Establishing a safe, medical officer-led intravitreal injection clinic: minimizing inadvertent crystalline lens injury

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Abstract

Purpose: To study the incidence of iatrogenic crystalline lens injury in a medical officer-led intravitreal (IVT) injection clinic and to evaluate the effect of a structured training programme designed to teach medical officers how to safely administer IVT injections.

Study design: Clinical audit.

Methods: The first phase of the clinical audit comprised a retrospective analysis of the consecutive numbers of IVT injections between January and December 2020. Outcome measures included incidence and risk factors of lens injury. Target incidence rate of iatrogenic crystalline lens injury was set at < 0.06%. Intervention was implemented in the form of a structured training programme over the course of 4 months. The programme encompassed a lecture and video on proper administration techniques, as well as a handout detailing the key points. Medical officers were guided, directly supervised, and assessed by a single ophthalmologist and were required to complete a logbook before being sanctioned to perform IVT independently. Re-audit was done on the consecutive numbers of IVT injections in the following year, between May 2021 and April 2022.

Results: Out of 1,952 IVT injections performed by medical officers pre-intervention, 3 cases of iatrogenic lens injuries were reported, corresponding to an incidence rate of 0.15%. One patient was uncooperative. No other risk factors were identified.

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Post-intervention, our target was achieved with zero injection-related lens injury out of 2,118 consecutive IVT injections.

**Conclusion:** A structured training programme results in highly skilled medical officers delivering a well-rounded service that improves the quality of care and reduces the rate of adverse events in a large overburdened tertiary centre. Training must be conducted on a regular basis due to the entry of new medical officers periodically.

**Keywords:** anti-vascular endothelial growth factor therapy, iatrogenic lens injury, intravitreal injection, structured training programme

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**Abstrak**

**Tajuk:** Penubuhan klinik suntikan intravitreal yang selamat di bawah pantauan pegawai perubatan: mengurangkan kecederaan tidak sengaja kepada kanta mata.

**Tujuan:** Menyelidik kejadian kecederaan tidak sengaja kepada kanta mata di dalam klinik suntikan intravitreal (IVT) yang dikendalikan oleh pegawai perubatan dan menilai kesan program latihan berstruktur yang direka untuk mengajar pegawai perubatan cara untuk memberikan suntikan IVT dengan selamat.

**Reka bentuk kajian:** Audit klinikal.

**Kaedah:** Fasa pertama audit klinikal terdiri daripada analisis retrospektif bagi jumlah suntikan IVT berturut-turut antara Januari hingga Disember 2020. Pengukuran hasil termasuk kejadian dan faktor risiko kecederaan kanta. Kadar kejadian sasaran bagi kecederaan kanta kristal iatrogenik ditetapkan pada < 0.06%. Intervensi dilaksanakan dalam bentuk program latihan berstruktur selama empat bulan. Program ini merangkumi ceramah dan video mengenai teknik pentadbiran yang betul, dan bahan rujukan yang menetapkan butiran penting disebarkan. Pegawai perubatan diberi arahan, diawasi secara langsung dan dinilai oleh seorang pakar oftalmologi, dan dikenal pasti tidak berjaya. Audit ulang diadakan pada jumlah suntikan IVT berturut-turut pada tahun berikutnya, antara Mei 2021 hingga April 2022.

**Keputusan:** Daripada 1,952 IVT yang dilakukan oleh pegawai perubatan sebelum intervensi, 3 kes kecederaan kanta mata dilaporkan, yang sepadan dengan kadar kejadian 0.15%. Satu pesakit tidak bekerjasama. Tidak terdapat faktor risiko lain yang dikenal pasti. Selepas intervensi, sasaran kami dicapai dengan tiada kecederaan kanta mata berkaitan dengan suntikan daripada 2,118 IVT berturut-turut.

