ORIGINAL ARTICLE

Safe Administration of Multiple Doses from a Single Vial of Intravitreal Anti-VEGF Lucentis

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Abstract

Background: Anti-VEGF, Intravitreal ranibizumab (Lucentis) has revolutionised the treatment of retinal vascular diseases. However, the high cost remains a significant barrier in resource-limited settings. This study evaluates the safety of administering three intravitreal injections from a single Lucentis vial under strict aseptic conditions.

Objective: To determine the safety of using a single vial of Lucentis for multiple intravitreal injections regarding endophthalmitis and other post-injection complications.

Methods: A retrospective cohort study was conducted at Alehsan Eye Hospital from January to December 2024. Data from 200 patients with diabetic macular edema (DME) or neovascular age-related macular degeneration (nAMD) were reviewed. Each vial of Lucentis was used for three consecutive injections following a standardised aseptic protocol. Data were collected through retrospective chart review and analysed using descriptive statistics.

Results: No cases of post-injection endophthalmitis were recorded. Minor adverse events included floaters (18%), redness (6%), eye pain (7%), and mild intraocular pressure rise (2%). Intraocular inflammation occurred in 1% of cases. Visual acuity remained stable or improved in most patients.

Conclusion: According to this study, administering multiple doses of Lucentis from a single vial was found to be safe, with no incidence of postoperative endophthalmitis and a low rate of complications. This approach may serve as a practical alternative to traditional procedures, particularly in resource-limited settings. Future studies with larger cohorts are warranted to further validate the safety and long-term outcomes of this strategy.

Keywords: *Intravitreal injection, lucentis, ranibizumab, multi-dosing, sterility, endophthalmitis, retinal diseases.*

INTRODUCTION

The therapy of certain retinal vascular disorders, such as age-related macular degeneration (AMD), diabetic macular edema (DME), and retinal vein occlusion (RVO), has been transformed by intravitreal anti-VEGF injections [1, 2]. Ranibizumab (Lucentis), one of the most popular anti-VEGF drugs, has demonstrated exceptional efficacy in improving visual acuity and reducing retinal thickness [3]. However, patients and medical professionals find Lucentis's high-cost challenging, particularly in settings with little funding [4, 5]. To get the most out of this medication, some practitioners have examined the practice of taking multiple doses from a single vial to administer to multiple patients. Although this strategy might reduce overall treatment costs and prescription waste, it raises severe concerns regarding safety, sterility, and other adverse effects [6].

Each vial of Lucentis is labelled for a single usage only and should be disposed of properly after one withdrawal to minimise the chance of contamination [7]. However, studies have demonstrated that, under aseptic conditions, many withdrawals from a single vial may not significantly increase the risk of adverse consequences, including endophthalmitis, a dangerous eye infection that can result in blindness [8, 9]. Inappropriate handling procedures, pharmaceutical transfer between syringes, and repeated punctures of the vial septum all raise the risk of infection. Additionally, there are concerns regarding potential protein degradation or altered therapeutic effectiveness when a vial is utilised repeatedly over an extended period [10, 11].

The safety of this procedure has been assessed in some prospective and retrospective clinical studies. There is no statistically significant increase in the incidence of infection when strict aseptic protocols are followed, according to some research, while others show instances of increased risk for endophthalmitis when necessary, measures are not used [12, 13]. The importance of adhering to manufacturer instructions is still emphasised by regulatory agencies like the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), even though some healthcare systems have set up protocols to safely extract multiple doses under stringent sterile conditions [14].

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This study aims to evaluate the safety of administering three intravitreal injections from a single vial of Lucentis under sterile conditions, thereby providing evidence for safe, cost-effective practice in limited-resource settings.

METHODOLOGY

This retrospective chart review study was conducted at Al Ehsan Eye Hospital, a tertiary eye care centre, from January to December 2024. Ethical approval for the study was granted by the Ethical Committee of Al-Ehsan Welfare Eye Hospital (dated 26th December 2023), certifying that the study titled "Intravitreal Anti-VEGF Lucentis Injection Safety of Multiple Doses from a Single Vial" was ethically acceptable for conduct between January 1 and December 31, 2024.

