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Original Research Article

Syringe Pumps Connected in Series with or Without a Carrier Infusion –Does It Matter?

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Abstract: It is common in the intensive care unit to have many syringe pumps connected to a stopcock manifold and then attached to the port of a central line. The treatment of such critical patients also involves the alteration of flow rates of these syringe pumps. There are varied practices with respect to how the syringe pumps are placed when connected to the central line. Three syringe pumps containing inert fluid with a prefixed amount of different measurable electrolytes were connected to a central line via stopcock manifold .These pumps were commenced at a predetermined flow rate .At the end of prefixed intervals the samples were analysed to assess the quantity of electrolytes in the fluid delivered at the end of a central line. Alteration in flow rates and their subsequent end effect was studied. Further an infusion pump was connected to the distal end of the manifold and the fluid mechanics with various permutations of flow rate were studied. As per the results of our study, when a carrier infusion pump was connected in series to multiple syringe pumps connected to the manifold , the initial 5 minutes showed a significant dilutional effect for the contents of the proximal infusion pump (closest to the central line port)when alteration were made to the other pumps. This laboratory experiment does seem to suggest that there seems to be a significant dilutional effect with the use of carrier infusion in series as compared to when the carrier infusion is not used when drug alterations are done . This study further lays an impetus to study the above experiment in vivo in order to ascertain whether this has biological relevance.
Keywords: intensive care unit, syringe pumps, infusion pump, carrier infusion

INTRODUCTION

Central venous catheters (CVC) are used extensively in Critical Care departments around the world for administering continuous infusion of inotropic, sedatives, vasopressors drugs via syringe pumps. Controlled drug delivery is important for patient safety when vasopressors and inotropes are used.

However when multiple drugs are connected via stopcock manifold to the CVC then changes made in any one pump may alter the drug delivery in a significant way. Many ICU's adopt the policy of connecting a carrier infusion with an inert fluid at the end of the stopcock manifold so that a continuous drug delivery is done with an aim to minimize these sudden drug dose changes

MATERIALS AND METHODS

The study was conducted in the laboratory of a tertiary care institute under controlled conditions. Fresh frozen plasma was used as an inert fluid to which a fixed quantity of different electrolytes (kcl, sodium bicarbonate, claclium gluconate) were added. This was done so that we could measure the amount of electrolytes by a standard automated analyser .

When added undiluted to the plasma the analyzer was unable to read the amount and hence the electrolytes were diluted to analyzable amount using micropipettes.

Three syringe pumps (B Braun- syringe pump model: perfusor compact) [1] and am Infusion Pump (B Braun- infusion pump model: infusomat P) [2] were used. Syringes used were 50 ml Becton Dickenson luer lock syringes. 200 cc IV extension tubing were used. Drugs used were Sodium bicarbonate (7.5% W/v, NaHCO3 893mmol/l, 10ml), Potassium chloride (15% W/v, pot chlor 160mg, 20meq K and Cl, 10ml) and Calcium gluconate (gluconate anhydrous 137.50mg,

10ml) and were diluted to a range of 1:50, 1:200 and 1:100 respectively using micropipette. The dilution was done with Micropipette – Finnpipette 100-1000ul & 10-100ul to get a reading on the machine. The samples were processed on 'Medicaeasystat. Biochemistry Blood gas & Electrolyte analyzer', Transasia Biomedical Ltd. [3] and 'COBAS Integra 400 Plus Biochemistry Autoanalyser', Roche Diagnostic International Ltd. [4] CVC used was of the standard make available in the market, it was a 3 lumen Arrow central line, Product no AK-12703, 7 Fr. x 6-5/16" (16 cm) Polyurethane CVC Kit [5]. The Distal port (brown colored) was used for the study.

METHODS

Step 1. Three syringe pumps were connected in series labeled as C, B and A with the help of stopcock manifold and 200 cc IV extension tubing along with A connected to distal port of CVC [Figure 1].