**Kesimpulan:** Program latihan berstruktur menghasilkan pegawai perubatan yang sangat mahir memberikan perkhidmatan yang menyeluruh yang meningkatkan kualiti penjagaan dan mengurangkan kadar kejadian yang tidak diingini di hospital tertiar yang besar dan sibuk. Latihan harus dijalankan secara berkala.
Introduction

Treatment options for retinal eye diseases have expanded over the years and intravitreal (IVT) drug delivery has emerged as the gold standard for treating many retinal disorders, especially after the introduction of anti-vascular endothelial growth factor (anti-VEGF) therapy. The benefit of IVT drug delivery is that it minimises systemic toxicity by targeting drug delivery directly to the posterior pole. The several common retinal disorders treated by IVT injection include neovascular age-related macular degeneration (AMD), diabetic macula oedema (DME), retinal vein occlusions, and choroidal neovascularisation.

These procedures are conventionally performed by ophthalmologists. In some developed countries, these procedures are only performed by retinal specialists. However, with the increasing number of patients that have to undergo this treatment, it is slowly being delegated to medical officers or non-medical ophthalmic health professionals. In the United Kingdom (UK), two-thirds of ophthalmic departments already have non-medical ophthalmic health professionals delivering IVT injections, according to a Royal College of Ophthalmologists paper from 2017 titled The Way Forward. Increasingly, Michelotti et al. reported that many ophthalmology departments in the UK are already training ophthalmic nurse injectors to undertake the procedure, which was previously only performed by ophthalmologists.

In a similar vein, there is a significant rise in the number of patients in our public healthcare system who require IVT anti-VEGF therapy to treat retinal diseases. The Department of Statistics Malaysia reported that, the percentage of Malaysians 65 and older is expected to rise from 5.0% in 2010 to 14.5% by 2040. In addition, the country’s aging population structures and rising life expectancy are expected to drive up the number of IVT injections.

Patients treated with anti-VEGF for wet AMD and DME require numerous injections and follow-up visits. Oftentimes, the limiting factor is an issue with capacity within the public hospital eye services to treat patients due to the large number of patients requiring injections and the high number of injections required per patient. There are simply not enough ophthalmologists to meet the demand. This necessitates training medical officers in the ophthalmology department to administer the injections to cater to a large number of injections and to ensure the smooth-running of the daily IVT injection clinic. Additionally, it is essential for trainees to attain proficiency in administering injections prior to their graduation.
as ophthalmologists. Simulation can be a valuable training tool for IVT injections to increase safety. It provides a standardised training experience for all trainees and allows practitioners to familiarise themselves with the procedure in a controlled environment before performing it on actual patients, helping to mitigate the many inherent risks of IVT injection. This consistency ensures that practitioners are well-prepared and follow best practices, which ultimately enhances patient safety.

Even though IVT injections improve vision in a variety of retinal diseases, each IVT injection poses the risk of adverse events. Repeated and long-term injections may lead to ocular and systemic complications. In a comprehensive systematic review, Jager et al. evaluated the prevalence of the most common serious adverse events associated with IVT injection and reported endophthalmitis, retinal detachment, iritis/uveitis, intraocular haemorrhage, ocular hypertension, cataract, and hypotony as some of the complications of the procedure. Retinal vein occlusions, anaphylactic reactions, and iatrogenic traumatic lens injury are among the other uncommon complications that have been identified.\(^7\)

Iatrogenic crystalline lens injury is a rare complication of IVT which occurs due to contact or penetration of the lens by the needle tip. Although it is uncommon, it should not be ignored because it can have significant visual consequences and can complicate future cataract surgery. Meyer et al. reported the overall incidence of traumatic lens injuries at 5 high-volume centres in Europe and South America over 36-months to be 0.006% (2/32,318).\(^8\) In the International IVT Bevacizumab Safety Survey, Fung et al. mentioned only 1 lens injury among 7,113 IVT injections (0.014%).\(^9\) Similarly, the VISION study observed that this complication is rare with only 5 lens injuries during 7,545 injections (0.067%).\(^10\)

This study was conducted to determine the incidence of this rare IVT complication and to assess the efficacy of a designed structured training programme to prepare medical officers to become competent in administering IVT injections safely and effectively while minimizing the complication of iatrogenic lens injury in a high-volume injection clinic operated by medical officers.

**Methods**

Before the audit, recently joined medical officers typically observe and assist senior medical officers during IVT injection sessions. Following this observational period, they are entrusted with the responsibility of conducting IVT injections themselves after participating in 2 to 3 sessions as observers.

