcation / demarkacja skóry | Necrosis, ulceration / martwica, owrzodzenie | Days to weeks / od dni do tygodni |
area. Because of the rounded tip there is less bleeding and bruising but also a lower risk of vascular occlusion.

Aspiration
There is still a lot of discussion whether to aspirate or not, and there are a couple of arguments for this. First of all the needle size is important, depending on the density of the filler itself. It is possible that not enough pressure is generated because the needle is too small or the filler is too thick. If we do not aspirate blood the result can be false negative.

There are studies on how long we should aspirate before injecting, in vitro used on rabbit ears [10] or tested on saline bags containing anticoagulated blood [11].

Results of the studies show that depending on the characteristics of the hyaluronic acid filler, but also on the needle size and duration of the aspiration a positive aspiration ranges between 30 and 65%. And what about aspiration with cannula? There is not much published data on this topic, however there are reports of aspirating blood when using a cannula.

You can imagine that the thinner the cannula, the sharper the end gets eventough it is rounded and with this a higher risk of perforating or entering a vascular structure.

Hyaluronidase
Hyaluronidase is an enzyme that degrades hyaluronic acid found in hyaluronic acid fillers. This enzyme is often used for the treatment of excessive quantities or wrongly placed hyaluronic acid fillers in the face [12]. The dosage for using hyaluronidase ranges in different protocols, depending on the amount of fillers used. In cases where hyaluronidase is applied for treating inflammatory and/or painful nodules an antibiotic or even steroids are necessary [13–14].

For emergency situations such as a vascular compromise there is still no international standard protocol on the dosage of the hyaluronidase but also not whether to repeat it, and if so when and how many times. Delorenzi was the first one to talk about high dose pulsed hyaluronidase. He observed that single site ischemia, such as a lip, healed better then larger areas affected by vascular adverse events. And thus he thought maybe the amount of hyaluronida-

Podczas korzystania z kaniuli potrzebny jest tylko jeden zaczep do włożenia kaniuli i leczenia dużego obszaru. Ze względu na zaokrąglone zakończenie występuje mniej krwawień i siniaków, ale także mniejsze ryzyko niedrożności naczyń.

Aspiracja
Wciąż jest wiele dyskusji na temat tego, czy aspirować, czy nie, i jest kilka argumentów na ten temat. Przede wszystkim ważny jest rozmiar igły, w zależności od gęstości samego wypełniacza. Możliwe, że nie wytworzy się wystarczający nacisk, ponieważ igła jest za mała lub wypełniacz jest za gruby. Jeśli nie będzie się aspirować krwi, wynik może być fałszywie ujemny.

Istnieją badania dotyczące tego, jak długo powinniśmy aspirować przed wstrzyknieniem, stosowane in vitro na uszach królika [10] lub testowane na workach z solą fizjologiczną zawierając antycogulacyjną krew przeciwzakrzepową [11]. Wyniki badań pokazują, że w zależności od właściwości wypełniacza kwasu hialuronowego, ale także od wielkości igły i czasu trwania aspiracji, dodatnia aspiracja wynosi od 30 do 65%. A co z aspiracjami przez kaniulę? Nie ma zbyt wielu danych na ten temat, jednak istnieją doniesienia o zasypaniu krwi podczas używania kaniuli.

Można sobie wyobrazić, że im cieńsza kaniula, tym ostrzejsze jest zakończenie, mimo że jest zaokrąglone, a przez to możliwe jest większe ryzyko perforacji lub dostania się do struktury naczyniowej.
se used was to little in the larger areas, thereby adjusting his protocol. Practitioners are still doing additional treatment such as vasodilators and hyperbaric oxygen therapy, whereas he states that if you use hyaluronic acid in high quantities within every hour, it has even better outcomes in monotherapy. The injected hyaluronic acid needs time to start degrading the hyaluronic acid filler, time depending on the crosslinking of the filler. The hyaluronic acid eventually diffuses through the arterial wall at some concentration rate. Low concentrations are far less effective since a couple of mechanisms are activated:

1. The hyaluronidase will be deactivated at some rate since the own body hyaluronidase will not be metabolised actively at this point.
2. Because of swelling fluid from leaky capillaries in the ischemic environment, there will be dilution of the hyaluronidase.
3. Finally when the ground substance degrades it will begin to diffuse away from the original injection site [15].

Discussion

First of all, it is important to inform your patients when to come back and what alarming symptoms are after treatment. There should not be a threshold for patients to call their physician when in doubt. When talking about preventing and managing complications, the most important is anatomical knowledge, keeping in mind that there are anatomical variations and there are no 100% safe zones to inject. Always be cautious and evaluate injected areas. One way of evaluating a treated area is to assess the capillary refill.

