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ORIGINAL CONTRIBUTION

Comparison of hyaluronic acid filler ejection pressure with injection force for safe filler injection

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Abstract

Background: Owing to the increase in the number of medical procedures performed every year, the frequency of filler injection-related complications has also increased. Although slow, gentle injections with low pressure are usually considered to be safe, the differences in ejection pressure during a filler injection remain to be determined. This study aimed to identify the optimal pressure during filler injections and evaluate its capacity to overcome the arterial blood pressure and reflux the filler material.

Methods: Twelve combinations of four hyaluronic acid (HA) fillers with different rheological properties and three needles of different diameters were assessed to determine the force exerted by the injection model. The ejection forces corresponding to varying injection forces were measured and HA filler ejection pressures were calculated.

Results: The highest and lowest injection forces were achieved using 30- and 25-G needles, respectively. In accordance with the expected ejection force, high ejection pressure was achieved by administering the HA filler under a high injection force. Irrespective of the injection force, the ejection pressure was likely to be higher than the vascular pressure at the time of entry into the vessel, rendering the injection dangerous.

Conclusion: During filler injection, penetration of blood vessels and intravascular injection can be avoided by approaching the target area gently using a cannula or needle.

KEYWORDS
ejection force, ejection pressure, hyaluronic acid filler, injection force

1 | INTRODUCTION

The administration of hyaluronic acid (HA) filler injections is one of the most common aesthetic procedures in modern medicine.[1] As such procedures become more common, the frequency of filler injection-related complications, such as visual compromise caused by intravascular occlusion, inevitably rises.[2-4] As filler injections are administered blindly, it is difficult to identify the exact moment at which a vascular complication arises.

The pathophysiology of vision loss associated with HA filler injection-related complications is presumed to be caused by the reflux of filler particles from the ophthalmic artery.[5] However, the influence of auxiliary conditions, such as the pressure required to overcome arterial pressure and amount of filler required to block the blood vessels, has not been established. Anatomical and rheological studies of filler materials have been conducted with the primary aim of preventing such complications.[6] However, adequate guidelines to

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guarantee safety during the administration of filler injections have yet to be established as most existing guidelines are based on expert consensus and not on evidence-based studies.[7,8]

Although previous studies have recommended the use of small-diameter needles to avoid intravascular injection, this approach remains controversial.[7,9,10] It is well accepted that a slow, gentle injection produces lower ejection pressure than a relatively faster injection. High injection forces are expected to be dangerous because they correspond to high ejection pressures and elevated risks of intravascular regurgitation. However, despite the general preference for a slow, gentle injection with low pressure, the pressure difference generated during such injections has not been measured. Further, no study has been conducted on the pressure generated during the injection of HA filler material from a syringe.[9,11] This study aims to determine the pressure exerted during the administration of filler injections and evaluate the sufficiency of the ejection pressure to overcome the arterial pressure and induce backflow.

2 | MATERIALS AND METHODS

2.1 | Materials

This study was conducted at the Daegu Research Center for Medical Devices and Rehabilitation Engineering, Korea Institute of Machinery & Materials (KIMM). Four HA fillers (e.p.t.q. S50, S100, S300, and S500; Jetema Co., Ltd.) with different rheological properties were used in this study (Table 1). Each filler was tested using 25-, 27-, and 30-G needles (Tae-Chang Co.), which are commonly used for filler injections. The inner diameters of the 25-, 27-, and 30-G needles were 0.26, 0.21, and 0.16 mm, respectively. The 1-ml syringe included within the package of the original filler product was used for all combinations.

2.2 | Methods

Injectability can be interpreted in terms of two types of forces: injection force, which is the initial force generated by the piston of the syringe when it is pushed, and ejection force, which is the force produced during the injection process. The former determines the smoothness of the injection process, while the latter can be used to calculate the ejection pressure (Figure 1).