A retrospective audit of the consecutive number of IVT injections between January and December 2020 was conducted. Outcome measures were the incidence and risk factors of lens injury. The progression and management of each respective case were also studied in detail. A target incidence rate of iatrogenic crystalline lens injury was set by our department at < 0.06%.
Following the first audit, a structured training programme for the medical officers was designed and implemented over a period of 4 months. Training of medical officers consists of the following components (Fig. 1):

- **Theory teaching**
  - Sterility
  - Anatomy of the eye
  - Step-by-step approach on how to deliver intravitreal injections

- **Observation**
  - Medical officers observe 50 injections performed by a competent doctor
  - Non-contact period for medical officer

- **Supervised injections**
  - 50 intravitreal injections are performed by the medical officer under close supervision of a competent doctor
  - All competencies must be signed off prior to the medical officer being able to independently administer injections

- **Practical assessment**
  - Medical officers are assessed by a competent ophthalmologist while performing the injections
  - All ten cases of injections need to be performed satisfactorily to obtain a pass

- **Logbook completion**
  - Trainee medical officers will need to document all observed cases, supervised cases and assessment cases in the designated logbook and submit it upon completion

**Independent injector status achieved**

*Fig. 1.* The Hospital Pulau Pinang medical officer training pathway to become independent practitioners.
• Theory course: The trainee medical officer was provided with a handout that contains fundamental information about the procedure. The course also included a lecture that covered fundamental information regarding the eye's anatomy and the theoretical aspects of delivering the injections (Appendix, Fig. 1). A video demonstration was also included.

• Observation: The trainee medical officer observed a minimum of 50 IVT injections administered by a competent doctor over 4 to 5 injection clinics.

• Injecting under supervision: A minimum of 50 injections were administered by the trainee medical officer under the supervision of a competent doctor. When this part of training was successfully completed, the trainee medical officer proceeded to the final evaluation.

• Practical assessment: The trainee medical officer performed 10 injections under observation of an ophthalmologist. Only when the medical officer had achieved 10 satisfactory cases, the practitioner was signed off to carry out injection sessions independently.

• Logbook completion (Appendix, Fig. 2): The trainee medical officer documented all observed cases, supervised cases, and assessment cases in the designated logbook and submitted it upon completion.

A re-audit was done on the consecutive number of IVT between May 2021 and April 2022. Outcome measures were the incidence of lens injury and risk factors of lens injury.

Results

Over a period of 12 months from January to December 2020, a total of 1,952 IVT injections were performed by medical officers. From those, 3 cases of iatrogenic lens injury were reported, corresponding to an incidence rate of 0.15% (3/1,952).

The breakdown of the 3 cases of iatrogenic lens injury were as follows (Table 1):

• Case 1: Iatrogenic lens injury was detected upon ophthalmic examination during follow-up. There was an evident track-like superotemporal posterior subcapsular cataract which corresponded with the site of IVT injection. The cataract remained quiescent on follow-up.

• Case 2: An ocular examination revealed iatrogenic lens damage during follow-up. There was an evident track-like superotemporal posterior subcapsular cataract that corresponded with the site of IVT injection. The patient developed a significant visually impairing cataract and underwent phacoemulsification with lower fluidic settings, anterior vitrectomy, and sulcus intraocular lens implantation.

• Case 3: Iatrogenic lens injury was only detected intraoperatively. The patient developed a white cataract 3 months post-IVT injection and was scheduled to undergo a cataract operation. Posterior capsule puncture was only discovered
The patient subsequently underwent pars plana vitrectomy and lensectomy.

Identification of risk factors was categorised into patient factors, procedural factors, and physician factors (Table 2). For patient factors, patients received a range of 3 to 12 injections before the complication occurred. None of the patients were hyperopic, with spherical equivalent ranging from plano to -1.25 and axial length of 23.37 mm to 24.20 mm. None of the patients had a narrow palpebral fissure. All the patients were in the supine position for the procedure. Only 1 of the 3 cases was documented to be anxious during the procedure and had significant head motion during the injection. None of the 3 did not report any pain during the injection. In all 3 cases, the injection was at the superotemporal quadrant of the left eye, 4 mm from the limbus, measured with a calliper. For the procedure, the size of the needle used was a standardised 31-gauge insulin needle, 8 mm in length. All 3 had 0.05 ml of medication injected into the eye. For physician factors, in all 3, the physician was standing at the head of the table while performing the procedure and all had a cumulative experience of at least 100 injections prior to the event.