Step 2. An infusion pump was connected to this circuit at distal/terminal end of the syringe pump labeled C [Figure 1].

Step 3. The syringe pumps C, B and A contained solutions of inert fluid (FFP) mixed with diluted Sodium bicarbonate, Potassium chloride and Calcium gluconate and baseline values of the electrolytes were ascertained in respective syringes in the dilutions mentioned above and a baseline value of Sodium, Potassium and Calcium were recorded by testing the samples from pump C, B and A respectively at the beginning of the study.

Step 4. Samples were collected at the distal end of the CVC at 2 min, 5 min, 10 min and 15 min for analysis of the content of respective electrolytes.

Step 5. The study was initiated by keeping the flow rate at 4 ml/h for syringe pumps C, B and A for a period of one hour. This caused the circuit to be primed with the FFP containing all 3 drugs.

Step 6. In order to study the effect of increasing the rate of a single syringe pump on the other infusions in series (as seen in real life) after one hour, the flow rate in syringe pump C was increased to 8 ml/h with syringe pump B and syringe pump A still having a flow rate of 4ml/h. The collected samples were measured for sodium, potassium and calcium at 2, 5, 10 and 15 min interval following which the flow rate of syringe pump C was reduced to 4 ml/h and again the circuit was allowed to be primed for one hour with all 3 syringe pumps with a flow rate of 4 ml/h.

Step 7. To study the effect of a pre-existing carrier infusion proximal to the syringe pumps in series an Infusion pump (D) was connected to the distal end of the stopcock manifold containing inert fluid (FFP) and had a flow rate of 4 ml/h, the same as syringe pumps C, B and A. In order to avoid discrepancy generated with sudden bolus effect the flow rate was maintained for 1 hour. Each further step was done at an interval of 1 hour.

Step 8. As explained earlier the exercise was again repeated i.e., the flow rate of syringe pump C was increased to 8 ml/h with infusion pump D, syringe pumps B and A at 4ml/h and the samples collected were measured for sodium, potassium and calcium at 2, 5, 10 and 15 min, following which the flow rate of syringe pump C was reduced to 4 ml/h, infusion pump D was disconnected and again the circuit was allowed to be primed for one hour with all 3 syringe pumps with a flow rate of 4 ml/h.

Step 9. As explained earlier the exercise was again repeated i.e., the flow rate in syringe pump B was increased to 8 ml/h with syringe pump C and A still having a flow rate of 4ml/h. The collected samples were measured for sodium, potassium and calcium at 2, 5, 10 and 15 min interval following which the flow rate of B was reduced to 4 ml/h and again the circuit was allowed to be primed for one hour with all 3 syringe pumps with a flow rate of 4 ml/h.

Step 10. After one hour, the infusion pump D was reconnected to the distal end of the stopcock manifold containing inert fluid (FFP) with a flow rate of 4 ml/h, the same as syringe pumps C, B and A, this was run for a period of one hour.

Step 11. After one hour had elapsed, the flow rate of syringe pump B was increased to 8 ml/h with infusion pump D, syringe pumps C and A at 4ml/h and the samples collected were measured for sodium, potassium and calcium at 2, 5, 10 and 15 min.

Step 12. All the above steps were repeated by another researcher. However both researcher were aware of which infusion was placed where and the same protocol for analysis was followed.

