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Original Article

# RESIDUAL VOLUMES AND FINAL WEIGHTS IN DIFFERENT TYPES OF PLASTIC INFUSION CONTAINERS

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**ABSTRACT**

**Objective:** To compare the residual volumes, the drained volumes, and the final weights of different infusion containers with different volumes and degrees of flexibility. The risk of drug error can be aggravated by a high residual volume remaining in a drained intravenous container. A high residual volume can also increase the final weight of the container after drainage.

**Methods:** A total of 80 infusion containers containing normal saline of four different brands (Viaflo® and Freeflex® flexible bags and KabiPac® and Ecoflac® Plus semi-rigid containers) in two different volumes (250 and 500 ml) were tested. Every container type was tested ten times under close-vent conditions. Residual and total drained volumes and weights of drained containers before and after drying were assessed.

**Results:** The residual volume that remained in the intravenous containers tested was lower than 2% of the declared volume, with only one exception (KabiPac® 250 ml), in which the residual volume was higher than 10% of the declared volume. Using gravity drainage, among the 250 ml containers, only one (Viaflo®) reached the full declared total drained volume of 250 ml. By contrast, among the 500 ml containers, only one failed to reach the declared drained volume. There were significant differences in favor of flexible bags in the final weights of containers after drainage, and in one case (250 ml KabiPac® semi-rigid container) the residual volume accounted for more than a half of the final container weight.

**Conclusion:** All four types of containers can be used with the same resulting quality of parenteral treatment. Selection of a specific type of container will be affected primarily by the price (both acquisition and waste disposal costs) and requirements of personnel for handling the container.

**Keywords:** Infusion therapy, Flexible, and semi-rigid containers, Residual volume



## INTRODUCTION

Infusion therapy is a method of drug delivery wherein the medication is slowly administered from the infusion container directly into the patient's vein through a needle or catheter, thus initiating a rapid and prolonged systemic response [1]. It is used when the patient's condition is too severe to be treated effectively with oral medications [2]. Intravenous therapy is used in the majority of in-patients [3] even though it is complex and relatively error prone [4]. Multiple steps are required in its preparation, administration, and monitoring [5]. Errors occurring at any stage of this process can cause serious adverse drug events, which may lead to increased morbidity and mortality [1]. One of the frequent medication errors during intravenous therapy is the delivery of an inadequate amount of the prescribed medication to the infusion container. This type of medication error is likely to be aggravated by a high residual volume remaining in the infusion container [6].

The role of the intravenous container and infusion set properties in the development of medication errors are of major importance. Nowadays, closed infusion systems are being preferred because they seem to be less associated with bloodstream infections than conventional open infusion systems [7].

A high residual volume in the infusion container may lead not only to the administration of an inadequate amount of the diluted active agent but also may increase the final weight of the empty container. This needlessly high weight results in more money being spent on waste disposal from the hospital budget.

The technological properties of the infusion container may also have an effect on the total volume of the fluid delivered, thus impacting the amount of the drug that the patient receives. Infusion containers can be categorized according to the declared volume or material of the intravenous container. Currently, various types of plastic compounds with different degrees of flexibility are the most common materials for intravenous containers. The two main types are flexible (fully collapsible) containers and semi-rigid containers with limited flexibility. Glass infusion bottles are still available, but their use is very limited because of the need for external venting to allow ambient air. Fully collapsible and semi-rigid containers can be used with infusion sets allowing gravity drainage under close-vent conditions.

In this study, we have compared the total drained volume, the residual volume of widely used infusion containers and the dependence of the residual volume on the final weight of the containers used.

## MATERIALS AND METHODS

### Infusion containers and infusion set

Four types of infusion containers, two fully collapsible (Viaflo® and Freeflex®) and two semi-rigid (KabiPac® and Ecoflac® Plus), were used for all the tests.

Commercially available medicinal products containing normal saline were used: *Fresenius 0.9% Sodium Chloride in Water for Injection* (Fresenius Kabi Italia S. r. l., Verona, Italy; Lot. No. Freeflex 250 ml: 14HD7104, 500 ml: 14HF7338, KapiPac 250 ml: 15HI617M1, 500 ml: 15HH341C1); *Sodium Chloride 0.9% Intravenous Infusion, 250 ml,* and *Sodium Chloride 0.9% Intravenous Infusion, 500 ml* (Baxter Healthcare Limited, Thetford, UK; Lot. No.: 250 ml: 15I13E4L, 500 ml: 14I02L40); and *Braun Sodium Chloride 0.9%* (B. Braun Melsungen AG, Melsungen, Germany; Lot No.: 250 ml: 14346450, 500 ml: 14402452).

