

Statements on the Safety of Permanent Soft Tissue Fillers in Europe

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Abstract Increasing reported complications associated with permanent soft tissue fillers have led the national medical societies and governmental institutes in Europe to send out warnings regarding their use. Regulation and legislation for the introduction of new products and the use of existing products are necessary to guarantee patient safety.

Keywords Complications · Permanent soft tissue fillers · Safety

In 2006, the Dutch Authority on Safety Issues in Healthcare (IGZ) sent out a warning regarding the use of permanent soft tissue fillers. This warning was sent at the advice of the Governmental Institute on Health and Environment (RIVM), which has produced an elaborate report on the safety of permanent soft tissue fillers [1]. In this report, the use of Artecoll, Liquid Silicone, Bio-Alcamid, Aquamid, Dermalive, and New Fill/Sculptra in the Netherlands is thoroughly evaluated and criticized.

Additionally, at about the same time, the International Committee for Quality Assurance, Medical Technologies

and Devices in Plastic Surgery (IQUAM) sent out a similar warning [2]. The IQUAM, an international professional medical and scientific organization committed to the surveillance of existing and new medical technologies, devices, and procedures in plastic surgery, is dedicated to their safe use and to the guarantee of patients' safety.

Both of the aforementioned reports are the result of a growing knowledge on the adverse effects of permanent soft tissue fillers. This report aims to share the knowledge of these two reports with the international aesthetic surgery community reading *Aesthetic Plastic Surgery*.

Published Reports

The governmental and legal regulation of soft tissue fillers varies widely from country to country. Approval often is gained after a short-term evaluation period in a limited clinical setting (only a few months).

The RIVM Report

The Dutch RIVM report clearly stated that the current published clinical data on permanent soft tissue fillers are insufficient for drawing conclusions concerning their safety in the long term. To date, described complications with these fillers are almost all related to case studies, retrospective data, or both, from which it is not possible to establish whether the cause of these complications are product related or a consequence of inexperienced treatment. Therefore, it is recommended that each product and its treatment technique be evaluated in prospective clinical studies assessing both the short- and long-term results.

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It is quite obvious that the risk of complications never can be ruled out, not even when the product is administered skillfully by an experienced physician. The risk of complications however increases if the physician has insufficient knowledge of the product and the way to use it properly (e.g. the injection technique and preparation of the product) or has insufficient knowledge of the specific indication for the use of the product [3–6].

The RIVM therefore recommends that permanent fillers may be used only by properly trained physicians with a relevant medical specialization, such as plastic surgeons and dermatologists who have demonstrable knowledge and experience of the product and its applications.

The IQAM Report

The IQAM report stresses that all permanent soft tissue fillers are associated with risks of infection and granuloma formation, which may lead to major disfiguration. The risks depend on the nature of the soft tissue filler, its volume used, the depth of injection, the site of injection and many other factors. Appropriate guidelines often are lacking, and as the clinical use of permanent soft tissue fillers expands rapidly, there is considerable overlap in application. More choices demand greater clinical judgment and continuing clinical trials to highlight the differences, the safety, the efficacy, and the evolution of the use of these materials. Substantial biochemical and biophysical differences exist between commercially available soft tissue fillers as well as variations in their substance and purity. Therefore, most of these products have not stood the test of time and thus should still be considered experimental.

Clinical studies on new permanent soft tissue fillers offered by manufacturers are mostly not sufficient to predict the incidence of late reactions. Therefore, continued long-term postmarketing surveillance by both manufacturers and notified bodies is essential. Physicians should remain alert to detect late adverse events and report them immediately to the competent authorities. It is the latter's responsibility to report regular updates to both patients and users on the latest insights concerning risks and adverse events with newly introduced soft tissue fillers.

The supply of fillers should be limited to trained physicians only. Therefore, IQAM urges governments to pass legislation to protect patients from unduly trained physicians and non-medical personnel injecting materials for various indications. The current position of IQAM is to sustain the ban on the use of liquid silicone as a permanent soft tissue filler in aesthetic plastic surgery.

Relatively high volumes of injected permanent fillers, especially hydrogels, are reported to cause severe irreversible damage and therefore have generated substantial concern. After reviewing the accumulated reports, IQAM

recommends that permanent hydrogels not be used due to the high incidence of severe complications.

Based on past experience IQAM states that Conformité Européennemarks (CE) and U.S. Food and Drug Administration (FDA) approvals are required steps in establishing the safety of medical devices, but are not necessarily sufficient. Post marketing surveillance revealing new adverse information should lead to reconsideration of the approval status.

Conformité Européenne and U.S. Food and Drug Administration

Artefill, a permanent filler composed of polymethylmethacrylate microspheres and bovine collagen, received pre-market approval by the FDA based on a prospective study, among other things [7, 8]. The “conditions of approval” include a postapproval study for the monitoring of long-term adverse effects.

The Dutch Society for Plastic and Reconstructive Surgery, in collaboration with the Dutch Society for Aesthetic Plastic Surgery, has defined guidelines on the use of permanent soft tissue fillers in the Netherlands. Presented in 2006 to the Dutch Authority on Safety Issues in Healthcare (IGZ) [9, 10], these guidelines were incorporated into the RIVM report. Currently, these guidelines are of importance in several lawsuits regarding malpractice in the soft tissue filling business. The Swiss Society for Plastic Surgery has banned the use of permanent soft tissue fillers since 2004 [11]. International Confederation for Plastic Reconstructive and Aesthetic Surgery (IPRAS) Secretary and former president of the German Society for Plastic Surgery, Marita Eisenmann Klein has sent out a serious warning on the use of permanent soft tissue fillers because of the growing number of reports on complications of permanent fillers [12].

Conclusion

We believe that, to date, the introduction and use of most permanent soft tissue fillers have in no way been subject to properly designed prospective scientific research and therefore should still be considered as fully experimental. The lack of properly designed prospective studies is impressive and undesirable. With the “oath of Hippocrates” in mind: “we should not harm our patients,” as physicians, we should be fully aware of our responsibility to treat our patients carefully and responsibly. The further introduction of these materials on the international markets should be carried out very cautiously to guarantee the safety of our patients.

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