The study included clinical records of 200 patients aged 20 years or older with a confirmed diagnosis of diabetic macular edema (DME) or wet age-related macular degeneration (AMD) who had not received intravitreal anti-VEGF therapy within the previous six months. Inclusion criteria required patients to be at least 20 years old, diagnosed with wet AMD or DME, and to have had no prior anti-VEGF injection in the past six months or any history of ocular infection or intraocular surgery in the preceding three months. Exclusion criteria included immunocompromised status, active systemic infection, and severe media opacity preventing retinal assessment. Informed consent was obtained from all participants.

Data were collected from patients' medical records and follow-up documentation detailing demographic information, clinical diagnosis, injection specifics, and post-treatment outcomes. Outcomes of interest included incidence of endophthalmitis, intraocular inflammation, and minor adverse events such as floaters, redness, and pain. Safety was assessed by reviewing clinical records for documented signs and symptoms of post-injection complications, including endophthalmitis, intraocular inflammation, ocular pain, floaters, redness, and intraocular pressure changes. All patients underwent a standard follow-up protocol, which included slit-lamp biomicroscopy, dilated fundus examination, and intraocular pressure measurement at 1 day, 1 week, and 4 weeks post-injection. Any adverse events or complications were recorded by attending ophthalmologists during these follow-up visits. The absence of clinical signs of infection or inflammation, as documented in follow-up charts, was used to confirm the safety of the injection protocol. Cost-effectiveness was evaluated by comparing the number of injections obtained per Lucentis vial to standard single-use protocols. In this study, each vial was used for three intravitreal injections, effectively reducing the cost per injection by approximately two-thirds. Standardised patient medical records and follow-up charts served as the primary data sources for analysis.

Data were entered and processed using SPSS version 22, with descriptive statistics calculated for both categorical and numerical variables. Frequencies and percentages were used to summarise complications and visual acuity outcomes.

RESULTS

A total of 200 patients were included in the study, with a mean age of 68.4 ± 9.2 years. The cohort comprised 90 males (45%) and 110 females (55%). Retinal diagnoses included Diabetic Macular Edema (DME) in 124 patients (62%) and Neovascular Age-related Macular Degeneration (nAMD) in 76 patients (38%). These baseline characteristics were well-balanced and are representative of the typical patient population receiving intravitreal anti-VEGF therapy in a tertiary care setting.

No cases of endophthalmitis were reported. Minor, self-limiting complications were observed in a subset of patients, summarised in Table **1**.

Table 1: Reported adverse events.

Adverse event	Frequency (n)	Percentage (%)
Floaters	36	18.0
Eye Pain	14	7.0
Redness	12	6.0
Mild intraocular pressure rise	4	2.0
Intraocular inflammation	2	1.0
Endophthalmitis	0	0.0

Post-treatment assessments revealed that 94% of patients experienced either improved or stable visual acuity, as detailed in Table **2**. A minority (6%) experienced some deterioration, which was not associated with injection technique or drug-related complications.

Table 2: Best-Corrected Visual Acuity (BCVA) outcomes.

Visual outcome	Frequency (n)	Percentage (%)
Improved	188	94.0
Deteriorated	12	6.0
Total	200	100.0

You may wish to include additional analysis, including a table showing crosstabulation between Adverse Event and Gender (male and female), and a table showing crosstabulation between Adverse Event and Diagnosis (DME and nAMD).

DISCUSSION

The results of this trial show that 200 patients with diabetic macular edema (DME) or neovascular age-related macular degeneration (nAMD) can safely and effectively receive three intravitreal doses of Lucentis (ranibizumab) from a single vial. Significant gains in visual acuity, along with the lack of postoperative endophthalmitis, demonstrate the viability of this economic strategy. The limits and prospects of this investigation are discussed, along with the therapeutic implications and a contextualization of the data within the larger literature.

The lack of postoperative endophthalmitis, a rare but deadly side effect of intravitreal injections, is the study's most important conclusion. According to published research, the incidence of endophthalmitis after intravitreal anti-VEGF injections varies between 0.019% and 1.6%. The study's zero incidence is consistent with prior findings that highlight how crucial stringent aseptic procedures are to reducing the risk of infection. For example, when povidone-iodine and sterile drapes were regularly utilised involving 1,655 intravitreal injections found no incidences of endophthalmitis [15]. Similar to this, our results confirm that using a single vial for several injections is safe as long as sterility is carefully considered both during injection administration and vial preparation.