Following an intervention period of 4 months, the re-audit conducted over a period of 1 year from May 2021 to April 2022 did not reveal any cases of iatrogenic lens injury out of a total of 2,787 IVT injections, corresponding to an incidence rate of 0%. The target incidence rate of iatrogenic crystalline lens injury of < 0.06% was achieved.

### Table 1. Summary of reported cases of iatrogenic lens injury

<table>
<thead>
<tr>
<th>Case number</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case detection</strong></td>
<td>During follow-up</td>
<td>During follow-up</td>
<td>Intraoperatively</td>
</tr>
<tr>
<td><strong>Signs of lens injury</strong></td>
<td>Track-like superotemporal posterior subcapsular cataract correlating with the site of injection</td>
<td>Track-like superotemporal posterior subcapsular cataract correlating with the site of injection</td>
<td>During cataract surgery for white cataract, pre-existing posterior capsule rupture was noted</td>
</tr>
<tr>
<td><strong>Progress</strong></td>
<td>No obvious progression, quiescent</td>
<td>Developed visually significant dense diffuse posterior subcapsular cataract</td>
<td>Nucleus drop occurred intraoperatively</td>
</tr>
<tr>
<td><strong>Management</strong></td>
<td>Observation and watchful waiting</td>
<td>Phacoemulsification with lower fluidic settings, anterior vitrectomy, sulcus intraocular lens implantation</td>
<td>Pars plana vitrectomy, lensectomy</td>
</tr>
</tbody>
</table>


**Discussion**

During IVT injection, the IVT needle path is in close proximity to the crystalline lens. This confers an increased risk of iatrogenic lens injury. Iatrogenic lens injury brings many consequences. It can be localised and quiescent, likely because a small lens wound could heal spontaneously due to the proliferation of the subcapsular epithelium, which would seal the wound before the intraventricular passage of ions and fluid. On the other side of the spectrum, cataract progression could occur and be visually significant, necessitating cataract extraction. Some signs to look out for include retroillumination to highlight any marks indicating injury from IVT, a visible capsular channel perforation on the posterior capsule of the lens, focal or diffuse posterior subcapsular opacification, progressive opacification of lens, and total white cataract due to liquefaction of the cortex.

**Table 2. Analysis of possible risk factors**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
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<tbody>
<tr>
<td>Number of previously received injections ((n))</td>
<td>7</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Patient’s refraction spherical equivalent ((\text{dpt}))</td>
<td>Plano</td>
<td>-1.25</td>
<td>-0.50</td>
</tr>
<tr>
<td>Axial length ((\text{mm}))</td>
<td>23.54</td>
<td>24.20</td>
<td>23.37</td>
</tr>
<tr>
<td>Small lid margin</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td>Patient position during injection</td>
<td>Supine</td>
<td>Supine</td>
<td>Supine</td>
</tr>
<tr>
<td>Anxious patient</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Head motion during injection</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Pain during injection</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Injected eye</td>
<td>OS</td>
<td>OS</td>
<td>OS</td>
</tr>
<tr>
<td>Location of injection</td>
<td>Superotemporal</td>
<td>Superotemporal</td>
<td>Superotemporal</td>
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**Procedure**

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<thead>
<tr>
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<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
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<tbody>
<tr>
<td>Size of used needle ((\text{gauge}))</td>
<td>31G</td>
<td>31G</td>
<td>31G</td>
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<tr>
<td>Applied volume ((\text{mL}))</td>
<td>0.05</td>
<td>0.05</td>
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**Physician**

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<th>Case 1</th>
<th>Case 2</th>
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<tr>
<td>Position of treating physician</td>
<td>Standing</td>
<td>Standing</td>
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<tr>
<td>Experience of medical officer in terms of number of injections ((n))</td>
<td>&gt; 100</td>
<td>&gt; 200</td>
<td>&gt; 200</td>
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</table>
Iatrogenic lens injury poses important surgical concerns that surgeons should be aware of. Hahn et al. reported a higher rate of intraoperative and postoperative complications in eyes with prior IVT injections, likely due to unidentified injury during IVT. Therefore, deliberate attention should be given to the posterior capsule during preoperative cataract assessment and intraoperatively in eyes with a prior history of IVT.