A total of 80 plastic intravenous containers containing normal saline were divided based on the nominal volumes (250 ml and 500 ml), a degree of flexibility of the plastic material, and brands into eight groups each consisting of ten containers. The GAMA IS-103® (Lot. No.: 140020, Gama Group a. s., Jimramov, Czech Republic) infusion set was used for all the tests.

The infusion containers tested differ in their physicochemical composition. All are made of PVC-free material.

The composition of Viaflo® is co-extruded. There are three layers in the container. The inner layer is made of chemically inert polyethylene. The middle and outer layers are made of polyamide and polypropylene, respectively. The infusion containers manufactured by Fresenius (Freeflex® and KabiPac®) are made of PVC-free materials. According to the manufacturer, the Ecoflac® Plus container is made of a pure medical grade polyethylene. All infusion containers are approved for use in the European Union. In table 1, the geometrical description of intravenous containers is summarized.

**Table 1: The height (A), width (B), and in semi-rigid containers with oval cross-section also the depth (C) of the infusion containers used and the length (D) and diameter (E) of the chimney are summarized**

| | Brand name | A | B | C | D | E |
|---|---|---|---|---|---|---|
| 250 ml | Viaflo® | 17.1 cm | 11.8 cm | N/A | 1.6 cm | 0.8 cm |
| | Freeflex® | 21.3 cm | 8.3 cm | N/A | 3.1 cm | 0.8 cm |
| | KabiPac® | 11.5 cm | 7.4 cm | 4.1 cm | 3.2 cm | 2.5 cm |
| | Ecoflac® Plus | 14.1 cm | 7.4 cm | 4.3 cm | 3.0 cm | 2.4 cm |
| 500 ml | Viaflo® | 26.8 cm | 11.8 cm | N/A | 1.6 cm | 0.8 cm |
| | Freeflex® | 20.2 cm | 12.2 cm | N/A | 3.1 cm | 0.8 cm |
| | KabiPac® | 16.3 cm | 9.1 cm | 5.1 cm | 3.2 cm | 2.5 cm |
| | Ecoflac® Plus | 18.2 cm | 8.1 cm | 5.5 cm | 3.0 cm | 2.4 cm |

**Measurements**

All the procedures were conducted under standard laboratory conditions. For the weight measurement, the KERN scale model 440-47 (accuracy 0.1 g) was used. The full weights of all containers were measured (M1) and, subsequently, the containers were spiked by the GAMA IS-103 infusion set. A standard draining rack to allow gravity drainage under close-vent conditions was used, and the solution was drained into a tared beaker. After gravity drainage, all the containers were weighed again (M2). The indirect method for the measurement of the residual volume was used. Plastic containers were opened to allow draining with laboratory paper until dry. Following that, the weights of empty plastic bags were measured again (M3). Residual volume was determined from the difference between the weights (M2-M3), and the volume was then calculated by using the density and weight of the solution. Similarly, the total drained volume was determined using the difference between the weight of the beaker after and before drainage. The density of the saline solution was taken into consideration.

**Statistical analysis**

Mean residual volume and SD were calculated. For the statistical analysis of the differences between containers, the one-way analysis of variance and subsequent post hoc Tukey's HSD test was used. Differences were considered to be statistically significant when $p<0.05$. The statistical analysis was performed using the Statistica Cz 12 software (Stat Soft CR, Prague, Czech Republic).