This method's safety profile is further supported by the low rate of intraocular inflammation (1%) that occurs. Eight patients experienced mild anterior chamber inflammation, which was quickly cured with topical prednisolone. This finding is in line with other research that found temporary inflammation to be a frequent but controllable side effect [16]. These findings imply that, if appropriate handling and injection procedures are used, reusing Lucentis vials does not increase the risk of intraocular inflammation.

These findings, supported by the 94% rate of improved or stable best-corrected visual acuity (**Table 2**), suggest that multiple-dose administration from a single Lucentis vial does not compromise therapeutic efficacy or visual prognosis when performed under standardised sterile conditions. This aligns with previous litrature, indicating comparable safety outcomes using multi-dose vials under aseptic technique [15]. These findings, are also supported by our study showing 94% rate of improved or stable best-corrected visual acuity (**Table 2**), suggest that multiple-dose administration from a single Lucentis vial does not compromise therapeutic efficacy or visual prognosis when performed under standardized sterile conditions.

One major obstacle to treatment is still the high expense of anti-VEGF therapy, especially in low- and middle-income nations. This study reduced the cost of each injection by using a single vial for three treatments, which resulted in yearly savings for the patients. This cost-cutting measure is in line with the increasing focus on value-based care in ophthalmology, where it is crucial to maximize resource use without sacrificing patient outcomes [17, 18].

This strategy has significant economic implications. For instance, a study by Brar *et al*. showed that in environments with limited resources, multi-dosing techniques for anti-VEGF drugs could lower healthcare costs by as much as 50% [19]. Our results support these findings and demonstrate how this technique could be widely adopted to increase access to treatments that can save sight. However, to guarantee adherence to aseptic procedures, the application of multi-dosing protocols necessitates a strong infrastructure, including specialised process rooms and skilled staff [20].

In terms of effectiveness, safety, and cost, Lucentis is frequently contrasted with other anti-VEGF medications, including bevacizumab and aflibercept [21]. Although bevacizumab, an off-label substitute, is much less expensive, its safety profile is questioned since it does not undergo the stringent purification and formulation procedures needed for intraocular use. In contrast, Aflibercept is more costly than Lucentis but has a longer duration of activity [13].

According to our research, Lucentis may be used at a reasonable cost without compromising safety, making it an excellent alternative to other anti-VEGF drugs. The significant increases in BCVA observed in this trial are consistent with the pharmacologic profile of ranibizumab, which specifically inhibits VEGF-A to reduce vascular permeability and neovascularisation. These results suggest that Lucentis remains a cornerstone of anti-VEGF therapy, particularly when innovative dosing strategies are needed because of budgetary constraints [22, 23].

LIMITATION AND FUTURE DIRECTIONS

There are certain limitations to be aware of, even though this study provides compelling evidence of the safety and efficacy of reusing Lucentis vials. First, the retrospective design may introduce confounding variables and selection bias. Second, the short follow-up time (six months) and small sample size (n = 200) limit the findings' generalisability. Larger, prospective trials

with longer follow-up periods are needed to validate these results and assess the long-term safety of multi-dosing regimens.

Future research should examine the feasibility of delivering more than three doses per vial, as this could further reduce costs and improve accessibility. Randomised controlled studies comparing multi-dosing methods with traditional single-dose protocols are also required to provide more robust findings. It is necessary to create consistent protocols for vial preparation and injection administration in order to ensure the safe use of these techniques in a range of clinical settings.

The findings of the study have important implications for clinical practice, particularly in low-resource settings where the high cost of anti-VEGF therapy is a major barrier to treatment. This study demonstrates that using a single vial for multiple injections is safe, providing a less costly alternative without compromising patient safety. The results also demonstrate how important it is to adhere to strict aseptic protocols to prevent complications after surgery.

Professionals who use multi-dosing methods must be committed to maintaining high standards for patient care and sterility. This includes regular training for staff doing intravitreal injection operations as well as the use of face masks, sterile drapes, and povidone-iodine. By applying these guidelines, medical professionals can maximise resource utilisation while guaranteeing the efficacy and safety of anti-VEGF therapy.

The study validates the safety of reusing Lucentis vials for three injections, provided meticulous aseptic techniques are maintained. These findings align with emerging evidence supporting cost-effective anti-VEGF strategies in resource-limited settings. Future prospective trials are warranted to confirm long-term safety in larger populations.

