Assessing and Monitoring for Intravascular Injections

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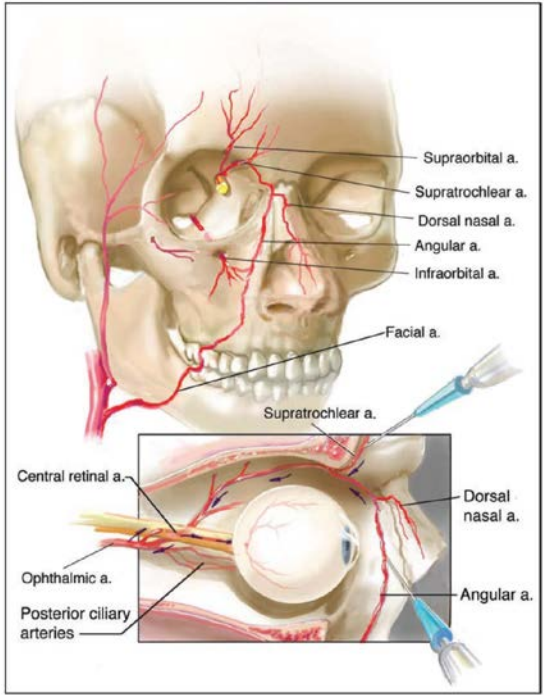
Intravascular Injection

- Dermal filler injections have been associated with serious adverse events
  - Skin necrosis
  - Ophthalmic complications, including blindness
  - Stroke
- Proposed mechanism
  - Vascular occlusion
    - Intravascular injection vs. external compression

Ophthalmic Adverse Events

- Intra-arterial injection
  → retrograde flow
  → ophthalmic artery
  → vision loss and other ophthalmic adverse events
- Numerous pathways to the ophthalmic artery



Beleznay K, Carruthers JDA, Humphrey S, Carruthers A, Jones D. Update on Avoiding and Treating Blindness From Fillers: A Recent Review of the World Literature. Aesthet Surg J. 2019;39(6):662-674

Incidence

- Incidence of serious adverse events such as blindness is unknown
- 48 published cases of partial or complete vision loss after filler from Jan 2015 – Sept 2018 (Beleznay et al, 2019)
- 92 vision-related Medical Device Reports (MDRs) from Aug 1, 2015 – Aug 1, 2020
- Estimated >2.7M soft tissue filler injections in 2019, with 79.4% hyaluronic acid filler injections*

*2019 American Society of Plastic Surgeons Annual Statistics Report

Clinical Signs/Symptoms

- Skin necrosis
  - Blanching
  - Violaceous mottling
  - Delayed pain
  - Ulceration
  - Scabbing
  - Scar
- Ophthalmic
  - Pain
  - Ptosis
  - Ophthalmoplegia
  - Partial vision loss
  - Blindness
- Stroke
  - Neurologic deficits

Premarket Vision Assessments

- In clinical studies, thorough assessment and monitoring for adverse events is essential for patient safety
- To date, common assessments have included:
  - Snellen visual acuity
  - Confrontational visual fields
  - Extraocular motility
- Performed before treatment, 30 minutes after treatment, and at follow-up visits
- Referral to retina specialist in the event of vision loss or other signs/symptoms of ophthalmic complications

Additional Safety Measures

- Increasing reports in literature and MDRs regarding certain anatomic locations, such as the nose and glabella
- Additional safety measures, such as dilated fundoscopic examinations, retinal photography, delayed contralateral treatment, and image-guided injections, may be needed to mitigate and/or characterize risk associated with intravascular injection
- Neurologic assessments
  - 18.8% of cases with blindness found to have central nervous system complications (Beleznay et al, 2019)

Risk Mitigation in Clinical Practice

- Increasing number of new dermal fillers, including new formulations, indications, and anatomic locations
- Increasing reports of adverse events
- Given the serious nature of adverse events associated with intravascular injection, FDA is interested in discussing the utility of implementation of approaches, through device labeling, for early detection of vascular occlusion in clinical practice

Panel Questions

The panel will be asked today to make recommendations for assessing and monitoring for intravascular injection in premarket clinical studies and in clinical practice.

This includes discussion of the impact of the indication for use and/or anatomic location for injection on the recommended assessments.

Premarket vs. Postmarket Risk Mitigation

- Premarket clinical studies typically utilize highly qualified physicians, such as plastic surgeons or dermatologists, with extensive experience with dermal filler injection
- Since initiation of vision assessments, vision loss secondary to intravascular injection has not been reported in studies supporting an approved PMA

Premarket vs. Postmarket Risk Mitigation

- In postmarket clinical use, the injector may not have adequate training to safely inject the device for a particular indication
- Well-trained and experienced providers may mitigate risk of complications
- Insufficient evidence quantifying the effectiveness of training or the types of training that may mitigate risk of adverse events

Postmarket Studies

- Premarket studies typically enroll 100-300 subjects
- Risk of less common adverse events such as intravascular injection may not be adequately characterized
- Postmarket studies may help to better characterize risks

Panel Questions

The panel will be asked today to make recommendations for additional safety measures to mitigate and/or characterize the risk associated with unintentional intravascular injection.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