

Evaluation of Regular Insulin Adsorption to Polypropylene Bag and Polyvinyl Chloride Infusion Set

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Abstract

Aim Clinical application of insulin infusion therapy is usually accomplished with regular human insulin. It is known that the regular insulin adsorbed to the hydrophobic surfaces and different approaches were implemented into the clinical practices. It was aimed to evaluate the rate of adsorption of insulin to PP bags and PVC infusion sets and stability of insulin during the infusion. **Methods** 100 IU insulin was added to PP bags containing 100 ml of 0.9% NaCl solution (n = 6). The infusion was started at a rate of 2 ml/h using infusion sets in the PVC structure. Insulin quantification was performed in the samples taken both from the bag and from the end tip of the infusion set during infusion. The stability of insulin solutions stored at room (+24°C) and refrigerator (+4°C) temperatures were compared. Samples were analyzed using reverse-phase high-performance liquid chromatography. **Results** No statistically significant difference was found between the concentrations of the samples taken from the bags stored at room and refrigerator temperatures at the 4th, 12th, and 24th hours (p>0.05). It was seen that the adsorption rate of insulin to PVC set was 57% and PP bags is at most 5% at the 24th hour. **Conclusion** When PP bags are used for insulin infusion, it is predicted that 24-hour change can be made instead of frequent change. In addition, losses caused by the high rate of insulin adsorption to PVC infusion sets should be considered and PP infusion sets would be the better option to use if available.

Evaluation of Regular Insulin Adsorption to Polypropylene Bag and Polyvinyl Chloride Infusion Set

Running Title: Clinical application of insulin infusion

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Abstract

Aim

Clinical application of insulin infusion therapy is usually accomplished with regular human insulin. It is known that the regular insulin adsorbed to the hydrophobic surfaces and different approaches were implemented into the clinical practices. It was aimed to evaluate the rate of adsorption of insulin to PP bags and PVC infusion sets and stability of insulin during the infusion.

Methods

100 IU insulin was added to PP bags containing 100 ml of 0.9% NaCl solution ($n = 6$). The infusion was started at a rate of 2 ml/h using infusion sets in the PVC structure. Insulin quantification was performed in the samples taken both from the bag and from the end tip of the infusion set during infusion. The stability of insulin solutions stored at room ($+24^{\circ}\text{C}$) and refrigerator ($+4^{\circ}\text{C}$) temperatures were compared. Samples were analyzed using reverse-phase high-performance liquid chromatography.

Results

No statistically significant difference was found between the concentrations of the samples taken from the bags stored at room and refrigerator temperatures at the 4th, 12th, and 24th hours ($p > 0.05$). It was seen that the adsorption rate of insulin to PVC set was 57% and PP bags is at most 5% at the 24th hour.

Conclusion

When PP bags are used for insulin infusion, it is predicted that 24-hour change can be made instead of frequent change. In addition, losses caused by the high rate of insulin adsorption to PVC infusion sets should be considered and PP infusion sets would be the better option to use if available.

What is already known about this topic?

- It is known that the regular insulin adsorbed to the surfaces of polyvinyl chloride bags and infusion sets, which are generally used in hospitals, and not to the polypropylene surfaces.
- There are different data about the adsorption rates and approaches were implemented into the clinical practices in the literature.
- There is a lack of information regarding the stability of the insulin solution at room temperature.

What does this article add?

- As a result of the study, it has been determined that insulin solutions are stable at both room and refrigerator temperatures over 24 h storage.
- It has been determined that the rate of adhesion of insulin to polyvinyl chloride surface is different from that stated in the literature.
- These results may change the clinical practice.

Introduction

Hyperglycemia is common in critically ill patients and is a modifiable risk factor that increases morbidity and mortality [1-4]. For many years, optimal treatment of hyperglycemia has been discussed in intensive care units [5]. The American Clinical Endocrinologists Association and the American Diabetes Association recommend keeping glucose levels between 140-180 mg/dL for glycemic control in critically ill patients [6,7]. In critically ill patients, continuous iv insulin infusion has been shown to be the best route to achieve glycemic targets and prevent glycemic fluctuations [7]. Clinical application of insulin infusion therapy is usually accomplished with regular human insulin [2,8]. It is known that the regular insulin adsorbed to the surfaces of polyvinyl chloride (PVC) bags and infusion sets, which are generally used in hospitals, and not to the polypropylene (PP) surfaces. However, there are different data about the adsorption rates in the literature [9-16]. Therefore different approaches were implemented into the clinical practices, such as changing the bag every 4 or 12 hours, to minimize the adsorption of insulin to the bag during the infusion [17-19].

In this study, it was aimed to evaluate the rate of adhesion of insulin solutions to PP bags and PVC infusion sets and stability times at room temperature (+24° C) during the infusion.

Methods

Chemicals

Insulin (Humulin R, Lilly²), PP bags (Polifarma²) and PVC infusion sets (Sapphire²) were obtained from a pharmaceutical warehouse. All the chemicals were analytical grade on preparing buffers and solutions. Acetonitrile was purchased from Merck (Darmstadt, Germany). Ultrapure water was purchased from the Milli-Q water system (Barnstead, USA).

Analytical Conditions

Chromatographic methods for insulin are included in the Turkish Pharmacopoeia [20]. In this study, insulin was analyzed by reverse phase high performance liquid chromatography (RP-HPLC) which the assay was validated according to international guidelines [21]. Briefly, the LC system (Agilent 1220 Infinity II) consisted of a gradient pump, a degasser, and a UV detector (Thermo Separation Products, USA). The separations were achieved by a C18 Phenomenex column (250 x 4.6 mm, 100Å, 5 µm i.d.) at room temperature. The mobile phase was acetonitrile:phosphate buffer (50:50 v/v, pH:3.0, 10 mM) and, solutions delivered at a flow rate of 1mL/min which gave the optimum chromatographic conditions. Injection volume was 20 µL and UV detection was performed at 214 nm.