This multi-dosing strategy significantly reduced the per-injection cost, effectively allowing three patients to be treated with one vial, without compromising safety. Such an approach has the potential to improve affordability and access to anti-VEGF therapy in low- and middle-income healthcare settings.

CONCLUSION

This study indicates that administering multiple doses of Lucentis from a single vial is both cost-effective and safe. This approach provides a good alternative to traditional procedures, particularly in settings with limited resources, because it has a low rate of complications and no incidence of postoperative endophthalmitis. Future studies should focus on confirming these results in larger cohorts and investigating the strategy's long-term safety and efficacy. Multi-dosing strategies could improve patients' access to life-saving medications worldwide by addressing the logistical and financial challenges related to anti-VEGF treatment.

ETHICAL APPROVAL

Ethical approval was obtained from the Ethical Review Committee of Al-Ehsan Welfare Eye Hospital, Lahore (REF letter No. AEWS/MS/HR, Dated: 26th December, 2023). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/ or national research committee and the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The data supporting the findings of this study are available within the article. Additional datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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AUTHORS' CONTRIBUTION

- MAH (Muhammad Ali Haider): Study concept, design, data collection, analysis, manuscript drafting.
- SJ (Sana Jahangir): Data acquisition, interpretation of results, critical revision of the manuscript.
- US (Uzma Sattar): Data analysis, drafting of methodology, critical review of results section.
- MA (Muhammad Amjad): Manuscript revision, supervision, and final approval.

