Deadspace : A Potential Error in Concentration of Medication During Dilutional Process in Neonates

ARUCHALEAN WATANACHAI, BSc*,
CHITTIWAT SUPRASONGSIN, MD*

Abstract

Objective : To evaluate the volume of deadspace (DS) and degree of errors in concentration of medications during medication dilution with needle removable syringe (NRS) compared to needle nonremovable syringe (NNRS).

Material and Method : 300 syringes were tested and divided into 3 groups as follows: The first group was 100 syringes of needle removable insulin 1 ml syringe (NRIS) with a 27 gauge needle (Terumo®), the second group was 100 syringes of NRIS with a 27 gauge needle (Nipro®) and third group 3 was 100 syringes of needle non removable insulin syringe (NNRIS) with a 27 gauge needle (Terumo®). All syringes with needle sets (without needle cover) were weighed with a Mettler electronic balance. Volume of DS was measured and calculated using a standard method. 10 syringes of each group were randomly selected to test for degree of errors in concentration of medications during the dilutional process using standard insulin (310 micro unit per ml) as a medication for dilution. All specimens were collected by ejecting all diluents into collecting tubes and insulin concentrations were measured using radioimmunoassay technique (insulin-CT biointernational, France) twice in each sample. Concentration was then calculated back and the results were noted and analysed.

Results : Means of DS in group 3 (2.4 ± 0.8 μl) was significantly less than group 1 (49.7 ± 00.9 μl) and group 2 (65.3 ± 0.7μl) (median = 2 microlitre). All three groups were significantly different from each other with the largest DS in group 2. After dilution, insulin concentrations from diluents in group 3 were still close to standard insulin (335 ± 28 *vs* 310 microunits/ml), whereas group 1 and 2 were significantly higher than group 3 (1.7 and 1.9 times) and standard insulin (1.8 and 2 times).

Conclusions : DS in NRIS is not negligible and is considered a potential source of error in the concentration of medications when it is used to dilute parenteral medications in the neonatal intensive care unit (NICU).

Key word : Deadspace, Neonatal, Needle Nonremovable Insulin Syringe, Needle Removable Insulin Syringe, Dilution, Concentration

WATANACHAI A & SUPRASONGSIN C
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* Research Center, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

Deadspace (DS) is defined as the volume of a solution retained in the hub and needle when the plunger of the syringe is fully depressed. DS can lead to the delivery of an inadequate dose of drug and result in a poor response in adults[1]. However small volumes of drug retained in DS may have a surprisingly higher effect on the newborn. Most medications are designed in the concentration that is proper for adults and children. In the neonatal intensive care unit (NICU), dilution of perenteral medication is needed. In general practice, an NICU nurse usually uses a 1 ml-syringe to dilute parenteral medication due to the small amount of medication. These syringes are designed as 2 types; needle removable syringe (NRS) and needle non removable syringe (NNRS). NRS is more popular for medication dilution because its needle can be changed after the dilutional process and eliminates the potential of bacterial contamination during the process. The amount of parenteral medication retained in the hub and needle may be negligble in adults, but not in newborn. This DS is a potential source of error when drugs are diluted using a syringe which contains a large DS. Therefore, this study was designed to assess the amount of DS and effect of DS that causes an error of drug concentration produced by DS using insulin as a model.

MATERIAL AND METHOD

Three hundred syringes were tested and divided into 3 groups as follows:

Group 1: 100 syringes of needle removable insulin 1 ml syringe (NRIS) with a 27 gauge needle (Terumo® syringe with needle tuberculin, Terumo corporation, Tokyo, Japan).

Group 2: 100 syringes of NRIS with a 27 gauge needle (Nipro insulin®, Nissho corporation, Osaka, Japan)

Group 3: 100 syringes of needle non removable insulin syringe (NNRIS) with a 27 gauge needle (Terumo® syringe U-100 insulin, Terumo corporation, Tokyo, Japan)

Study volume of DS

All syringes, with needle sets (without needle cover) were weighed with a Mettler electronic balance (Mettler- Toledo model AG 245, Greifense, Switzerland) The reproducibility of the balance had a standard deviation of 0.02 mg and was calibrated before use. Sterile water was drawn in the standard manner with 0.5 ml. Then the plunger was pushed all the way through until it hit against the hub of the syringe. All air bubbles were evacuated wherever possible. The syringe with the needle was dried and reweighed. DS was calculated using the weight gain difference between the first and second measure. It was assumed that 1 g of sterile water retained equal to 1 ml of DS.

