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Clinical Investigation: Central Nervous System Tumor

Iodine 125 Brachytherapy With Vitrectomy and Silicone Oil in the Treatment of Uveal Melanoma: 1-to-1 Matched Case-Control Series

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Summary

Radiation retinopathy is a frequent, blinding, and poorly treatable morbidity associated with brachytherapy after iodine 125 for the local treatment of uveal melanoma. We describe the first clinical evidence that using silicone oil 1000 centistokes as a vitreous attenuating substance to "shield" iodine 125 from healthy nontumor ocular tissues may result in improved anatomic and visual outcomes in a 1-to-1 matched case-control series.

Purpose: We initially reported the radiation-attenuating effect of silicone oil 1000 centistokes for iodine 125. The purpose of this report was to compare the clinical outcomes in case patients who had iodine 125 brachytherapy with vitrectomy and silicone oil 1000 centistokes with the outcomes in matched control patients who underwent brachytherapy alone.

Methods and Materials: Consecutive patients with uveal melanoma who were treated with iodine 125 plaque brachytherapy and vitrectomy with silicone oil with minimum 1-year follow-up were included. Control patients who underwent brachytherapy alone were matched for tumor size, location, and sex. Baseline patient and tumor characteristics and tumor response to radiation, final visual acuity, macular status, central macular thickness by ocular coherence tomography (OCT), cataract progression, and metastasis at last follow-up visit were compared. Surgical complications were also determined.

Results: Twenty case patients met the inclusion criteria. The average follow-up time was 22.1 months in case patients and 19.4 months in control patients. The final logMAR vision was 0.81 in case patients and 1.1 in control patients ($P = .071$); 8 case patients and 16 control patients had abnormal macular findings ($P = .011$); and the average central macular thickness by OCT was 293.2 µm in case patients and 408.5 µm in control patients ($P = .016$). Eleven case patients (55%) and 1 control patient (5%) had required cataract surgery at last follow-up ($P = .002$). Four patients in the case group and 1 patient in the control group experienced metastasis ($P = .18$). Among the cases, intraoperative retinal tear occurred in 3 patients; total serous retinal detachment and macular hole developed in 1 case patient each. There was no case of rhegmatogenous retinal detachment, treatment failure, or local tumor dissemination in case patients or control patients.

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Conclusions: With up to 3 years of clinical follow-up, silicone oil during brachytherapy for the treatment of uveal melanoma resulted in fewer abnormal maculas, lower central macular thickness on OCT, and a trend toward better final visual acuity in comparison with matched control patients who underwent brachytherapy alone.

Introduction

Melanoma arising from the choroid and ciliary body is the most common primary intraocular cancer (1). Iodine 125 is the most common source of radiation used for local brachytherapy of uveal melanoma in North America; its efficacy was established by the Collaborative Ocular Melanoma Study (COMS) (2-4).

The adverse effects of plaque brachytherapy include vision loss, maculopathy and optic neuropathy, cataract, and radiation-associated proliferative retinopathy. Visual acuity in the treated eye generally declines at a rate of approximately 2 lines per year, and nearly 45% of patients may lose ambulatory vision (≤20/200) in the treated eye by 3 years of follow-up (5). Radiation maculopathy, which manifests as cystoid macular edema, macular ischemia, and chorioretinal atrophy, has been reported to occur in 18% to 43% of treated eyes within 5 years after brachytherapy (6, 7). In the COMS study, photographic and angiographic evidence of radiation-associated macular pathology was as high as 75% at 5 years (8). The typical onset occurred 18 to 24 months after treatment (6, 9).

The risk factors for radiation maculopathy, optic neuropathy, and proliferative radiation retinopathy include total radiation dose to the affected structures, proximity of the tumor to the affected structures, and systemic conditions such as diabetes mellitus (7, 10, 11). No treatment for radiation maculopathy or optic neuropathy has been proved to be effective in a randomized clinical trial.

Radiation injury to vital structures may be shielded with the use of materials that have a higher effective atomic number and density than tissue. We have reported for the first time the use of silicone oil 1000 centistokes as an attenuating substance for iodine 125 radiation (12). Ahuja et al (13) have recently corroborated our findings. In our initial report of this technique, we used cadaver eyes, an in vitro model, and Monte Carlo simulation to compare the radiation-attenuating effects of various vitreous substitutes in clinical use with the effects of normal saline. Among silicone oil 1000 centistokes, silicone oil 5000 centistokes, heavy oil, and perfluorocarbon liquid, the empirical data and theoretical calculations both demonstrated that silicone oil 1000 centistokes had the greatest radiation-attenuating effect in the human eye of 55% compared with saline (12). Therefore, the use of intraocular silicone oil 1000 centistokes during iodine 125 brachytherapy may limit the exposure of healthy tissues in the path of the radiation.

This study investigated the clinical evidence that silicone oil 1000 centistokes may reduce radiation-related ocular complications related to iodine 125 brachytherapy in patients treated for uveal melanoma.

Methods and Materials

The study was performed in accordance with the United States Health Insurance Portability and Accountability Act of 1996 and was approved by the Office of the Human Research Protection Program (Institutional Review Board) of the University of California, Los Angeles.

The inclusion criteria for case patients were that the patient was treated for uveal melanoma with iodine 125 plaque brachytherapy and silicone oil 1000 centistoke placement, and there was a minimum follow-up time of 1 year.

Control patients were those treated for uveal melanoma with plaque brachytherapy without concurrent vitrectomy or silicone oil placement. Control patients were matched, in order of priority, for tumor height (within 1.0 mm), sex, and tumor location. Data were collected from the control patients at the follow-up visit closest to an equivalent time point corresponding to the date of last follow-up visit of the matched case patient.

Information on patient demographics, tumor height and location (distance from tumor apex to nerve, and to fovea), preoperative and postoperative at last follow-up logMAR vision, lens status, macular status, ocular coherence tomography (OCT), and metastasis were retrospectively collected. The prescribed radiation dose was calculated in the same manner as the COMS (ie, 85 Gy to tumor apex), with a dose rate of approximately 0.5 Gy/h. The method outlined by Task Group 43 of the American Association of Physicists in Medicine (14) was followed. In brief, iodine 125 seeds were modeled as point sources, and water equivalence of the methyl methacrylate used to cement the seeds to the gold plaque was assumed. The plaques were sized with a 3-mm margin beyond the tumor on all sides.

Iodine 125 plaque surgery consisted of fine needle biopsy of the lesion and plaque placement followed by intraoperative ultrasonography by an experienced ultrasonographer to check for plaque position and lesion coverage, and followed by vitrectomy with silicone oil placement. The details of the brachytherapy plaque placement procedure have been described elsewhere (15-19). Briefly, fundus examination was performed on the affected eye, followed by monitored anesthesia care with retrobulbar anesthesia. A 360° conjunctival peritomy was performed, followed by isolation of the 4 rectus muscles with 2-0 silk suture. Transpupillary transillumination was used to mark the anterior border of the tumor. If the rectus muscles or their