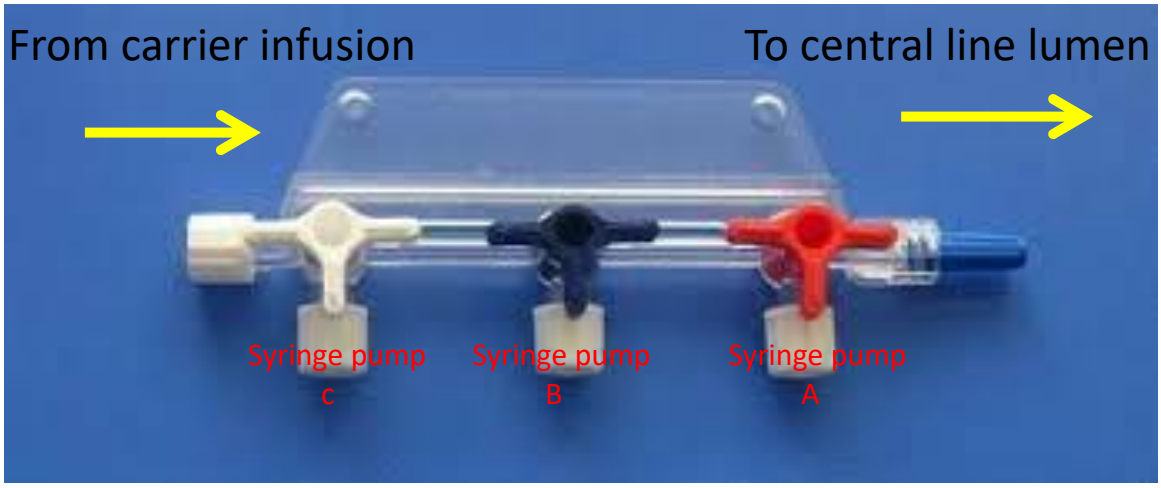

Fig-1: Syringe pump experiment scheme

After data collection was done, the data entry was done in Excel and data analysis was done with the help of Statistical package for social sciences (SPSS) Software version 15 [6] and Sigma plot Version 11 [7].

Quantitative data was presented with the help of Mean, Standard deviation, Median and IQR. Comparison among study group was done with the help of One-way Repeat measure ANOVA test per results of normality test and multiple pairwise comparisons among group was done with Holm-Sidak method. (Calculation attached at the appendix)

P value less than 0.05 was taken as significant level. Please refer to Appendix, Table 1, 2 and 3 for full statistical analysis.

RESULTS

A change in the electrolytes delivered from syringe pump A was seen in the initial 2 minutes when alteration in flow rate of syringe pump c was done with carrier infusion pump connected in series . A significant change was also noted in electrolytes delivered from syringe pump A at 5 minutes with alteration in flow rate of syringe pump B with carrier infusion pump connected in series. With flow alterations in syringe pump C and B, were done, not much change was found in the collected electrolyte.