Study effect of DS to insulin concentration after dilution

Ten syringes of each group were randomly selected. Standard insulin (310 micro unit per ml) was used as the medication for dilution. Insulin was drawn slowly to 0.3 ml without air bubbles then ejected out to 0.1 ml. Sterile water was slowly drawn in the same syringe up to 1 ml level without air bubbles. All specimens was collected by ejecting all the diluent into collecting tubes. Insulin levels in the diluents were measured using the radioimmunoassay technique (insulin-CT biointernational, France) twice in each sample. Concentrations were then calculated back and the results were noted and analysed.

Statistical analysis

SPSS version 9.01 for windows was used for analysis. Kruskal Wallis test and Mann Whitney test were performed. A p-value of 0.05 was taken to be significant.

RESULTS

Volume of DS are presented in Table 1. Means of DS in group 3 which was the non removable needle group (2.4 ± 0.8 μl) is significantly less than group 1 (49.7 ± 00.9 μl) and group 2 (65.3 ± 0.7μl) (median = 2 microlitre) using Kruskal Wallis test (data did not pass the homogeneity test).

Using the Mann Whitney test to test the difference among groups, all three groups were significantly different from each other with the largest DS in group 2.

Study effect of DS to insulin concentration after dilution

Table 2 depicts the means of insulin concentration in all three groups compared to standard insulin. In group 3, insulin concentration after dilution was still close to standard insulin (335 ± 28 μl micro units *vs* 310 μl), whereas, group 1 and 2 were significantly higher than group 3 and standard insulin. Means

Table 1. Estimated weight, volume of deadspace and concentration of insulin created by deadspace in each group.

	Estimated weight of DS (mean ± SE) (milligram)	Estimated volume of DS (mean ± SE) (microlitre)	Estimated concentration of insulin in DS (unit) (if using 100 units per ml of insulin)
Group 1 NRIS (Terumo®)	49.7 ± 0.9*	49.7 ± 0.9	5
Group 2 NRIS (Nipro®)	65.3 ± 0.7*	65.3 ± 0.7	6.5
Group 3 NNRIS (Terumo®)	2.4 ± 0.1*	2.4 ± 0.1	0.2

NRIS = Needle removable insulin syringe,
NNRIS = Needle nonremovable insulin syringe,
DS = Deadspace, SE = Standard error.
*$p < 0.001$ when compared to the other two groups.

Table 2. Concentration of insulin in deadspace of all three groups.

	Concentration (mean ± SE) (microunit per millilitre)
Standard insulin	310
Group 1 NRIS (Terumo®)	540 ± 54
Group 2 NRIS (Nipro®)	617 ± 45*
Group 3 NNRIS (Terumo®)	335 ± 28**

NRIS = needle removable insulin syringe,
NNRIS = needle nonremovable insulin syringe,
SE = standard error.
* $p = 0.31$ when compared to group 1
** $p = 0.032$ when compared to group 1 and 0.008 when compared to group 2

of insulin levels in group 1 was 1.7 times and group 2 was 1.9 times that of group 3 and equal to 1.8 times and 2 times of standard insulin.

DISCUSSION

The deadspace of a syringe is usually not available as part of the product information. In a general nursery intensive care unit, dilution of medication for parenteral use is common. Avoiding contamination to serious infection is the first priority in clinical practice in neonatal intensive care units (NICU). Using a needle removable needle syringe to dilute parenteral medications is generally accepted in pediatric intensive care units due to aseptic technique. However, the effect of DS is usually neglected. In the past, insulin was usually prepared in two strengths; a more dilute concentration (20-40 units per ml) for neonates and higher concentration (100 units per ml) for children and adults. Even with the lower concentrations, hypoglycemia was usually reported in neonates after using a glass syringe[2]. Nowadays, only higher concentration insulin is available. The necessity to dilute insulin for the treatment of neonatal hyperglycemia is unavoidable. A plastic syringe which is used as disposable syringe has less DS[3] and has become more popular. However, there are two types of insulin syringe on the market; a needle removable insulin syringe (NRIS) and a needle non removable insulin syringe (NNRIS). Both types are equally popular. Unfortunately NRIS is more popular in neonatal practice when used to dilute parenteral medication in the NICU because the needle can be change after the dilutional process.

This study shows that an NRIS has an unneglectable volume of DS (5 and 6.5 microlitre). Using insulin as a model (100 units per ml), this DS contributed to a loss of 5 and 6.5 units per injection. Type 1 diabetes patients who inject insulin two times per day, will loose at least 10-13 units of insulin per day.

The most pronounced effect of DS is the potential error in concentration of the diluted medication. The authors demonstrated that higher insulin concentrations (1.8 and 2 times of standard insulin) were obtained when using the same needle of NRIS to draw both insulin and sterile water during the dilutional process as generally practiced in NICU. Higher insulin concentrations can cause hypoglycemia in patients who need insulin treatment. The hazard effect is more pronounced if an NRIS is used to dilute special emergency medications such as adrenaline.

