



Solution for Dead Space Problem in Ranibizumab Syringe System

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Authors' contributions

This work was carried out in collaboration between all authors. Authors OK and SB designed the study, wrote the protocol. Author SB wrote the first draft of the manuscript. Authors BC and FT managed the literature searches, analyses of the study and the experimental process. All authors read and approved the final manuscript.

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ABSTRACT

Intravitreal injection of drugs that inhibit the actions of vascular endothelial growth factor bring high economic burden for the health systems. We evaluated the amount of drug volume retained in two different types of syringes with billed and non - billed rubber stopper. Difference between two syringe types is 0.037 g. This indicates a significant amount of volume loss due to dead space between syringe and needle. Consequently, a simple change of design of rubber stopper of the plunger as billed form may reduce significant amount of drug loss due to dead space volume.

Keywords: Anti-vascular endothelial growth factor; dead space volume.

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1. INTRODUCTION

Intravitreal injections of vascular endothelial growth factor (VEGF) drugs for neovascular age-related macular degeneration (AMD) is the current preferred treatment modality, which requires a high economic burden for the health systems. On average each patient receives monthly injected, at least 6 anti-VEGF injections in a one year period, mainly ranibizumab 0.5 mg in volume of 0.05mL. If this treatment regimen can be applied successfully, the choroidal neovascular membrane usually stabilizes and generally regresses leaving a satisfactory visual acuity.

The commercial presentation of Lucentis is in a 3 ml vial with a chlorobutyl rubber stopper containing 0.23 ml of ranibizumab; a blunt 18-gauge filter needle and a 30-gauge injection needle are also included in the package (http://www.novartis.com.au/PI_PDF/luc.pdf). All the system is presented in a single closed package, to provide 0.05 mL of 10 mg/mL solution for intravitreal injection. Apart from concerns for sterility during drug removal, one drawback of this system is that syringe system has a significant dead space. The surgeon should withdraw all the fluid volume from the vial into a tuberculin syringe through a 18-gauge filter needle to obtain the desired injection volume and then insert a 30-gauge needle for intravitreal injection. All through this process we experience a great amount of drug volume sequestered at the dead spaces of both syringe and needle hubs (Fig. 1).



Fig. 1. We can see the drug volume sequestered due to dead spaces after injection of ranibizumab (Lucentis®)

2. MATERIALS AND METHODS

We evaluated the amount of fluid retained in two different types of syringes following injection (Fig. 2). Firstly, ten syringes with non-billed rubber stopper of Lucentis and 10 syringes with billed rubber stopper of 1ml tuberculine were weighed in a high precision bascule. In a second phase we filled the syringes with distilled water, removed air bubbles then pushed the syringe piston to the end. Afterwards, the syringes were immediately weighed again.



Fig. 2. A: Two different types of syringes: syringes with non - billed rubber stopper B: Syringes with billed rubber stopper

2.1 Data Analysis

Statistical analyses were performed using the Mann-Whitney U test. A p-value of less than 0.05 was considered to show a statistically significant result.

3. RESULTS AND DISCUSSION

Mean weight of syringes with billed and non-billed rubber stopper was 2.3264 ± 0.00823 and 2.4067 ± 0.0084 g, respectively. Following injection, mean weight of the experiment syringes with billed or non-billed rubber stopper was 2.3838 ± 0.0134 and 2.5011 ± 0.0063 , respectively. Volume of dead space was 0.0944 g for syringe with non-billed rubber stopper and 0.0574 g for syringe with billed rubber stopper ($p=0.001$).

Wolf et al. [1] indicated that an extra volume of 0.137 ml is required to obtain 0.05 ml of medicine. Ribeiro et al. [2] reported a volume loss of 0.05 ml from aspiration needle. Montero

et al. [3] reported that residual amount of drug due to dead space in needle with 30 and 18 gauge was 0.051 g (51 μ l=0.0051ml) and 0.073 g (73 μ l=0.0073ml), respectively. We showed that difference between two syringes was 0.037 g. This indicates that a significant amount of volume loss is due to dead space between syringe and needle.

Lucentis pre-filled syringe has been specifically designed to reduce the risk of adverse events to patients and to enhance the treatment process in the clinic. This new injection technology offers the potential for improved safety for patients through a reduction in non-sterile preparatory steps and the inclusion of more safety features, such as a non-retractable plunger [4]. On the other hand, remaining drug volume between syringe and needle hub might still be a problem for this pre-filled syringe system.

4. CONCLUSION

Consequently, design of pre-filled syringe system with billed rubber stopper will reduce significant amount of drug loss due to dead space volume. Also prevention of dead space loss may help to reduce cost of the drug. Moreover, suggested change in injection technique can be used for all intravitreal injection of small volumes such as aflibercept [5].

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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