GRAPHICAL REPRESENTATIONS

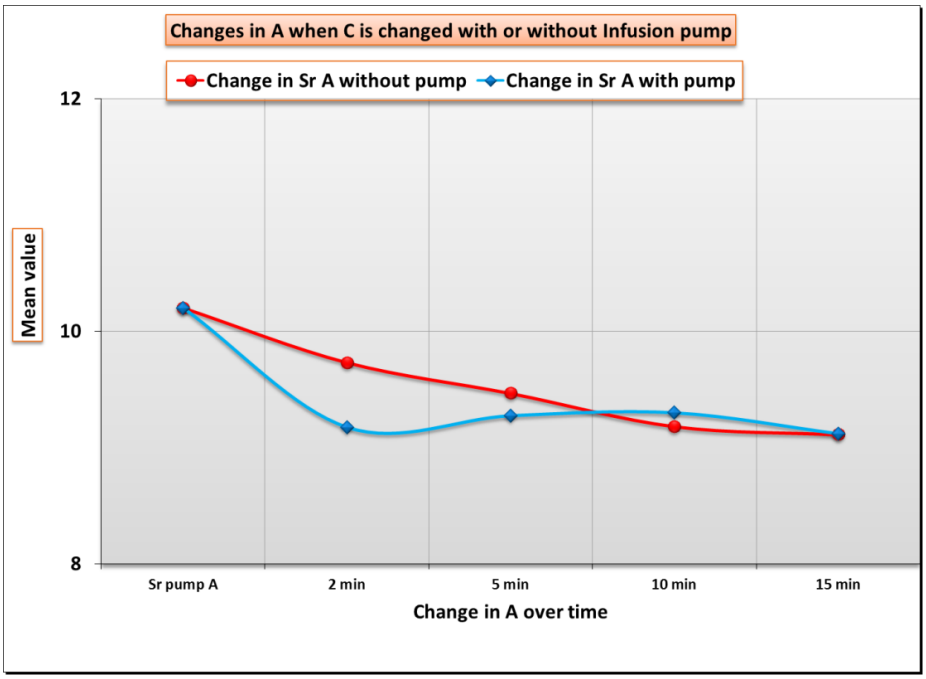

Fig-2: Changes in A when C is changed with or without infusion pump

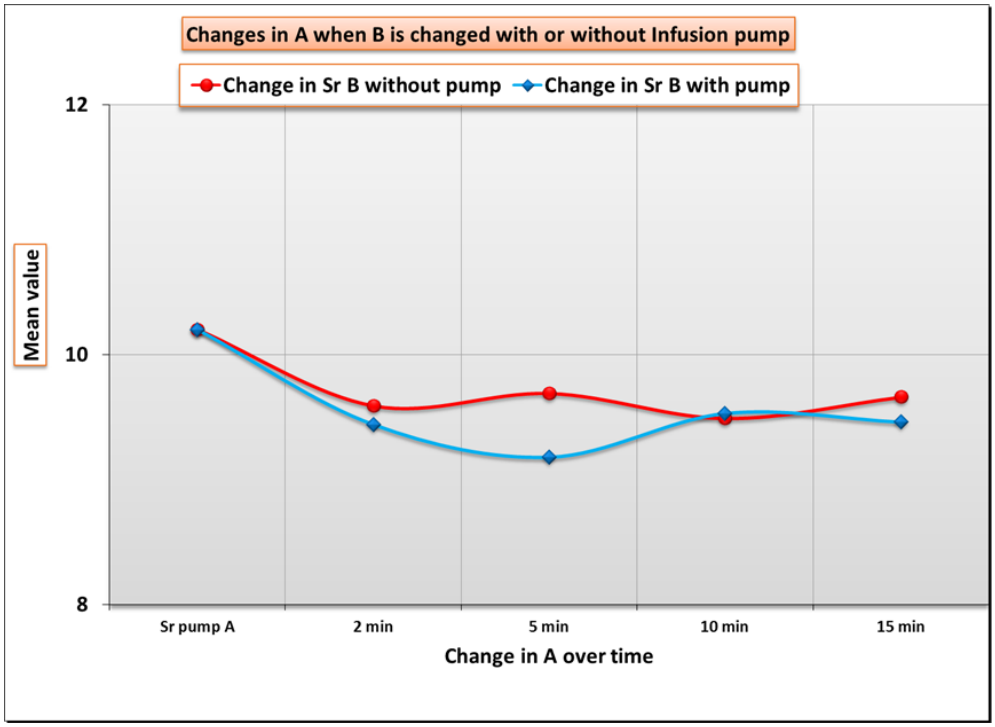

Fig-3: Changes in A when B is changed with or without infusion pump

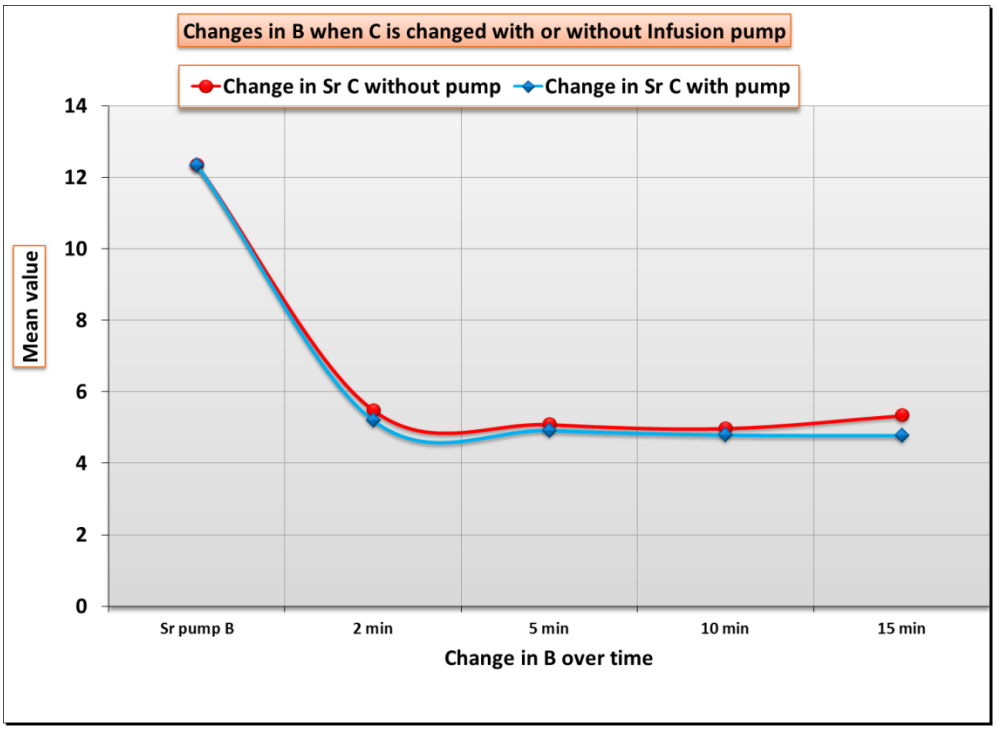

Fig-4: Changes in B when C is changed with or without Infusion pump

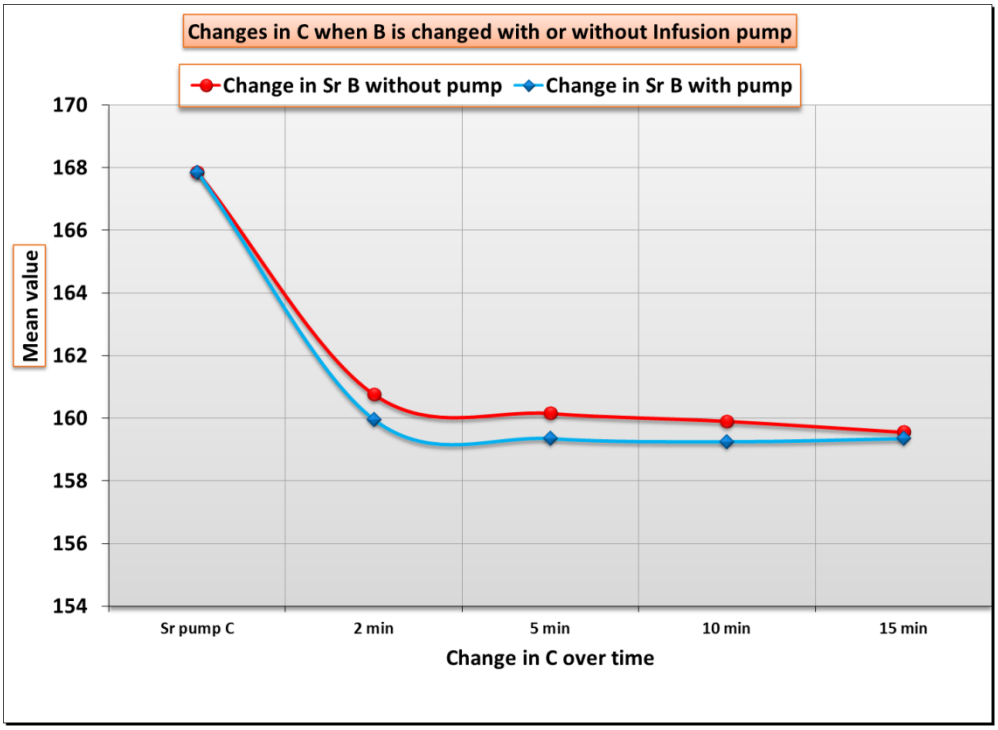

Fig-5: Changes in C when B is changed with or without infusion pump

DISCUSSION

Concentrated infusions of highly potent medications like vasopressors, hypnotics and analgesics are used regularly in the intensive care unit. There are wide variation of practices in the drug delivery systems worldwide. It is often not possible to use dedicated separate lines for such drugs which logically seems the right way. In most patientsin the intensive care unit these medications are placed one after the other connected to a single dedicated line. It is standard practice in many units (including the author's unit)to place a "carrier infusion" at the proximal end (piggy-backed) so that there is a constant flushing of these drugs into the system. This also ensures some amount of dilution of the concentrated drug thus reducing the impact of an accidental bolus. However the carrier flow cannot be very high as many patients (like in renal failure, cardiac failure, Acute respiratory distress syndrome etc) in the intensive care will be on fluid restriction. Due to this reason the carrier flow rates in intensive care units (and in the author's unit) are around 4 to 10 ml/hr and hence the said rate in our study.

