Technical Note

Estimation of heparin leak into the systemic circulation after central venous catheter heparin lock

Mohsen Agharazii, Isabelle Plamondon, Marcel Lebel, Pierre Douville and Simon Desmeules

CHUQ-L’Hôtel Dieu de Québec Hospital, Division of Nephrology, Department of Medicine, Laval University, Québec, Canada

Abstract
Background. Although most catheter problems in haemodialysis are related to infection or clotting, bleeding associated with the heparin lock is of clinical importance especially during peri-operative conditions. The objective of this in vitro study is to estimate the volume of heparin that may leak into the circulation immediately after performing a catheter lock.

Methods. Different volumes (ml) of a dextrose solution were used to perform a catheter lock on haemodialysis catheters. The tip of the catheter was placed in a test tube containing water for a pre-specified period. The final concentrations of dextrose in the test tube were used to determine the volume of solution that leaked from the catheter.

Results. When the total lumen volume was filled, the catheter leak was estimated to be 0.59±0.03 and 0.71±0.04 ml after 15 and 25 s, respectively. There was a continuous leak of 1.23±0.41, 2.20±0.34 and 3.38±0.23 ml at 5, 15 and 30 min, respectively, after performing a catheter lock on a catheter with a total lumen volume of 4.5 ml. The catheter leak was significantly reduced when only 3.7 ml of solution was used to fill the total lumen volume of 4.5 ml.

Conclusion. The present study demonstrates a significant early and late leakage from the catheter that occurs after performing a catheter lock. When applied to heparin, the volume of the unwanted catheter leak may result in adverse clinical events, especially following haemodialysis sessions and during peri-operative periods. However, these results are hypothesis-generating, and clinical studies are necessary to evaluate the efficacy of underfilling.

Introduction
Catheter-associated haemodialysis problems are mostly related to infection or catheter dysfunction as a result of clotting at the tip of the catheter or formation of a fibrin sheet. A catheter lock with a highly concentrated heparin solution is often used to maintain the catheter’s permeability. Recently, based on activated partial thromboplastin time measurements after heparin lock, it was shown that a clinically relevant amount of heparin enters the systemic circulation [1,2]. Clinical observations indicate that the amount of heparin that leaks into the circulation could, in part, result in minor or major bleeding.

The objective of the present in vitro study is to estimate the amount of heparin that enters the systemic circulation after performing a heparin lock. For practical reasons, we used a solution containing dextrose as a surrogate marker for the amount of heparin that enters the systemic circulation.

Materials and methods

Materials
Two types of catheters were used for this study: (i) a Quinton (Mahurkar) dual-lumen 16 cm catheter with an arterial lumen volume of 1.2 ml and a venous lumen volume of 1.3 ml (Tyco Healthcare group LP, Mansfield, MA); and (ii) a pre-curved Opti-flow PC-2 catheter with an arterial lumen volume of 2.2 ml and a venous lumen volume of 2.3 ml (Bard Access Systems, Salt Lake City, UT). A solution containing 278 mmol/l of dextrose and 200 mmol/l of potassium chloride was measured out in 3 ml syringes and used to lock the...
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catheters in pre-specified volumes. The concentration of dextrose and potassium chloride was calculated in order to cover a wide reliable range of final concentrations of these molecules. The dextrose concentrations were shown to be in a more reliable range (range: 1.5–15.8 mmol/l) than those of potassium (1.0–13.7 mmol/l). Therefore, the dextrose concentration was used to determine the catheter leak. The volume of the lumen and the precision of the 3 ml syringes were tested and were extremely reliable.

Procedure

The catheter was flushed with 20 ml of water in a sink. The tip of the catheter was placed into a test tube filled with a 15 cm column of water. The syringes were filled with the pre-measured amount of the solution and then injected into each lumen. The catheter was withdrawn and the solution that remained in the test tube (representing the blood compartment) was sent to the laboratory for measurement of dextrose concentration. Using the final concentration of dextrose in a sample of test tube, we calculated the volume of dextrose concentration. Using the final concentration of dextrose in a sample of test tube, we calculated the volume of the catheter leak using the following equation:

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\frac{[\text{Solute}]_{\text{Test Tube}} \, (\text{mmol/L}) \times \text{Test Tube Volume} \, (\text{L})}{[\text{Solute}]_{\text{Catheter-lock}} \, (\text{mmol/L}) \times \text{Catheter-Lock Volume} \, (\text{L})} = \text{Ratio of Solute Leak}
\]

The quantity of the solute in the test tube divided by the initial quantity of solute injected in the catheter is referred to as the ratio of solute leak. Volume leak is calculated by multiplying the ratio of solute leak by the injected volume as described with the following equation:

Catheter leak (l) = ratio of solute leak × injection volume (l)

Experiment 1

Each experiment was performed three times with two haemodialysis catheters at three different volumes as follows: (i) volume of each lumen; (ii) volume of each lumen minus 0.1 ml; and (iii) volume of each lumen minus 0.2 ml. Each experiment was also conducted at two different lengths of bathing time in the test tube, one for 15 s and one for 25 s.