**RESULTS**

Fig. 1 summarizes the final residual volumes in drained infusion containers with total volumes of 250 ml and 500 ml. The lowest residual volume was observed in the Viaflo® flexible bags (1.3±0.2 ml for 250 ml). For the Freeflex®, the increase in residual volume was 2.0-fold compared with Viaflo®. The significantly highest residual volume was observed in the KabiPac® semi-rigid container (a 25.2-fold increase compared with Viaflo® with $p<0.001$). The residual volume in semi-rigid Ecoflac® Plus containers was 3.0-fold higher in comparison with Viaflo®. Similar results were obtained in containers with the declared volume of 500 ml. The lowest residual volume was observed in Viaflo® flexible packs (1.4±0.3 ml). Flexible Freeflex® containers retain a 2.8-fold higher residual volume than Viaflo® plastic bags. Similarly, for KabiPac® 500 ml, a 13-fold increase in the residual volume was observed compared with Viaflo®. The residual volume of this semi-rigid container significantly differs from all the other containers tested ($p<0.001$). For the semi-rigid Ecoflac® Plus containers, a 2.9-fold increase in the residual volume was observed, very similar to the flexible Freeflex® containers. None of these differences was statistically significant in comparison with Viaflo®.

An important indicator of the quality of parenteral administration systems is the ability to deliver the declared volume of the drug to the patients. In fig. 2, the results of total drained volume for all the containers tested with the declared volumes of 250 ml and 500 ml are summarized. In containers with the declared volume of 250 ml, the exactly declared volume of 250 ml was drained only from the Viaflo® flexible pack. For both KabiPac® and Freeflex®, the differences were significant, with $p<0.05$ and $p<0.001$ for Freeflex® and KabiPac®, respectively. For semi-rigid KabiPac® containers, the drained volume was only 84% of the declared volume. The semi-rigid Ecoflac® Plus plastic container did not differ significantly from Viaflo®, but it's drained volume did not reach 250 ml. As shown in fig. 2, in the group of 500 ml containers, only the KabiPac® semi-rigid plastic container failed to reach the declared drained volume (472.2±5.9 ml with $p<0.001$, compared with all the other containers tested). Similarly to the group of containers with the declared volume of 250 ml, the highest drained volume of 500 ml containers was obtained in Viaflo® flexible bags.

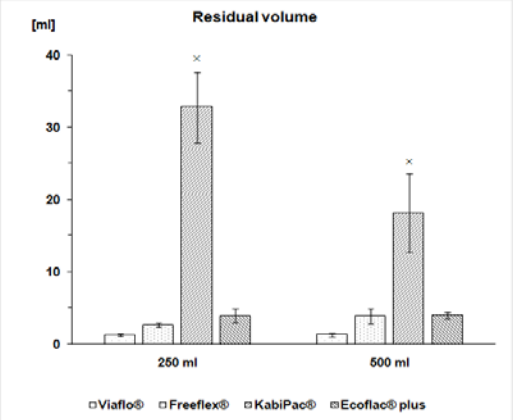


**Fig. 1: Final residual volumes after gravity drainage under closed-vent conditions for different container types, volumes, and brands. KabiPac® significantly differs from the other 250 ml as well as 500 ml containers tested. Data are expressed as means±SD, n = 10. × p<0.001 KabiPac® 250/500 vs. Viaflo® 250/500, Freeflex® 250/500 and Ecoflac® Plus 250/500**

An interesting result was also found concerning the final weight of empty containers after drainage. The results in fig. 3 summarize the mean empty weights of all containers. The lowest weights were obtained for both flexible Viaflo® bags; 12.3±0.2 g for containers with the declared volume of 250 ml and 16.4±0.3 g for 500 ml containers. The residual volume represents 11% and 9% of the measured total weight for Viaflo® containers, respectively.

The highest final empty container weight was observed in KabiPac® for both volume sizes; a 4.7-fold increase for 250 ml and a 3.5-fold

increase for 500 ml containers compared with Viaflo® flexible packs (all p<0.001). Only the flexible Freeflex® containers did not differ significantly from Viaflo® bags. For the KabiPac® containers, the amount of the residual volume represents 56% and 37% of the total drained container weight, respectively. The corresponding values for flexible Freeflex® containers were 20% for 250 ml containers and 23% of the final total weight for 500 ml containers. Semi-rigid Ecoflac® Plus containers significantly differed from flexible Viaflo® bags; a 2.4-fold increase for containers with the volume of 250 ml and a 2.2-fold increase for 500 ml containers (all p<0.001). For these semi-rigid containers, the weight of the residual volume accounts for 14% and 11% of the total measured drained container weight, respectively.