The effect of the alteration of any of the syringe pump flow rates in the presence of carrier infusion on flow has not been studied. By this experimental laboratory study we strived to understand this. As seen by the results of the study, demonstrated in the graphical analysis (Fig 2) it does seem to suggest that there was an increased dilutional effect on the contents of the syringe pump closest to the patient(syringe pump A) when the flow rate of the first syringe pump(syringe pump c) closest to the carrier infusion pump was increased. This dilutional effect was maximally seen at 2 minutes. This dilutional effect was also noticed in the same pump (i.e closest to the patient) maximally at 5 minutes when the middle syringe pump flow rate was increased with carrier infusion on(fig 3)However it was noticed that none of the dilutional effects were noticed when there was no carrier infusion on. Another observation was that alteration of flow rate from the two pumps closer to the carrier(syringe pump B and C) does not cause any change in electrolytes delivery in either. Moreover this observation remains same irrespective of the presence or absence of carrier infusion (figure 4 and 5).

In conclusion it does seem to suggest that the dilutional effect is maximal within the first 5 minutes for the pump closest to the central line and farthest from the carrier infusion when alterations of flow rates are made to the other pumps connected to the manifold of stop cocks.

Hence this study indicates that port selection in a stopcock manifold is very important when a carrier infusion is on flow.

In a clinical scenario this would translate as a significant change on the hemodynamics of a patient on such drug delivery systems with carrier infusions. Whether this trial hold biological relevance can be ascertained only by replicating the above experimental study in vivo. However the study on fluid dynamics does leads to some interesting findings which may hold clinical significance.

CONCLUSION

Continuous intravenous medications are a principal means of drug delivery in critically ill patients and these medications are infused via CVC's and syringe pumps. To the best of our knowledge, there are no published studies assessing whether drug delivery kinetics depend on the design or port selected for connecting a drug infusion to the delivery system [8], however one study which was a mathematical performed study had contradicting results [9].

This laboratory experiment does seem to suggest that there seems to be a significant dilutional effect with the use of carrier infusion in series as compared to when the carrier infusion is not used when drug alterations are done in the syringe pumps connected in parallel. This interaction as demonstrated by our experiment should be understood in order to avoid unintentional clinical effects which would lead to wide variation in the delivery of extremely potent drugs like vasoactive ,hypnotic and analgesic medications. This study further lays an impetus to study the above experiment in vivo in order to ascertain whether this has biological relevance.