2.3 | Injection force testing

A MultiTest 2.5-*d* device (Mecmesin Limited) was used to measure the forces produced by the injection model. To assess the physical and mechanical aspects of the relevant powers and forces, 12 combinations of HA fillers and needles were selected. The machine was programmed to push and displace the syringe plunger at a constant speed. The injection force was determined by analyzing the results corresponding to the speed (12 mm/min). Plunger displacement and injection force measurements were recorded at intervals of 0.1 s using a data acquisition system. Representative profiles are depicted in Figure 2. Data analysis of the injection force profiles was conducted by calculating the average value of the injection force plateau. The injection force was measured three times.

2.4 | Ejection force testing

An external air compressor (BBT-001 Beetle Bug Air Compressor; Yamato Comp) was designed to apply the designated forces to the piston of the syringe (Figure 3). Injection forces of 9.56, 15, 20, 30, and 40 N were applied. The HA filler, S100, was administered using a 25-G needle.

The experimental setup was designed to mimic the necessary subdermal ejection pressure exerted by the filler flow generated by the manual injection force. Ejection force is defined as the force used to push the syringe to inject the filler, and it was measured by connecting one syringe to another syringe prefilled with approximately 0.2 ml of filler on the opposite side. As the filler was displaced out of the syringe under a constant injection force exerted by the air compressor, the plunger of the opposite syringe was displaced correspondingly. This displacement stopped when the tip of the plunger touched the digital force detector (Imada Co), which recorded the ejection force exerted on the plunger tip of the second syringe. The force exerted on the plunger tip during the ejection of the filler from the opposite syringe was considered as the ejection force.

The injection of HA filler using an air compressor creates a constant and reproducible force and flow resistance, which allows for the measurement of differences between injection forces. The ejection force was measured three times and used to calculate the ejection pressure, which was defined as the force applied per unit area at the needle tip.

TABLE 1 Rheological data of the fillers

	Concentration (mg/mL)	Storage modulus (Pa)	Loss modulus (Pa)	Tan delta	Complex viscosity (Pa·s)	Frequency (Hz)
S50	24	29.31	16.17	0.55	53.24	0.1
S100	24	50.80	21.06	0.41	87.52	0.1
S300	24	130.52	37.32	0.28	216.05	0.1
S500	24	264.50	52.87	0.19	429.31	0.1

FIGURE 1 Schematic depicting the injection and ejection forces and ejection pressure

2.5 | Statistical analysis

All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc). Differences between the injection forces achieved using needles of varying dimensions and the corresponding ejection pressures were compared using a Mann-Whitney test. *p*-values < 0.05 were considered statistically significant.

3 | RESULTS

3.1 | Injection force

The injection forces achieved using the tested fillers are summarized in Table 2. The 25-, 27-, and 30-G needles exhibited significant differences in the injection force produced ($p < 0.001$). The 30- and 25-G needles achieved the highest and lowest injection forces, respectively. No significant differences were observed in filler characteristics with respect to needles of same diameter. Furthermore, increasing the viscosity of the filler did not significantly increase the injection force.

3.2 | Ejection pressure

The values of the injection and ejection forces and internal and ejection pressures within S1, and the internal cross-sectional areas of S1 and S2 are summarized in Table 3. Application of a 40 N injection force yielded the highest ejection force (28.03 ± 0.15 N). The lowest mean ejection force (2.24 ± 0.06 N) corresponded with the combination of the S100 HA filler with a 15 N injection force. An injection force of 9.56 N was used to inject the S100 HA filler, but the corresponding ejection force could not be measured. Ejection forces of 6.80 ± 1.91 and 9.42 ± 0.08 N were achieved using injection forces of 20 and 30 N, respectively. Overall, the ejection force was significantly dependent on the applied injection force.

The lowest mean ejection pressure of 572.67 ± 11.68 mm Hg was achieved using a low injection force of 15 N, and even the lowest ejection pressure was higher than the arterial pressure. Mean ejection pressures of 1601.67 ± 443.71, 2202.00 ± 12.29, and 6549.67 ± 24.79 mm Hg corresponded to the 20, 30, and 40 N injection forces, respectively.