Experiment 2

Each experiment was done three times with the pre-curved Opti-flow PC-2 haemodialysis catheter at three different volumes as follows: (i) volume of each lumen or 4.5 ml for both lumens; (ii) volume of each lumen minus 0.2 ml or 4.1 ml for both lumens; and (iii) volume of each lumen minus 0.4 ml or 3.7 ml for both lumens. Samples from the test tube were obtained at 5, 15 and 30 min after catheter lock. A stirrer was used to ensure the homogeneity of the sample.

Statistical analyses

The data were analysed using SPSS 11.5 for Windows (SPSS Inc., Chicago, IL). The results were expressed as the mean ± SEM. Three-way analysis of variance (ANOVA) was used to evaluate the effects of the two different catheters, the three sets of intra-luminal volume and two different bathing times for the first experiment. For the second experiment, two-way ANOVA was used to evaluate the three sets of intra-luminal volume and three different bathing times. Bonferroni correction was used for the post hoc multiple comparisons of the observed means.

Results

Experiment 1

The total amount of intra-catheter fluid that mixed with the test tube water was dependent upon the volume of solution used to fill up the catheter and the bathing duration. There were no significant differences between the two types of catheters. Figure 1 shows the early catheter leak.

Experiment 2

Across all volumes used for the catheter lock, the average catheter leaks at 5, 15 and 30 min were statistically different from each other (\(P < 0.02\)). Across all bathing times, the average catheter leak increased significantly along with the increased volume of solution used for the catheter lock (3.7 ml < 4.1 ml and 4.5 ml, \(P < 0.03\); 4.1 ml < 4.5 ml, \(P = 0.17\)). Table 1 shows the increasing quantity of catheter leakage that occurred over time together with the increasing catheter lock volume.
Discussion

The patency of the dialysis catheter continues to remain a clinical challenge. Infections or thrombosis cause the most clinically relevant complications of these catheters [3]. Guidelines on vascular access, published by the National Kidney Foundation Dialysis Outcomes Quality Initiative (DOQI), do not include any recommendations for filling catheters so as to prevent thrombosis or bleeding [4]. Heparin lock alters coagulation studies [5], and bleeding complications related to heparin lock have been reported [1,3,6]. Significant catheter leak is also supported from catheter lock performed with gentamicin [7].

In a preliminary study, we performed the same experiment with heparin. However, measuring heparin levels in water is much more complex and requires many intermediate steps that compromise the reliability of the test. We therefore used dextrose as surrogate marker of heparin diffusion for practical reasons. The present study showed that a clinically significant catheter leak occurs immediately after performing a catheter lock. This early catheter leak is followed by an ongoing leak that continues to occur over a 30 min period of observation. It should be considered, however, that in vivo the catheter is placed in central veins and is surrounded by a high blood flow. In our experiment, the tip of the catheter was under a constant hydrostatic pressure of 15 cm of water, whereas in vivo, the catheter is submitted to the rhythmical changes in vena cava superior diameter and hydrostatic pressure that occurs with each heart beat. It is unlikely that an early catheter leak with dextrose solution would be much different from that with heparin since the early catheter leak is most likely to be dependent on the propulsion of fluid that takes place immediately following catheter lock. Assuming that 5000 IU of heparin is diluted in order to fill the total lumen volume, depending upon the volume of the lumen, a patient can receive somewhere between 1700 and 3400 IU of heparin within 25 s after a heparin lock is performed. This quantity of heparin is of clinical importance in a number of clinical settings including peri-operative periods, per-operative installation of catheters, and at the end of a dialysis session when the aPTT is already abnormal. In vivo, however, a late catheter leak might not occur at the same rate as shown in our experiment. It is possible that a higher density of blood could hinder the rate of a late catheter leak that might occur in vivo.

In conclusion, the results of this in vitro study show a significant catheter leakage that occurs after catheter lock. Although underfilling may seem a safer alternative in clinical conditions where there is a high risk of bleeding, our results remain preliminary and hypothesis-generating. Clinical studies are therefore necessary to evaluate the efficacy and safety of underfilling.

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Conflict of interest statement. None declared.

References

5. Stas KJ, Vanvalleghem J, De Moor B, Keuleers H. Trisodium citrate 30% vs heparin 5% as catheter lock in the interdialytic period in twin- or double-lumen dialysis catheters for intermittent haemodialysis. Nephrol Dial Transplant 2001; 16: 1521–1522

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