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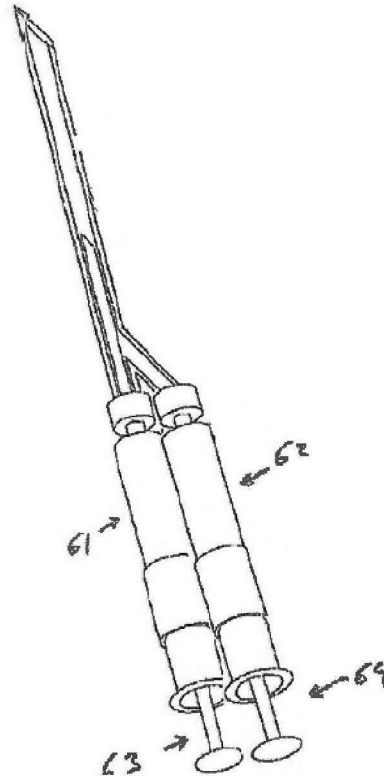
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(54) Title: OPHTHALMIC SYRINGE



(57) Abstract: The present invention provides a device for use in ophthalmology. In particular, the present invention provides a device for use in intravitreal administration of ocular agents. The present invention also provides methods of delivering one or more drugs to a human eye and methods for treating an ophthalmic disease, disorder, or condition.

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OPHTHALMIC SYRINGE**RELATED APPLICATIONS**

This application claims priority to U.S. Provisional Application Serial Number 60/717,865 filed September 16, 2005, Attorney Docket No. EYE-036P, which is hereby
5 incorporated in its entirety by reference.

FIELD OF THE INVENTION

The present invention relates to methods of administering ophthalmic medicines and devices related thereto. In particular, the invention relates to intravitreal injection using an ophthalmic syringe and needle.

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BACKGROUND OF THE INVENTION

Intravitreal (IVT) injection has been used in the treatment of human ocular disease for nearly a century beginning in 1911 as means to introduce air for retinal tamponade and repair of detachment (J. Ohm, *Albrecht von Graefes Arch Ophthalmol* 1911; 79:442-450). Over the past two decades, the use of intravitreal injection has gained increasing acceptance
15 in the therapeutic management of many intraocular diseases, particularly disorders affecting the posterior segment of the eye (Jager *et al.*, *Retina* 24:676-698, 2004). IVT injection is increasingly being incorporated into management of ocular diseases and the number of approved products for IVT injection is anticipated to grow on the basis of promising results from ongoing clinical studies. Currently formivirsen sodium (Vitravene®, Novartis AG,
20 Basel, Switzerland), ranibizumab injection (Lucentis™, Genentech, Inc., South San Francisco, CA) and pegaptanib sodium (Macugen®, (OSI) Eyetech, Inc. NY, NY) are three medicines approved by the Food and Drug Administration as IVT injections.

Advantages of IVT injection of medicines and diagnostics include the achievement of maximum vitreal concentrations while minimizing toxicity attributed to systemic
25 administration. While these advantages are becoming widely appreciated, the ophthalmology community turns its focus to various complications potentially associated with IVT injection. Risks of IVT injection, some vision threatening, include endophthalmitis, retinal detachment, iritis/uveitis, inflammation, intraocular hemorrhage, ocular hypertension, hypotony,

pneumatic retinopexy, and cataract (R.D. Jager *et al.*, *Retina* 24:676-698, 2004 and C.N. Ta, *Retina*, 24:699-705, 2004).

Endophthalmitis is a condition in which the tissues inside the eyeball become inflamed and is generally caused by bacterial infection. The most common sources of
5 bacteria causing postoperative endophthalmitis are believed to be the patient's conjunctiva or eyelids. Unless treated effectively, endophthalmitis can rapidly lead to severe vision loss or blindness. The relative risks of developing postoperative endophthalmitis depend on a
number of factors, including the presence of eyelid or conjunctival diseases, the patient's
general health, the use of immunosuppressant medications, the type of intraocular surgery,
10 and intraoperative complications. Of these factors, intraoperative complications, particularly breaks in the posterior capsule with vitreous loss, carry the greatest risk for the development of endophthalmitis.

Although intravitreal injection is a simple procedure with a small wound, it has been demonstrated that bacteria potentially introduced by the procedure are sufficient to induce
15 endophthalmitis, which is likely due to the inability of the vitreous to clear the infectious microorganisms. Other equally plausible explanations for the apparent high risk of endophthalmitis after intravitreal injections may be the very limited sample size as well as publication bias. It is important, nevertheless, to minimize the risk of developing
endophthalmitis by reducing or eliminating bacteria from the ocular surface at the time of the
20 injection and to strictly adhere to aseptic technique. The use of topical antibiotics has been shown to reduce conjunctival and eyelid bacterial flora, which may in turn also decrease the risk of endophthalmitis.

Because transient increases in intra-ocular pressure (IOP) may cause mild discomfort and can be associated in rare instances with irreversible damage to retinal ganglion cells
25 and/or retinal vascular occlusion, many investigators reported using prophylactic and/or therapeutic measures to prevent increases in IOP after IVT injection. These have included the use of aqueous paracentesis, preoperative treatment with pressure-lowering agents and digital massage or the use of a Honan IOP reducer.

Particulate contaminants present in a drug, in a syringe, or in or on materials used at
30 the time of injection also may have the potential to induce detrimental effects when injected into the vitreous. This has been demonstrated in the case of glove lubricants, which are

highly inflammatory when injected into the posterior ocular chamber (H.S. Park, *Korean J. Ophthalmol.* 1997; 11:51-59).

Other serious complications rarely occurred after IVT injection, making it difficult, in most instances, to determine whether these were truly injection-related or simply sporadic, unrelated comorbidities.

Serious adverse events are for the most part transient and/or treatable, and the risks of serious adverse events reported after IVT injection is low. Even so, there is a need for improved devices and methods for IVT injection. The risks and benefits of IVT injection will likely carry increased weight in patient and clinician treatment as more treatment options become available.

Guidelines for IVT injection are continuing to evolve (L.P. Aiello *et al.*, *Retina*, 24:S3-S19, 2004). For example, povidone iodine and an antibiotic are administered prior to IVT injection. Also, IVT injections are generally performed with a sterile surgical drape and lid speculum in place and a 27 or 30 gauge needle is typically used with an injection site 3.5-4.0 mm posterior to the limbus.

As new treatment modalities for macular diseases become available, the number of intravitreal injections administered is expected to increase dramatically. For example, intravitreal injection of the vascular endothelial growth factor (VEGF) inhibitor, Macugen®, has become available for the treatment of age-related macular degeneration. Also, intravitreal injections of triamcinolone acetonide are now commonly used for the treatment of macular edema.

The prevalence of endophthalmitis after intravitreal injection of anti-VEGF agents is unknown. Due to the very limited data regarding the rate of endophthalmitis after intravitreal injections, it is difficult to speculate about the true prevalence of endophthalmitis after these types of procedures. The increased use of intravitreal injections for the delivery of these agents to the retina will provide data regarding the prevalence and risk factors for post-injection endophthalmitis and in the future define a more accurate rate of endophthalmitis.

Drug delivery into the eye is challenging because the anatomy, physiology and biochemistry of the eye includes several defensive barriers that render ocular tissues

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