Sample Preparation

In the study, solutions containing 1 IU/mL concentration (n = 6) were prepared by adding 100 IU insulin to PP bags containing 100 ml of 0.9% NaCl solution. Also, PVC infusion sets were used. In the experimental setup established in accordance with clinical practice, the infusion rate of the solutions was determined as 2 IU/hour through the infusion pump. 600 µL samples were taken from the bag at the beginning of the infusion (hour 0), as well as from the bag and at the end tip of the infusion set at the end of the 1st, 2nd, 4th, 12th and 24th hours. In each sample taken, insulin quantification was made. This experimental procedure was carried out simultaneously with 6 separate insulin solutions prepared at room temperature. As a result of the analysis of the samples taken from each bag and set at specified times, the adsorption rates of insulin to PP bag and PVC infusion set were evaluated.

Also, to evaluate the stability of insulin solutions at room temperature during infusion, the analysis results of samples taken from insulin solutions stored at room (+25°C) and refrigerator (+4°C) temperatures at 0, 4, 12 and 24 hours were compared.

Statistical analysis

Statistical evaluation was performed using Student's t-test and the *p* values [?]0.05 were considered statistically significant. In the beginning (0 hours), insulin solutions in PP bags are the control group.

Results

The samples required to evaluate the amount of insulin adsorbed to PP bags were collected simultaneously from 6 separate infusion bags. In the analysis of these samples, the insulin concentration rate of 100% was accepted at baseline (0 hours). The insulin concentration rates of the samples taken from PP bags at the 1st, 2nd, 4th, 12th, and 24th hours of the infusion were determined as 95%, 98%, 98%, 95%, and 100%, respectively (Table 1).

The samples required to evaluate the amount of insulin adsorbed to the PVC infusion set were collected simultaneously from the end tips of the 6 separate infusion sets. The insulin concentrations of the samples collected at the 1st, 2nd, 4th, 12th, and 24th hours of the infusion were determined as 43%, 40%, 30%, 21% and 35%, respectively (Table 1).

To evaluate the stability of the insulin solution at room temperature, the insulin concentrations of the solutions in PP bags stored at room (+25degC) and at refrigerator (+4degC) temperatures were compared. The insulin concentration in the PP bag, stored at + 4deg C, was initially considered 100% (0 hours). No statistically significant difference was found between the concentrations of the samples taken from the bags stored at room and refrigerator temperatures at the 4th, 12th, and 24th hours ($p>0.05$) (Figure 1).

Discussion

Adsorption is a nonspecific phenomenon that occurs with every solid particle. This phenomenon is particularly important with insulin, because it alters the rate of drug delivery to patient, and finally impacts glycemic control [18]. In order to minimize insulin loss due to adsorption and optimal glycemic control, appropriate clinical practices should be determined according to the rate of insulin adsorbed to the bag and set used during infusion.

In this study, the insulin concentration rates of the samples taken from PP bags at the 1st, 2nd, 4th, 12th, and 24th hours were determined as 95%, 98%, 98%, 95%, and 100%, respectively. Accordingly, it has been shown that the rate of insulin adsorption to PP bags is at most 5%, and this rate decreases after the first hour of infusion. In a study by Jakobson et al. it was shown that insulin adsorbed 10% to the PP bag at the first hour of infusion, and then this rate was decreased while insulin was administered at a rate of 1 ml/h. Similarly, the maximum adsorption rate was achieved at the 1st hour and then reduction was determined in both studies [10]. The difference between the maximum adsorption rates is thought to result from the difference in infusion rates. It is reported that the rate of adsorption increases with a slower infusion rate [10,16-22].

The insulin concentration of the samples taken from the end tip of the PVC infusion set, at the 1st, 2nd, 4th, 12th, and 24th hours were detected as 43%, 40%, 30%, 21% and 35%, respectively. Accordingly, it was seen that the adsorption rate of insulin to PVC set was 57% at the 1st hour and 65% at the 24th hour. In the study conducted by Zahid et al., it was shown that the adsorption rate of insulin to the PVC neonatal tube was approximately 55% at 3 hours and 15% at 24 hours [16]. It is thought that the high adsorption rate determined in our study may be due to the surface area difference of the sets used in both studies. In the study of Trissel et al., it was reported that the 24-hour adsorption rate of insulin to the PVC bag was 35%. However, in Trissel's study, the sample was taken from the PVC bag at the beginning and after 24 hours storage, not during infusion [15]. Although the methods of both studies are different, it has been shown that the maximum adsorption rate was within the first 4 hours and then reduction in this rate was detected. So, changing the bag every 4 hours, which is frequently applied in clinical practice, leads to an increase in insulin loss.

It is thought that changing PVC and PP bags every 24 hours is more appropriate in terms of both preventing insulin loss and reducing workload. Besides, economic advantages of changing insulin solution bag every 24 hours versus 4 hours should be considered in terms of minimization of manpower (time spend for administration frequency and preparation), sources (bag and solution) and insulin loss. However, the stability of the insulin solution is of concern when using the bags for 24 hours. Also, there is no information on the stability of the insulin solution at room temperature in the package insert. As a result of the analysis, the insulin solution has been shown to maintain its stability for 24 hours at room temperature.

Conclusion

As a result of the study, it has been determined that insulin solutions are stable at both room and refrigerator temperatures over 24 h storage. When PP bags are used for insulin infusion, it is predicted that 24-hour change can be made instead of frequent change. In addition, losses caused by the high rate of insulin adhesion to PVC infusion sets should be considered and PP infusion sets would be the better option to use if available.

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