In summary, this study demonstrated that DS in NRIS is a potential error in concentration when it is used to dilute parenteral medications in the NICU.

Newborn patients who need a very small amount of medication; dilutional of medication is unavoidable. Therefore, an NNRIS is recommended to avoid this potential error. Awareness of contamination is still needed and can be prevented by a good aseptic technique. Moreover, in normally use, an NNRIS can save more medications than an NRIS when medication is administered without dilution.

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ผลของปริมาตรคงค้างปลายหลอดฉีดยาที่มีต่อความผิดพลาดของความเข้มข้นของยาหลังการเจือจางยาเพื่อใช้ในเด็กทารกแรกเกิด

อรัชลีพห์ วัฒนชัย, วทบ, จิตติวัฒน์ สุประสงค์สิน, พบ**

วัตถุประสงค์ : เพื่อประเมินปริมาตรคงค้างปลายหลอดฉีดยา (Deadspace) และความผิดพลาดของความเข้มข้นของยา เมื่อทำการเจือจางยาด้วยหลอดฉีดยาชนิดที่ถอดหัวเข็มได้เทียบกับชนิดที่ถอดหัวเข็มไม่ได้

วัสดุและวิธีการ : ทำการทดสอบหลอดฉีดยาอินสุลินขนาด 1 ซีซี พร้อมเข็มเบอร์ 27 จำนวน 300 ด้าม โดยแบ่งเป็น 3 กลุ่มคือ กลุ่มแรก เป็นชนิดถอดเข็มได้ (Terumo®) กลุ่มที่ 2 เป็นชนิดถอดเข็มได้ (Nipro®) และกลุ่มที่ 3 เป็นชนิดถอดเข็มไม่ได้ (Terumo®) กลุ่มละ 100 ด้าม และทำการชั่งหลอดฉีดยาพร้อมเข็ม (ไม่รวมคลุมเข็ม) ด้วย เครื่องชั่งเบ็ทเทลอ ทำการวัดปริมาตรคงค้าง ในแต่ละกลุ่มและเปรียบเทียบ จากนั้นสุ่มหลอดฉีดยากลุ่มละ 10 ด้ามมาวัดความเข้มข้นของอินสุลินหลังการเจือจาง เพื่อหาความผิดพลาดของความเข้มข้นของยาหลังการเจือจางยา โดยใช้อินสุลินขนาดมาตรฐาน (310 ไมโครยูนิตต่อมิลลิลิตร) เป็นยาในการเจือจางโดยวิธี radioimmunoassay (insulin–CT biointernational, France) โดยแต่ละตัวอย่างจะวัด 2 ครั้ง จากนั้นทำการคำนวณความเข้มข้นกลับ และนำผลมาวิเคราะห์

ผลการศึกษา : พบว่าค่าเฉลี่ยของปริมาตรคงค้างในกลุ่มที่ 3 (2.4 $\pm$ 0.8 ไมโครลิตร) ต่ำกว่ากลุ่มที่ 1 (49.7 $\pm$ 0.9 ไมโครลิตร) และกลุ่มที่ 2 (65.3 $\pm$ 0.7 ไมโครลิตร) อย่างมีนัยสำคัญทางสถิติ (มัธยฐาน = 2 ไมโครลิตร) พบว่าปริมาตรคงค้างในทั้ง 3 กลุ่มแตกต่างกันเองอย่างมีนัยสำคัญทางสถิติ และปริมาตรคงค้างมีมากที่สุดในกลุ่มที่ 2 การศึกษาความเข้มข้นของอินสุลินเพื่อเปรียบเทียบกับอินสุลินมาตรฐาน พบว่ากลุ่มที่ 3 ได้ความเข้มข้นใกล้เคียงกับอินสุลินมาตรฐานที่สุด (335 $\pm$ 28 *vs* 310 ไมโครยูนิตต่อมิลลิลิตร) ขณะที่กลุ่มที่ 1 และ 2 สูงกว่ากลุ่มที่ 3 (เป็น 1.8 และ 1.9 เท่า) และอินสุลินมาตรฐาน (เป็น 1.8 และ 2 เท่า) อย่างมีนัยสำคัญทางสถิติ

สรุป : ปริมาตรคงค้างในหลอดฉีดยาชนิดถอดเข็มได้มีความสำคัญที่ละเลยไม่ได้ เนื่องจากเป็นสาเหตุสำคัญที่ทำให้เกิดข้อผิดพลาดของความเข้มข้นของยาหลังการผสมยา

คำสำคัญ : ปริมาตรคงค้างในหลอดฉีดยา, ทารกแรกเกิด, หลอดฉีดยาชนิดถอดหัวเข็มได้, หลอดฉีดยาชนิดถอดหัวเข็มไม่ได้, การเจือจาง, ความเข้มข้น

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* สำนักงานวิจัย, คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10400