The structured training programme guides the medical officers to be well-versed in the safe execution of the procedure. Some important tips pointed out by Su et al. include an accurate selection of needle entry points and angles, appropriate anaesthesia, the importance of stable head fixation, and a comprehensive understanding of the patient’s condition before carrying out the procedure. The programme also provides the medical officers with adequate exposure during the initial observation period prior to performing the procedure itself. The other positive ramification is that medical officers play a more active role in the patients’ treatment.

We acknowledge a few study limitations. First and foremost, the study is limited by its retrospective design. The initial challenge of setting up the training programme was that time must be set aside to provide training and to conduct assessments amidst an overburdened, busy clinic. There may also be the possibility of under-reporting of case morbidities. Among the 3 case morbidities reported pre-intervention, 2 of the eyes did not have documented lens trauma in the patient records, so it is very likely that this inadvertent interaction generally occurs unknowingly. Some cases might not be picked up during follow-ups, especially cases that are quiescent. There may also be cases where the patient does not notice changes in vision due to pre-existing poor vision. Longer post-intervention surveillance might be more reflective of the impact of the intervention.

**Conclusion**

The indications and need for IVT injections continue to grow, and the burden of treatment is beginning to extend beyond ophthalmologists to trainees. Streamlining the training process allows for maintaining high-quality standards and allows medical officers in training to establish a safe, efficient, and cost-effective medical-officer-led IVT injection clinic. The structured training programme is effective in reducing the rate of adverse events in a large overburdened tertiary centre. Nevertheless, it is ideal if a competent ophthalmologist or a senior medical officer could be available for consult while medical officers are performing the procedure should the need for help or urgent complications arise.
Declarations

Ethics approval and consent to participate
This study is registered with NMRR, ID-22-01536-QK4. Retrospective studies do not require ethics approval nor informed consent.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgements
None to declare.

References


Appendix

**INTRAVITREAL INJECTION TECHNIQUE**

1. Confirm consent and correct eye.
2. Instil topical Alcaine into fornix of eye being injected.
3. Instil 5% povidone-iodine into fornix of eye being injected.
4. Clean around eye with 10% povidone. Dry.
5. Drape the eye.
6. Prepare solution in syringe with a 20G needle in correct volume and make sure air bubble expelled prior to injection.
   - Ranibizumab 0.5mg/0.05ml
   - Afibercept 2mg/0.05ml
7. Apply lid speculum.
8. Measure 4.0mm (phakia)/3.5mm (pseudophakia/ aphakia) posterior to limbus with caliper.
9. Keep caliper in place to stabilize the globe.
10. Inject anti-VEGF at superotemporal/inferotemporal quadrant into intravitreal cavity by inserting needle perpendicular, aim towards centre of the globe.
11. Keep syringe in place, replace caliper with cotton tip applicator and cover injection site upon removal of syringe.
12. Instil a drop of topical ciprofloxacin immediately post-injection.
13. Check that patient has at least CF vision post-injection.
14. Clean eye and discharge patient with topical antibiotic eye drops and warning signs of infection/ RD.

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*Fig. 1. (A-H) The handouts for theory teaching and compilation of CME slides.*
## INTRAVITREAL INJECTION LOGBOOK

### A  
**OBSERVED (50 cases)**

<table>
<thead>
<tr>
<th>No.</th>
<th>Date</th>
<th>Diagnosis</th>
<th>Procedure</th>
<th>Complications</th>
<th>Remarks</th>
<th>Supervised by (Sign)</th>
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### B  
**PERFORMED UNDER SUPERVISION (50 cases)**

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### C  
**PERFORMED UNDER SUPERVISION (10 cases)**

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