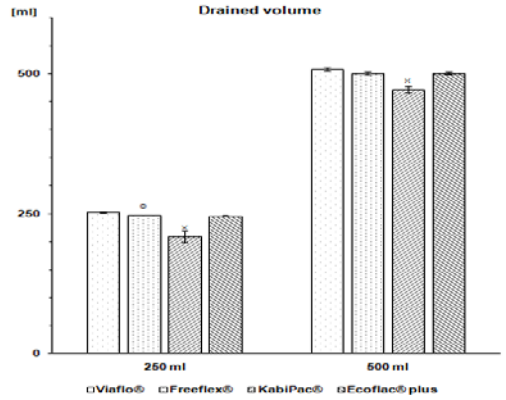


**Fig. 2: The mean drained volume after gravity drainage under closed-vent conditions for different container types, sizes, and brands. In the group with the declared volume of 250 ml, only Viaflo® reached the declared drained volume and significantly differed from Freeflex® and KabiPac®. In the group of 500 ml containers, only KabiPac® did not reach the declared volume and significantly differed from the other containers tested. Data are expressed as means±SD, n = 10. ○ p<0.05 Viaflo® 250 vs. Freeflex® 250; × p<0.001 Viaflo® 250 vs. KabiPac® 250 × p<0.001 KabiPac® 500 vs. Viaflo® 500, Freeflex® 500 and Ecoflac® Plus 500**

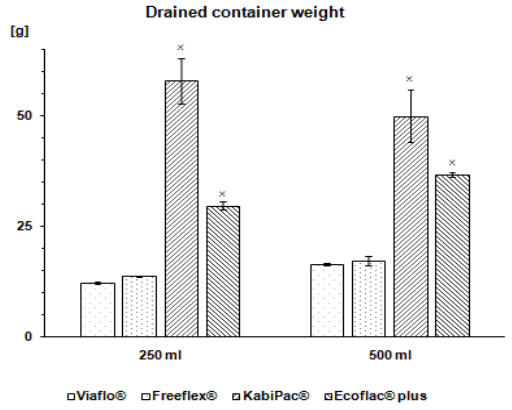


**Fig. 3: Comparison of the mean final weight of empty containers after gravity drainage. Viaflo® showed the significantly lowest final weight compared with Ecoflac® Plus and KabiPac® for containers with the declared volume of 250 ml as well as 500 ml (× p<0.001). Data are expressed as means±SD, n = 10. × p<0.001 Viaflo® 250/500 vs. KabiPac® 250/500, and Viaflo® 250/500 vs. Ecoflac® Plus 250/500, Freeflex® 250/500 vs. KabiPac® 250/500 and Freeflex® 250/500 vs. Ecoflac® Plus 250/500**

## DISCUSSION

Parenteral treatment is error prone. There are several steps where critical mistakes can occur, and some mistakes may be, at least, aggravated by the properties of infusion containers and administration system. Bloodstream infections in critically ill patients in intensive care units are probably the most serious and potentially fatal errors. A solution prepared for parenteral administration in an infusion container may be contaminated by microorganisms from a contaminated air influx [8]. This can occur when external venting is required for the full drainage of fluid as in the case of glass bottles or non-flexible plastic containers. Both flexible and semi-rigid plastic containers made of PVC or non-PVC materials can be used with a closed infusion system to prevent the administered solution from being contaminated by microorganisms from the external air [7]. This is the reason why we only used a closed infusion administration system for our study.

A closed infusion set may slightly increase the residual volume in semi-rigid infusion containers as was previously shown [9]. Despite this, we decided to use the closed infusion set, taking into account the fact that all the infusion packages tested are recommended to be used with a closed set. The high residual volume can have various consequences for the quality of parenteral treatment. Patients may suffer from an inadequate administration of medication, particularly those treated with antibiotics for a severe infection wherein an inadequate dose may increase the risk of treatment failure or the incidence of microbial resistance [10]. The admixed drug remains in the residuum, and this amount of active agent cannot be delivered to the patient. The residual volume is likely to depend greatly on the flexibility of the infusion bag and the properties of the infused solution. The properties of the infusion container affect the residual volume and the flow rate of intravenous fluid administration [11]. However, the flow rate depends on the liquid height in the bag, as was demonstrated previously [12].

