A Comparison of Characteristic Properties and Qualitative Difference between Three Kinds of Triamcinolone Acetonide

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Objective: To conduct a study comparing 3 triamcinolone acetonide preparations in terms of their particle surface observed with a scanning electron microscope, their particle size distribution, and sedimentation in order to discuss their ability to facilitate visualization during vitreous surgery and the clinical results.

Methods: Kenacort-A®, the newer form of MaQaid, and the older form of MaQaid® were used. A scanning electron microscope and a measuring device were used. Sedimentation was measured based on ultraviolet and visible light absorption spectra.

Results: Observation of the particle surface revealed that small particles of the older form of MaQaid® had clumped together, and they contained numerous voids. It had a small mean particle dia (almost the same size as the newer form of MaQaid® and Kenacort-A®). Kenacort-A® was dispersed while the older form of MaQaid® had numerous clumps and ascending particles, and a large sedimentation volume. Small sedimentation volume and few clumps were noted on the newer form of MaQaid®.

Conclusion: The newer form of MaQaid® had a particle distribution like that of Kenacort-A®, so it should provide good visibility. Moreover, it is free of preservatives, so it may prove to be a useful aid to visualize the vitreous during vitreous surgery.

Key words: Triamcinolone acetonide, Vitreous surgery, Visualizing aids

INTRODUCTION

Visualization of the intraocular contents with a dye (chromovitrectomy) has become an essential technique for vitreous surgery over the past few years. Triamcinolone acetonide (TA) is one such dye. Peyman et al. [1] reported using TA to better visualize the vitreous with TA during vitreous surgery in 2000, and Sakamoto et al. [2] reported similar use of TA in 2002. Since that time, TA has been widely used to safely and reliably perform artificial posterior vitreous detachment [3]. TA for intramuscular injection and intraarticular injection (Kenacort-A®) was initially used off-label for vitreous surgery in Japan, but Japanese clinical trials of another TA agent, MaQaid®, revealed that it was a safe and effective aid to visualize the vitreous during vitreous surgery. Accordingly, MaQaid® was approved in 2010, and it is now in wide use.

Kenacort-A® contains an additive in the form of a surfactant (polysorbate 80), so it readily forms a uniform suspension. In contrast, MaQaid® contains no additives whatsoever, so it forms clumps. The older form of MaQaid® that was sold initially provided a somewhat different level of visibility than Kenacort-A®, causing a sense of a discrepancy among surgeons who had grown accustomed to the latter. To remedy this situation, a new TA agent of MaQaid® was developed to improve visibility in June 2012 [4]. The current study compared the particle surface, particle size distribution, and sedimentation of various TA agents in order to essentially examine their characteristics.

MATERIALS AND METHODS

The triamcinolone agents used were the older form of MaQaid®, the newer form of MaQaid®, and Kenacort-A®.

1. The particle surface of each triamcinolone agent was observed with a scanning electron microscope.
2. The particle size distribution in each triamcinolone agent was measured by measurement of particle size with laser diffraction method.
3. The sedimentation of each triamcinolone agent was measured based on ultraviolet and visible light absorption spectra (suspension concentration: 1 mg/mL, diluent: BSS Plus, measurement times: 0, 2, 4, 6, 8, and 10 min, measurement wavelength: 660 nm) in accordance with the methods of Moshfeghi et al. [4] In order to determine sedimentation macroscopically, triamcinolone agents were prepared in concentrations close to the concentration used chemically (11 mg/mL), and sedimentation after 10 min was filmed.

RESULTS

Use of SEM to observe the particle surface of each triamcinolone agent

SEM revealed that small particles of the older form of MaQaid® had clumped together and that the particles contained numerous voids. Since the newer form of MaQaid® and Kenacort were mainly constructed on large particles, there was no void (Fig. 1).

Particle size distribution in each triamcinolone agent

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The older form of MaQaid® had a small mean particle dia., while the newer form of MaQaid® and Kenacort-A had almost the same particle size distribution (Fig. 2).

**Sedimentation of each triamcinolone agent**

Sedimentation property is shown in Fig. 3. Kenacort-A® gradually precipitated in the 10 min it was left to stand. The newer form of MaQaid® had sedimentation property quite close to that of Kenacort-A®, but the older form of MaQaid® precipitated faster than the other 2 agents. Kenacort-A was dispersed while the older form of MaQaid® had numerous clumps, numerous ascending particles, and a large sedimentation volume. Sedimentation of the newer form of MaQaid® was noted, but a small sedimentation volume and few clumps were noted. Kenacort-A® presumably remained dispersed since it contained an additive in the form of a surfactant (polysorbate 80).

**DISCUSSION**

Over the past few years, vitreous surgery has been safely and reliably performed because of advances in surgical procedures and surgical instruments. Outcomes have improved and indications for surgery have expanded. Advances in surgical aids have made a substantial contribution to these changes. Since Peyman et al. [1] and Sakamoto et al. [2] reported using TA in posterior vitreous detachment, a number of surgeons have used TA as an aid to visualize the vitreous during vitreous surgery. The use of TA improves visibility during vitreous surgery and it allows a vitrectomy to be performed safely and reliably. TA is a poorly water-soluble corticosteroid which is made of white crystalline particles. A white suspension is made with TA particles which are mixed with 0.9% saline or BSS Plus ophthalmic solution. This suspension adheres to the vitreous gel, which is transparent, so the
Vitreous gel becomes distinctly visible. Kenacort-A® and MaQaid® are both TA agents. In Japan, Kenacort-A® comes as a suspension while MaQaid® comes as particles. Kenacort-A® contains additives such as a preservative that is harmful to ocular tissue (benzyl alcohol) [5, 6] and carmellose [7], which can raise the intraocular pressure. These additives had to be removed to use Kenacort-A®. In contrast, MaQaid® contains no additives whatsoever, so there is no need to rinse this agent off. Additives are thought to be one cause of aseptic endophthalmitis, and the risk of aseptic endophthalmitis had been reduced since MaQaid® was produced with no additives [8, 9].

Kenacort-A® was originally used in clinical practice because it has few clumps and it produces a uniform suspension. Kenacort-A® came as a suspension and it contained polysorbate 80 as a surfactant, so its TA particles were readily dispersed and it tended to provide a uniform suspension.

TA particles readily clump together, so MaQaid® , which contained only TA particles, tended to have large clumps (agglomerates). Small particles of MaQaid® aggregated and contained voids, so they tended to ascend when injected into the vitreous. In light of these facts, the manufacturer of MaQaid® , Wakamoto Co., Ltd., modified the TA particles in its product in June 2012. The company modified its method of manufacture and it increased the particle size distribution.

This made the MaQaid® more like Kenacort-A® (Fig. 3) since it had fewer clumps and it had particles with few voids (Fig. 1).

The current study found that after a change in the TA particles used, the newer form of MaQaid® had few large clumps (which would affect visibility) and it provided outstanding visibility. In addition, the newer form of MaQaid® better entwined with the vitreous and its particles tended not to ascend. A precipitation test was conducted to ascertain the reasons for these changes. The test revealed MaQaid® with different TA particles had a faster rate of sedimentation than Kenacort-A® and the newer form of MaQaid® with the conventional TA particles. Macroscopic examination revealed a smaller volume of sedimentation in a test tube and relatively even dispersal of MaQaid®. Thus, the disparity on vitreous visibility between old and new MaQaid® could be affected TA characteristics such as particle shape, sedimentation property and dispersal of particles. Additional studies need to be conducted to examine these characteristics in greater detail.

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CONFLICT OF INTEREST
No author has a financial proprietary interest in any material or method mentioned.

REFERENCES