4 | DISCUSSION

The findings of this study showed that the ejection pressure exerted by a filler injection was higher than the arterial pressure, irrespective of the injection force applied. However, both the ejection force and pressure significantly depended on the injection force.

Ejection pressure is directly related to the ejection force and corresponds with the injection force. In clinical practice, the injection force is usually estimated by measuring the force exerted on the syringe plunger. However, physicians are incapable of controlling the injection force precisely and prone to injecting fillers using forces slightly higher than the injection force needed to displace the syringe plunger.

According to the Hagen-Poiseuille law, under a constant flow rate and fluid viscosity, the loss of pressure through the needle is inversely proportional to the square of the radius (inner diameter) of the needle and directly proportional to the length of the needle. During ejection

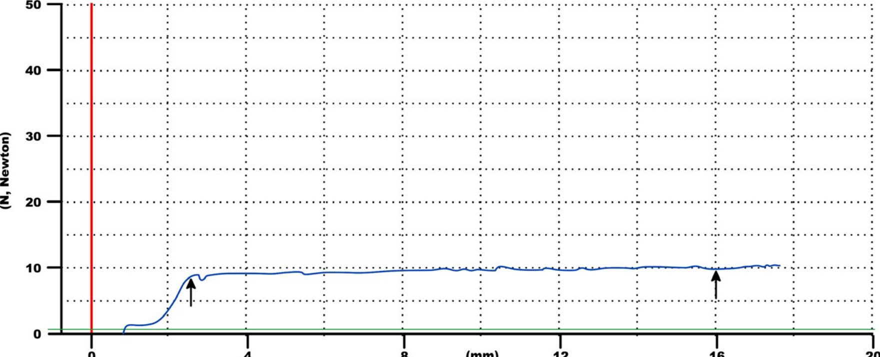

FIGURE 2 e.p.t.q. S100 lidocaine exhibited an injection force of 9.56 N corresponding to the 25-G needle. The arrows in the figure indicate the range used during the data analysis in order to determine this average value