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Appendix

Data:

Table 1: Distribution of study group

Table No : Distribution of study group as per,		
ST Gr		
ST Gr	Frequency	Percent
Calcium (A) (1:100)	2	33.3
Potassium (B) (1:200)	2	33.3
Sodium (C) (1:50)	2	33.3
Total	6	100.0

Table 2: A post hoc analysis using Holm-Sidak method was applied, baseline versus 15 min and baseline versus 10 min, this paired difference was found to be significant

ST Gr = Calcium (A)(1:100)					
Change in A when C is changed without Infusion Pump					
Study Group	N	Mean	Std. Dev	One way RM analysis of variance	
Vol in Syringe pump A	2	10.20	0.30	F Value	P Value
C increased to 8ml/Hr (2 min)	2	9.73	0.51	12.453	0.016
C increased to 8ml/Hr (5 min)	2	9.47	0.21	Difference is significant	
C increased to 8ml/Hr (10 min)	2	9.18	0.35		
C increased to 8ml/Hr (15 min)	2	9.11	0.03		
All Pairwise Multiple Comparison Procedures (Holm-Sidak method):					
Comparison	P	P<0.050			
A vs. C 8ml/Hr (15 min)	0.036	Yes			
A vs. C 8ml/Hr (10 min)	0.041	Yes			
Change in A when C is changed with Infusion Pump					
Study Group	N	Mean	Std. Dev	One way RM analysis of variance	
Vol in Syringe pump A	2	10.20	0.30	F Value	P Value
C increased to 8ml/Hr with Inf pump (2 min)	2	9.18	0.33	355.906	<0.001
C increased to 8ml/Hr with Inf pump (5 min)	2	9.28	0.33	Difference is significant	
C increased to 8ml/Hr with Inf pump (10 min)	2	9.30	0.28		
C increased to 8ml/Hr with Inf pump (15 min)	2	9.12	0.25		
All Pairwise Multiple Comparison Procedures (Holm-Sidak method):					
Comparison	P	P<0.050			
A vs. C 8ml/Hr with Inf pump 2 min	<0.001	Yes			
A vs. C 8ml/Hr with Inf pump 5 min	<0.001	Yes			
A vs. C 8ml/Hr with Inf pump 10 min	<0.001	Yes			
A vs. C 8ml/Hr with Inf pump 15 min	<0.001	Yes			
C 8ml/Hr with Inf pump 2 min vs. C 8ml/Hr with Inf pump 10 min	0.034	Yes			
C 8ml/Hr with Inf pump 10 min vs. C 8ml/Hr with Inf pump 15 min	0.048	Yes			
Change in A when B is changed without Infusion Pump					
Study Group	N	Mean	Std. Dev	One way RM analysis of variance	
Vol in Syringe pump A	2	10.20	0.30	F Value	P Value
B 8ml/hr without Inf pump with C 4ml/hr (2 min)	2	9.59	0.82	1.576	0.335
B 8ml/hr without Inf pump with C 4ml/hr (5 min)	2	9.69	0.01	Difference is not significant	
B 8ml/hr without Inf pump with C 4ml/hr (10 min)	2	9.49	0.16		
B 8ml/hr without Inf pump with C 4ml/hr (15 min)	2	9.66	0.18		
Change in A when B is changed with Infusion Pump					
Study Group	N	Mean	Std. Dev	One way RM analysis of variance	
Vol in Syringe pump A	2	10.20	0.30	F Value	P Value
B increased to 8ml/Hr with Inf pump (2 min)	2	9.44	0.03	4.839	0.078
B increased to 8ml/Hr with Inf pump (5 min)	2	9.18	0.06	Difference is not significant	
B increased to 8ml/Hr with Inf pump (10 min)	2	9.53	0.30		
B increased to 8ml/Hr with Inf pump (15 min)	2	9.46	0.25		

Table 3: Changes in drug delivered by syringe pump C when flow rates are changed of syringe pump B and vice versa with or without carrier infusion pump

