A systematic review of permanent and semipermanent dermal fillers for HIV-associated facial lipoatrophy

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CRD summary
This review concluded that permanent and semi-permanent dermal fillers decreased the visible effects of human immunodeficiency virus-associated facial lipoatrophy, with high patient satisfaction, and that safety appeared to be favourable in the short-term. These conclusions appear to be over optimistic, given the limited and sometimes conflicting evidence presented, and should therefore be interpreted with caution.

Authors' objectives
To assess the safety and efficacy of injectable semi-permanent and permanent dermal fillers, compared with other injectable facial augmentation techniques, for the management of facial lipoatrophy as a result of highly active antiretroviral therapy for human immunodeficiency virus (HIV) infection.

Searching
PubMed, EMBASE, CINAHL, Current Contents, the Cochrane Library, ClinicalTrials.gov, NRR, metaRegister of Controlled Trials, and ANZCTR were searched, without language restriction, from inception to July 2008; search terms were reported.

Study selection
Studies of patients receiving facial injectable semi-permanent or permanent dermal fillers to reduce the visibility of fat loss from antiretroviral-associated facial lipoatrophy were eligible for inclusion. Trials, comparative studies, and case series (with pre-test and post-test outcomes), with a sample size of 40 participants or more, were eligible. Studies of patients, who had received facial filling within three months of the start of the study, were excluded. The treatments in included studies varied, but polylactic acid or polyacrylamide gel was commonly used; the number of injections given ranged from one to seven. Autologous fat transfer was a comparator treatment in three studies.

Two reviewers independently selected studies for inclusion, with disagreements resolved through consensus.

Assessment of study quality
The authors stated that studies were assessed on criteria such as the methods of randomisation and allocation concealment (for RCTs), blinding, sample size, and the ability of the study to measure the true effect. The authors did not state how many reviewers performed this quality assessment.

Data extraction
Data were extracted by one reviewer and checked by another.

Methods of synthesis
A narrative synthesis was presented, grouped by outcome.

Results of the review
Eleven studies were included: one randomised controlled trial (RCT; n=100 patients), one pseudo-RCT (n=59), two non-randomised comparative studies (n=448), and seven case series (n=520). Two studies reported a power calculation and one of these was the RCT; no other study quality results were reported. One case series only included successfully treated patients. In most studies, the duration of follow-up was one year or less.

The RCT, which compared semi-permanent filler treatment with no treatment, reported significant increases in tissue depth for two facial areas after treatment, but no significant increases in tissue volume. The pseudo-RCT and a non-randomised study found that all treatments improved skin thickness, but there were no significant differences between treatments. Six case series indicated significant increases in skin thickness following treatment.
Improvements in quality of life were reported in many studies, but often only for some of the dimensions. The RCT reported significant improvements in lipoatrophy scores in more treated compared with untreated patients. One comparative study reported no difference in appearance between three filler products. Another comparative study reported improvements in a lipoatrophy score with each of three fillers. Two case series reported improvements in most or all of the patients.

Treatment led to reductions in skin thickness, ratings of lipoatrophy, or patient satisfaction during follow up in four studies. Fillers generally appeared to cause no serious short-term adverse events, but lumps were reported as occurring in seven studies and in three of the studies 40% of patients or more developed lumps.

**Authors’ conclusions**
Permanent and semi-permanent dermal fillers achieved their objective, which was to decrease the visible effects of HIV-associated facial lipoatrophy, with high patient satisfaction. Safety appeared to be favourable in the short-term.

**CRD commentary**
This review addressed a clear question, supported by appropriate inclusion criteria. Attempts were made to identify all relevant studies by searching databases and registries for studies in any language. Suitable methods were used to reduce the risks of reviewer error and bias for the processes of data extraction and study selection, but the authors did not report whether such methods were used to assess study quality. No characteristics of the populations studied were provided, so it is not possible to assess the generalisability of the results. The results were not tabulated for all the studies with relevant outcomes (e.g. patient satisfaction). Detailed quality assessment results were not reported (levels of evidence were stated), making it difficult to assess the reliability of the studies. A narrative synthesis appears to have been appropriate in light of the heterogeneity of treatments.

The authors’ conclusions appear to be over optimistic, given the limited and sometimes conflicting evidence presented, and should therefore be interpreted with caution.

**Implications of the review for practice and research**

*Practice:* The authors did not state any implications for practice.

*Research:* The authors recommended research into long-term safety and efficacy, facial changes, gender differences, short- and long-term quality of life, and the development of training standards for injection techniques. They also commented on the need for improved study design and reporting of methods.

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