There is unpublished data from injectors on aspiration. We know that aspiration does not give a 100% guarantee for a safe injection, however, when using an unprimed needle the success of aspirating blood is much higher, at least tested in saline bags filled with blood. This will remain an interesting topic until more studies can educate us.

When facing a vascular complication it is important to be prepared. Always have enough hyaluronidase to use a high dose pulsed protocol since this is becoming the standard in most practices. However you could imagine that other ways of treating a vascular complication are still used so that the patient gets the most optimal treatment there is.

Discussion

Przede wszystkim ważne jest, aby poinformować pacjentów, kiedy powinien wrócić do gabinetu i jakie niepokojące objawy mogą wystąpić po leczeniu. W przypadku wątpliwości pacjenci powinni mieć możliwość telefonicznego skontaktowania się z lekarzem. Mówiąc o zapobieganiu i zarządzaniu powikłaniami, najważniejsza jest wiedza anatomiczna. Należy pamiętać, że istnieją różnice anatomiczne i nie ma 100% bezpiecznych stref do wstrzyknięcia. Zawsze należy być ostrzegawczo i należy ocenić miejsce wstrzyknięcia. Jednym ze sposobów oceny leczonego obszaru jest ocena składu włośniczko-wego. Istnieją niepublikowane dane dotyczące aspiracji. Wiadomo, że aspiracja nie daje 100% gwarancji bezpiecznej injekcji, jednak przy użyciu niepirogennej igły skuteczność aspiracji krwi jest znacznie wyższa, co najmniej testowana w wor-
If you are not sure whether a complication has occurred, either make sure the patients gets a strict follow up, or start dissolving the filler in the treated area.

Conclusions

Hyaluronidase can be used for small corrections after treatment with hyaluronic acid fillers and to treat larger complications such as vascular occlusion. Fortunately most of the complications associated with hyaluronic acid fillers are mild and even self-limiting.

There are many strategies to reduce the risk of complications associated with hyaluronic acid fillers.

First of all anatomy is key. Secondly good knowledge of side effects and differentiation between early and late onset complications is important.

It is advisable to aspirate, and if so at least for 10 seconds. Always have an emergency set for complications, including hyaluronidase in large quantities whereas for now it is the best treatment for vascular adverse events.

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References / Piśmiennictwo
1. Aesthetic medicine market research report jun 2019.
2. Beasley KL et al. Hyaluronic acid fillers: A comprehensive review. Facial plast Surg. 2009;25(2):086–094.

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3. Funt D et al. Dermal fillers in aesthetics: an overview of adverse events and treatment approaches. Clin Cosmet Investig Dermatol. 2013;6(1):295–316.
4. Abduljabbar MH et al. Complications of hyaluronic acid fillers and their managements. Journal of Dermatology & Dermatologic Surgery. 2016;7:100–106.
5. Lafaille P et al. Fillers: Contraindications, side effects and precautions. J Cutan Aesthet Surg. 2010;3(1):16–19.
6. King M. Management of Tyndal Effect. J Clin Aesthet Dermatol. 2016;9(11):6–8.
7. Dr Treacy’s casebook-Aesthetic medicine:2014;10:52–54.
8. Chatrath et al. Soft-tissue filler-associated blindness: A systematic review of case reports and case series. Plastic and Reconstructive Surgery – Globan Open, 2019;7(4):2173.
9. Wu Sufan et al. Anatomic study of ophthalmic artery embolism following cosmetic injection. Journal of Craniofacial Surgery. 2017;28(6):1578–1581.
10. Casabona G. Blood aspiration test for cosmetic fillers to prevent accidental Intravascular injection in the face. Dermatol Surg. 2015;41(7):841–847.
11. Van Loghem JA et al. Sensitivity of aspiration as a safety test before injection of soft tissue fillers. J. Cosmet. Dermatol. 2018;17(1):39–46.
12. Cavallini M et al. The role of hyaluronidase in the treatment of complications from hyaluronic acid dermal fillers. Aesthetic Surgery Journal. 2013;3(8):1167–1174.
13. Menon H, Thomas M, D’silva J. Low dose of hyaluronidase to treat over correction of HA filler—a case report. J Plast Reconstr Aesthetic Surg. 2010;63:416–417.
14. Narins RS, Coleman WP, Glogau RG. Recommendations and treatment options for nodules and other filler complications. Dermatol Surg. 2009;35:1667-1671.
15. Delorenzi C. New High Dose Pulsed Hyaluronidase Protocol for Hyaluronic Acid Filler Vascular Adverse Events. Aesthet Surg J. 2017;37(7):814–825.

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