ST Gr = Sodium (C)(1:50)					
Change in C when B is changed without Infusion Pump					
Study Group	N	Mean	Std. Dev	One way RM analysis of variance	
Vol in Syringe pump C	2	167.85	1.34	F Value	P Value
B 8ml/hr with A & C 4ml/hr (2 min)	2	160.75	0.64	80.02	<0.001
B 8ml/hr with A & C 4ml/hr (5 min)	2	160.15	0.49	Difference is significant	
B 8ml/hr with A & C 4ml/hr (10 min)	2	159.90	0.14		
B 8ml/hr with A & C 4ml/hr (15 min)	2	159.55	0.21		
All Pairwise Multiple Comparison Procedures (Holm-Sidak method):					
Comparison	P	P<0.050			
C vs. B 8ml/hr (15 min)	0.00	Yes			
C vs. B 8ml/hr (10 min)	0.00	Yes			
C vs. B 8ml/hr (5 min)	0.00	Yes			
C vs. B 8ml/hr (2 min)	0.00	Yes			
Change in C when B is changed with Infusion Pump					
Study Group	N	Mean	Std. Dev	One way RM analysis of variance	
Vol in Syringe pump C	2	167.85	1.34	F Value	P Value
B increased to 8ml/Hr with Inf pump (2 min)	2	159.95	0.92	112.84	<0.001
B increased to 8ml/Hr with Inf pump (5 min)	2	159.35	0.35	Difference is significant	
B increased to 8ml/Hr with Inf pump (10 min)	2	159.25	0.07		
B increased to 8ml/Hr with Inf pump (15 min)	2	159.35	0.49		
All Pairwise Multiple Comparison Procedures (Holm-Sidak method):					
Comparison	P	P<0.050	Diff is		
C vs. B 8ml/Hr with Inf pump (15 min)	<0.001	Yes	Sig		
C vs. B 8ml/Hr with Inf pump (10 min)	<0.001	Yes	Sig		
C vs. B 8ml/Hr with Inf pump (5 min)	<0.001	Yes	Sig		
C vs. B 8ml/Hr with Inf pump (2 min)	<0.001	Yes	Sig		

ST Gr = Potassium(B)(1:200)

Change in B when C is changed without Infusion Pump

Study Group	N	Mean	Std. Dev	One way RM analysis of variance	
Vol in Syringe pump B	2	12.35	0.32	F Value	P Value
C increased to 8ml/Hr (2 min)	2	5.49	0.58	152.09	<0.001
C increased to 8ml/Hr (5 min)	2	5.10	0.32	Difference is significant	
C increased to 8ml/Hr (10 min)	2	4.99	0.30		
C increased to 8ml/Hr (15 min)	2	5.35	0.57		

All Pairwise Multiple Comparison Procedures (Holm-Sidak method):			
Comparison	P	P<0.050	
B vs. C 8ml/Hr (10 min)	<0.001	Yes	
B vs. C 8ml/Hr (5 min)	<0.001	Yes	
B vs. C 8ml/Hr (15 min)	<0.001	Yes	
B vs. C 8ml/Hr (2 min)	<0.001	Yes	

Change in B when C is changed with Pump

Study Group	N	Mean	Std. Dev	One way RM analysis of variance	
Vol in Syringe pump B	2	12.35	0.32	F Value	P Value
C increased to 8ml/Hr with Inf pump (2 min)	2	5.21	0.01	964.899	<0.001
C increased to 8ml/Hr with Inf pump (5 min)	2	4.93	0.11	Difference is significant	
C increased to 8ml/Hr with Inf pump (10 min)	2	4.81	0.05		
C increased to 8ml/Hr with Inf pump (15 min)	2	4.79	0.03		

All Pairwise Multiple Comparison Procedures (Holm-Sidak method):			
Comparison	P	P<0.050	
B vs. C 8ml/Hr with Inf pump 2 min	<0.001	Yes	
B vs. C 8ml/Hr with Inf pump 5 min	<0.001	Yes	
B vs. C 8ml/Hr with pump 10 min	<0.001	Yes	
B vs. C 8ml/Hr with pump 15 min	<0.001	Yes	