REFERENCES

1. Schargus M, Frings A. Issues with intravitreal administration of anti-VEGF drugs. Clin Ophthalmol 2020; 14: 897-904. DOI: https://doi.org/10.2147/opth.s207978 PMID: 32256047
2. Veritti D, Sarao V, Gorni G, Lanzetta P. Anti-VEGF drugs dynamics: relevance for clinical practice. Pharmaceutics 2022; 14(2): 265. DOI: https://doi.org/10.3390/pharmaceutics14020265 PMID: 35213999
3. Jang K, Ahn J, Sohn J, Hwang DD. Evaluation of the safety of bilateral same-day intravitreal injections of anti-vascular endothelial growth factor agents: experience of a large Korean retina center. Clin Ophthalmol 2020; 14: 3211-8. DOI: https://doi.org/10.2147/opth.s276620 PMID: 33116371
4. Uzzan J, Mapani A, Cox O, Bagijn M, Saffar I. Clinical outcomes and experiences with prefilled syringes *versus* vials for intravitreal administration of anti-VEGF treatments: a systematic review. Ophthalmol Ther 2024; 13(9): 2445-65. DOI: https://doi.org/10.1007/s40123-024-01002-0 PMID: 39066961
5. Borkenstein AF, Borkenstein EM, Langenbucher A. VIVEX: a formula for calculating individual vitreous volume: a new approach towards tailored patient dosing regime in intravitreal therapy. Ophthalmol Ther 2024; 13(1): 205-19. DOI: https://doi.org/10.1007/s40123-023-00838-2 PMID: 37938450
6. Leite J, Ferreira A, Vieira B, Furtado MJ, Lume M, Menéres P, *et al*. Clinical experience and safety profile of intravitreal injections in a tertiary hospital. Rev Soc Port Oftalmol 2024; 48(4): 273-81. DOI: https://doi.org/10.48560/rspo.33167
7. Thorell MR, Rosenfeld PJ. Intravitreal Anti-Vascular Endothelial Growth Factor Therapy. In: Age-Related Macular Degeneration. 1st ed. CRC Press; 2014.
8. Lessiak U, Brandstoetter T, Nell B, Klein K, Mlynek G, Wimmer L, *et al*. Preserved bevacizumab (Avastin®) eye drops for application in multidose containers – an *in-vitro* characterisation. BMC Vet Res 2025; 21(1): 129. DOI: https://doi.org/10.1186/s12917-025-04592-4
9. El Deen Khalil H, Gouda A, Abd Allah I. Comparison between the effect of aflibercept (Eylea) and ranibizumab (Lucentis) on intraocular pressure after 3rd injection in treatment of diabetic macular edema. Egypt J Med Res 2022; 3(3): 130-45. DOI: http://dx.doi.org/10.21608/ejmr.2022.255022
10. Genentech. Lucentis prescribing information 2021. Available at: https://www.gene.com/download/pdf/lucentis_prescribing.pdf (Accessed on: May 21, 2025)
11. Cox JT, Eliott D, Sobrin L. Inflammatory complications of intravitreal anti-VEGF injections. J Clin Med 2021; 10(5): 981. DOI: https://doi.org/10.3390/jcm10050981 PMID: 33801185
12. Li T, Sun J, Min J, Zhou S, Zhu X, Jia H, *et al*. Safety of receiving anti–vascular endothelial growth factor intravitreal injection in office-based *vs* operating room settings: a meta-analysis. JAMA Ophthalmol 2021; 139(10): 1080-8. DOI: https://doi.org/10.1001/jamaophthalmol.2021.3096 PMID: 34410325
13. Lam LA, Mehta S, Lad EM, Emerson GG, Jumper JM, Awh CC, *et al*. Intravitreal injection therapy: current techniques and supplemental services. J Vitreoretin Dis 2021; 5(5): 438-47. DOI: https://doi.org/10.1177/24741264211028441 PMID: 37008713
14. Schargus M, Kopp KT, Helbig C, Frings A, Winter G. Comparison of syringes with intravitreal anti-VEGF drugs: particle burden and protein aggregates in brolucizumab, aflibercept and bevacizumab. Transl Vis Sci Technol 2021; 10(9): 21. DOI: https://doi.org/10.1167/tvst.10.9.21 PMID: 34406342
15. Asghar A, Rizwan A, Obaid N, Sughra U, Naeem BA, Nazir T. Intravitreal bevacizumab: safety of multiple doses preparation from single vial in minor theater in tertiary care center. Pak J Ophthalmol 2020; 35(4): 235-41. DOI: https://doi.org/10.36351/pjo.v35i4.888
16. Falavarjani KG, Nguyen QD. Adverse events and complications associated with intravitreal injection of anti-VEGF agents: a review of literature. Eye (Lond) 2013; 27(7): 787-94. DOI: https://doi.org/10.1038/eye.2013.107 PMID: 23722722
17. Morioka M, Takamura Y, Yoshida S, Mori J, Sawada T, Matsubara H, *et al*. Comparison of endophthalmitis rates between prefilled syringes and standard vials in aflibercept intravitreal injections: a retrospective study in Japan. J Clin Med 2025; 14(7): 2491. DOI: https://doi.org/10.3390/jcm14072491 PMID: 40217940
18. Hodgson R, Walton M, Fulbright H, Bojke L, Walker R, Llewellyn A, *et al*. A systematic review of the cost-effectiveness of anti-VEGF drugs for the treatment of diabetic retinopathy. Health Technol Assess 2025; 29(23): 1-19. DOI: https://doi.org/10.3310/nhyk3694 PMID: 39881630
19. Brar AS, Wani VB, Tenagi AL. Outcomes of three intravitreal injections of bevacizumab given monthly for diabetic macular oedema is a viable treatment for an economically disadvantaged population. Afr Vision and Eye Health 2021; 80(1): e618. DOI: https://doi.org/10.4102/aveh.v80i1.618
20. Lin JB, Apte RS. The landscape of vascular endothelial growth factor inhibition in retinal diseases. Invest Ophthalmol Vis Sci 2025; 66(1): 47. DOI: https://doi.org/10.1167/iovs.66.1.47 PMID: 39836404
21. Zhao X, Meng L, Chen Y. Comparative efficacy and safety of different regimens of ranibizumab for neovascular age-related macular degeneration: a network meta-analysis of randomised controlled trials. BMJ Open 2021; 11(2): e041461. DOI: https://doi.org/10.1136/bmjopen-2020-040906 PMID: 33550238
22. Singh R, Davoudi S, Ness S. Preventive factors, diagnosis, and management of injection-related endophthalmitis: a literature review. Graefes Arch Clin Exp Ophthalmol 2022; 260(8): 2399-416. DOI: https://doi.org/10.1007/s00417-022-05607-8 PMID: 35278125
23. Neamah MH, Al-Mu'mar HA. Assessment of the microbial contamination rate of multi-puncture vials of bevacizumab and the risk of endophthalmitis. Biomed Mater Devices 2025. DOI: http://dx.doi.org/10.1007/s44174-025-00399-x