In this study, we tested all four infusion containers widely used in both our country and the whole European Union. The volumes of 250 ml and 500 ml are the most widely used volumes of infusion containers. Because the smaller volumes as 50 ml or 100 ml are not equally popular in all countries, we did not test them in this study although we presume that a lower nominal volume of infusion container might be associated with an even greater proportion of the residual or dead volume [6, 13]. All four types were found to be able to deliver almost the complete amount of the admixed drug. There were no statistically significant differences in the total drained volume of normal saline between the infusion containers of different materials and flexibility, with an exception of the 250 ml KabiPac® semi-rigid container, which significantly differed from all the other containers tested. In this particular case, the delivered amount of the admixed active drug may be less than 90% of the required dose. This may be harmful to patients treated with medications with a low therapeutic range. A high residual volume might cause serious consequences, particularly when a drug with a narrow therapeutic range is admixed to the infusion container. A patient may be under dosed and suffer from inadequate treatment due to the delivery of an incorrect dose. On the other hand, the administration of a slightly lower amount of saline alone is usually harmless. For this reason, we suggest that flexible bags are more appropriate for the delivery of drugs with a low therapeutic margin.

Our results are consistent with the conclusion of Lannoy *et al.*, [6]. They tested the impact of the infusion containers used on the residual volume. Similarly, flexible bags provided a lower residual volume than semi-rigid plastic containers. While in the aforementioned study a higher residual volume in all the semi-rigid containers was found, our study shows that the newer semi-rigid Ecoflac® Plus container is comparable with fully collapsible infusion bags both in terms of residual volume and total drained volume. The novelty of our work is the use of containers made of newer plastic materials than in the previously mentioned studies. The biggest progress in the material of the container has been shown in semi-rigid Ecoflac® Plus. Ecoflac® B. Braun used in the previous study was more rigid and provides a larger residual volume than Ecoflac® Plus shown in our study.

Obviously, a solution with admixed drug may remain not only in the infusion container but also in the lines and drip chamber of the infusion set. Ideally, this amount should be constant, and the dead volume should depend predominantly on the amount of the residual volume in the infusion container.

Waste disposal usually costs a considerable sum of money from the hospital budget. The amount typically depends on the weight of the waste being disposed of. We found out that the residual volume remaining in an empty container after drainage may make up an important part of the weight of the container. In general, for flexible containers, the amount of the residuum did not significantly increase the weight of the containers in both volume sizes, but in the case of semi-rigid plastic containers, the weight of the residuum made up an important part of the total weight. Thus, we suggest that the material and flexibility of the infusion container may not only considerably influence the total weight of the containers but, in particular, the final weight of the container after drainage, which is also significantly dependent on the total volume of the residuum of the solution. This may increase the weight of the waste as well as the cost of waste removal. From this perspective, both tested collapsible containers (Viaflo® and Freeflex®) seem to be more advantageous.

In general, all the infusion containers tested are of approximately the same high quality. We showed that Viaflo® flexible bags provided the lowest residual volume, lowest final weight, and highest drained volume. By contrast, KabiPac® semi-rigid containers provided the highest residual volume, highest final weight, and lowest drained volume. On the other hand, a major advantage of these containers is their low cost, which is significantly different from the cost of the other containers tested produced by Fresenius, i.e. the Freeflex® flexible bags. These containers are of similar quality in terms of all the measured parameters compared with Viaflo® flexible bags. The quality of the Ecoflac® Plus infusion containers was similar to that of the other containers tested, and their parameters measured in our study were usually in between those of the Viaflo® and KabiPac® containers.

This study was carried out purely under laboratory conditions, which determines its limits. In common practice, a number of different external factors exist that can affect the total volume of the administered infusion.

## CONCLUSION

In conclusion, all four types of containers can be used with the same resulting quality of parenteral treatment. Selection of a specific type of container will be affected primarily by the price (both acquisition costs and waste disposal costs) and requirements of personnel for handling the container. Flexible bags or semi-rigid containers made of new materials are more appropriate for the delivery of drugs with a low therapeutic margin. These bags are able to deliver almost the entire nominal volume. All flexible bags had a lower weight than semi-rigid containers, and lower weight means lower cost for waste removal. On the other hand, we did not test all volumes available in our country, especially those under 250 ml, because they are not so popular in our country.

## ACKNOWLEDGMENT

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## CONFLICT OF INTERESTS

The authors have declared that there is no conflict of interest.

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