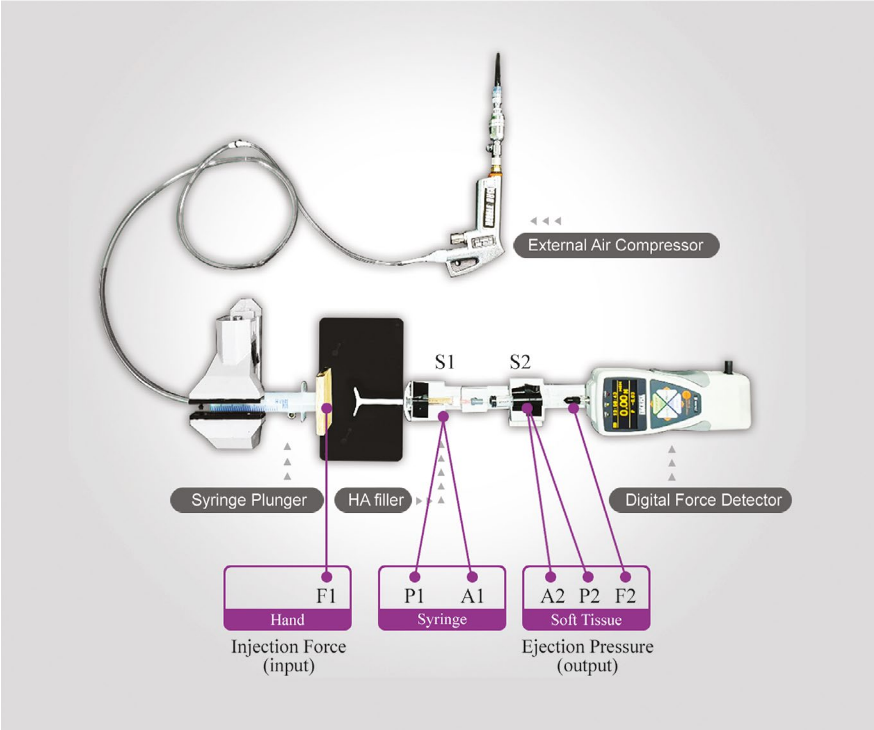

FIGURE 3 Instrumental setup for the ejection force experiments. S1 denotes the filler-filled syringe, S2 denotes an additional syringe connected to S1, and A1 denotes the internal cross-sectional area of S1. The diameter of S1 is approximately 6.3 mm, and the internal cross-sectional area of S1 is 3.12 mm^2. A2 denotes the internal cross-sectional area of S2, which is 3.22 mm^3. F1 denotes the injection force (controlled by adjusting the air compressor using a digital force detector before initiating each experiment), F2 denotes the ejection force (measured after the filler enters S2, causing the plunger of S2 to come into contact with the force detector sensor), P1 denotes the internal pressure within S1 (calculated by dividing F1 by A1), and P2 denotes the ejection pressure (calculated by dividing F2 by A2)

TABLE 2 Injection force (N) comparison of the different needle diameters

	25G	27G	30G	*p*-values
s50	8.71 ± 0.01	13.96 ± 0.14	25.41 ± 0.09	<0.001
s100	9.56 ± 0.06	13.69 ± 0.07	26.84 ± 0.16	<0.001
s300	9.5 ± 0.04	12.8 ± 0.15	24.29 ± 0.01	<0.001
s500	8.29 ± 0.21	11.14 ± 0.06	33.20 ± 1.95	<0.001

Note: Values are presented mean ±standard deviation.

pressure measurements, only one type of filler and needle (25-G) were used to minimize its variability with respect to the internal diameter, length, and surface characteristics of the needle. As the 25-G needle is relatively large for a filler procedure, we intended to measure the ejection pressure that corresponded to a relatively low injection force. The effect of filler viscosity on injection force was controlled by measuring the ejection pressure using only one type of filler. Furthermore, different pressure conditions that could be exerted on the syringe were simulated to verify the effect of the injection force and determine the corresponding ejection pressure. The ejection pressure was confirmed to be higher than expected in all filler injection procedures performed in this study, irrespective of the initial injection force. Under all tested scenarios, it exceeded normal blood pressure by at least 50%. Additionally, the ejection pressure corresponding to a 15 N injection force was calculated to be at least five times higher than normal blood pressure (<120/80 mm Hg). Thus, the results of this study indicate that even a carefully administered injection with a low injection force can significantly increase blood pressure. As the ejection pressure is not proportional to the injection force and higher than the blood pressure at the time of ejection, the injection force should be as low as possible during filler injection. Table 3 shows the variations in ejection force with respect to the initial injection force of differing pairs of fillers and needles. However, since we only tested particular fillers and needles, this relationship cannot be generalized to other filler-needle combinations. Therefore, a follow-up experiment should be conducted to measure the relationships between the injection and ejection forces corresponding with combinations of three other types of fillers and needles.

When the injection force was experimentally set to 9.56 N, the pressure exerted by the first cylinder did not exceed the static frictional force of the plunger of the second cylinder. Thus, the ejection force could not be measured in this case ("undetectable" in Table 3). The placement of the pressure sensor could have been improved by placing it within the cylinder, enabling direct measurement at the plunger level. However, as this was expected to drastically increase the number of experimental errors and uncertainties, a more stable experimental design was proposed instead.

No significant differences in injection forces were observed when fillers with different properties were injected using needles of identical dimensions (Table 2). Because of the nature of deep dermal or subcutaneous fillers, the injection force was high in certain cases. Therefore, to maintain a high elastic modulus, high viscosity should be maintained, which necessitates a high injection force. However, by controlling the injection force, the HA fillers tested in this experiment exhibited a constant elastic modulus. The viscosity of the filler did not induce any variations in injection force with respect to the needle dimensions due to the manufacturer's control of the filler properties of this series.

