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In-Vitro Evaluation of Pre-Injection Aspiration as Safety Checkpoint for Hyaluronic Fillers

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Background/Objectives: In 2017, about 2.1 million procedures using hyaluronic acid (HA) fillers were performed in the United States. While complications are rare, knowledge regarding their prevention and management are crucial. Intra-arterial injection can cause visual impairment and local skin damage, including necrosis. The use of pre-injection aspiration has become controversial regarding its usefulness as some clinicians believe aspiration of blood is not possible. However, no study on pre-injection aspiration has thoroughly examined physiochemical and rheological properties, which can help predict behavior of HA fillers. Our study investigated the utility of pre-injection aspiration as a safety checkpoint for HA fillers.

Methods: An in-vitro model consisted of fresh whole blood collected in EDTA-coated vacutainers that were pressure equalized. Syringes containing HA filler were inserted, and plungers were each pulled back at 0.2cc and 0.5cc volumes to mimic pre-injection aspiration. The plunger was held at this distance until flashback was visualized or until 30 seconds had passed. Syringes of 10 commonly used HA fillers were evaluated: Allergan (Pringy, France) Juvederm Ultra Plus XC, Juvederm Ultra XC, Juvederm Volbella, Juvederm Vollure, and Juvederm

Voluma; Galderma (Uppsala, Sweden) Restylane Defyne, Restylane Lyft, Restylane Refyne, and Restylane Silk; and Merz (Raleigh, N.C.) Belotero Balance. Product original syringes and their package provided needles were utilized. Values for physiochemical and rheological properties at 0.1 Hz were gathered.

Results: For the 10 HA fillers, the values for HA concentration, G' , G'' , and G^* varied. Using a multivariable regression model ($R^2=.8324$; $F=12.42$; $p<.0001$), HA concentration ($p=.0016$) and G^* ($p=.0017$) were shown to positively affect time to flash, while G' ($p=.0017$) and G'' ($p=.0029$) were shown to negatively affect time to flash. Needle gauge ($p=.1641$) and pullback distance ($p=.3263$) did not show any significant effect in this model. However, when comparing pullback distance using a paired analysis for each HA filler, 0.5cc pullback distance had a significantly decreased mean time to flash than 0.2cc (8.86 vs 10.86; $p=.0389$). All HA fillers, except for Restylane Defyne, showed a decreased time to flash with 0.5cc vs 0.2cc pullback distance. A significantly greater decrease in time to flash between 0.5cc and 0.2cc pullback distance was associated with HA concentration $>21\text{mg/ml}$ (4.5 vs 0.57; $p=.0166$), $G' <153\text{Pa}$ (4.4 vs 0; $p=.0024$), and

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$G^* < 155\text{Pa}$ (4.4 vs 0; $p=.0024$), while G'' showed no significant difference.

Conclusion: Pre-injection aspiration may have utility as a safety checkpoint for HA fillers. Practitioners may have to adjust pullback distance of the plunger and waiting time to visualize the flashback based on physiochemical and rheological properties.