However, as the cross-sectional areas of arterioles are larger than that of the needles used, the post-injection blood pressure is expected to be lower than the calculated result. A previous study

TABLE 3 Ejection force of the S100 lidocaine using a 25-G needle

No.	F1 (N)	A1 (mm^2)	P1 (MPa)	F2 (N)	A2 (mm^2)	P2 (Pa)	P2 (mm Hg)
1	9.56	3.12	UD	UD	3.22	UD	UD
	15	3.12	0.481438.15	2.4	3.22	74641.72	559.86
	20	3.12	641917.54	5	3.22	155503.58	1166.37
	30	3.12	962876.30	9.5	3.22	295456.81	2216.11
	40	3.12	1283835.07	28	3.22	870820.06	6531.69
2	9.56	3.12	UD	UD	3.22	UD	UD
	15	3.12	481438.15	2.5	3.22	77751.79	583.19
	20	3.12	641917.54	8.8	3.22	273686.31	2052.82
	30	3.12	962876.30	9.4	3.22	292346.74	2192.78
	40	3.12	1283835.07	27.9	3.22	867709.99	6508.36
3	9.56	3.12	UD	UD	3.22	UD	UD
	15	3.12	481438.15	2.5	3.22	77751.79	583.19
	20	3.12	641917.54	6.6	3.22	205264.73	1539.61
	30	3.12	962876.30	9.35	3.22	290791.70	2181.12
	40	3.12	1283835.07	28.2	3.22	877040.21	6578.34

Abbreviations: A1, internal cross-sectional area of the filler-filled syringe; A2, internal cross-sectional area of another syringe connected to the filler-filled syringe; F1, injection force; F2, ejection force; P1, internal pressure in the filler-filled syringe; P2, ejection pressure; UD, undetectable.

described the average volume of the supratrochlear artery to be 0.085 ml.[12] Additionally, due to the elasticity of the vessel walls, the force is dissipated across all contact surfaces within the vessel after filler injection. Further, the cross-sectional area can be altered at the moment at which the needle tip penetrates the blood vessel. In such a case, the pressure of the ejected filler will be lower than the pressure within the needle. It is also necessary to analyze the effect of ejection pressure on the vessels themselves, especially with respect to the hydrostatic pressure within them. Thus, confirmation that the ejection pressure within the blood vessel exceeds the normal blood pressure requires more accurate experimental design. However, the experiments presented in this study indirectly confirmed that the pressure at the time of ejection was significantly higher than normal blood pressure irrespective of the initial injection force.

Thus, injection of soft tissue fillers near ophthalmic artery branches, such as the dorsal nasal, supratrochlear, and supraorbital arteries, should be administered carefully to prevent vascular compromise and intravascular injection.

5 | CONCLUSION

The results of this study demonstrate that high ejection pressures can be achieved during filler injections using low injection forces. The lowest computed pressure at the time of injection (15 N) was observed to be at least five times higher than the systolic blood pressure. Thus, adequate awareness should be promoted among physicians regarding the potential dangers posed by intravascular filler injections irrespective of the initial injection force. To the best of our knowledge, this is the first study that has gathered quantitative data on ejection pressure during the administration of filler injections.

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CONFLICT OF INTEREST

Won Lee was previously employed as an investigator, speaker, and consultant for Jetema Co., Ltd (Seoul, South Korea). The hyaluronic acid fillers from the e.p.t.q. series were sponsored by Jetema Co. None of the other authors have any conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

Yongkoo Lee and Seung Min Oh involved in substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data. Won Lee and Eun-Jung Yang involved in drafting the manuscript or revising it critically for important intellectual content. Each author participated sufficiently in the work to take public responsibility for appropriate portions of the content; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ETHICAL STATEMENT

This manuscript contains experimentation and does not contain research on human or animals. Review by Ethics Committee is not applicable for this study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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