

AN EVALUATION ON PATENCY OF A CHRONIC VENOUS CATHETER

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INTRODUCTION

Access to the circulatory system in laboratory rats is desirable in many areas of study including pharmaceutical discovery and product registration studies, endocrinology, and cardiovascular dynamics. Pharmacokinetic studies in rats are most effectively and humanely performed with a chronically implanted catheter system that allows for repeated blood sampling from an animal with minimal restraint. Once a catheter is successfully implanted, the amount of time that it reliably remains patent (patency life), with or without flushing, will set practical limits on its use. The patency life can be affected by many factors including catheter material, flushing regimen, and lock solutions used to fill the lumen of the catheter to prevent reflux of blood and development of clots within the catheter. Since the 1960's, silicone has found widespread use in medical applications. More recently, polyurethane has rapidly gained acceptance in human and laboratory medical devices and catheters. Many catheter materials have been well studied and their advantages and disadvantages have been described (1-4). There are, however, very few reports on how long a catheter can maintain patent without manipulation and how flushing affects catheter patency and animal health.

Catheter flushing regimens are commonly used, and are sometimes used to extend the duration of catheter patency. This study was designed to compare the duration of patency of unmanipulated with flushed indwelling jugular vein catheters in rats.

MATERIAL AND METHODS

Animals:

In this study, 40 adult male CD rats (*Rattus norvegicus*) (CrI: CD (SD)) produced by Charles River Laboratories (Portage, Michigan) weighing between 245 and 275 grams were used. The study was approved by the institution's Animal Care and Use Committee. The animals were maintained in polycarbonate cages in a dedicated rodent surgical complex that was kept at $21 \pm 2^\circ\text{C}$ with a relative humidity of $60 \pm 5\%$ and a 12/12 hour light/dark cycle. Commercially produced, sterilized feed, bedding and water were provided ad libitum. All conditions of animal preparation and use were in accordance with recommendations set forth in the *Guide for the Care and Use of Laboratory Animals*. The animals were of VAF® (specific pathogen free) health status which was verified by an in-room sentinel system.

Surgical Procedure:

The animals were anesthetized with ketamine (43 mg/kg) and xylazine (8.7 mg/kg) administered intraperitoneally. All surgical procedures were conducted using aseptic techniques. The ventral neck and dorsal scapulae areas were shaved and the skin prepared using povidone iodine (Betadine™) and isopropyl alcohol. A 1 cm cranial-caudal incision was made at the ventral neck to expose one jugular vein. A 0.5 cm skin incision was made at the scapular region. The jugular vein was isolated and tied off cranially using non-absorbable suture material. A small incision was made in the jugular vein and a silicone catheter was inserted into the vein and a ligature subsequently tied around the catheterized vessel to fix the catheter in place. The catheter was locked with 50% heparinized dextrose. The end of the catheter was sealed with a metal plug. The catheter was subcutaneously tunneled and exteriorized through the incision in the scapular region. A skin pocket was created and the extra tubing was tucked into the pocket. The end of the catheter was secured with a wound clip to the skin. Immediately following surgery, the animal was placed in a heated cage until it was fully recovered. Postoperative

analgesic (Buprenorphine, 0.02 mg/kg) was given immediately following the completion of the procedure.



Experimental Design:

The catheterized rats were randomly allocated into four groups with ten animals per group. Catheters were not manipulated between days 0-6 in all groups. Beginning on day 7, the catheters of rats in group 1 were flushed every 3 days for 28 days using aseptic techniques. The flushing regimen included removal of the old lock solution, flushing with saline and relocking with the lock solution (50% heparinized dextrose). Groups 2-4 were not manipulated in any way until the catheters were evaluated for patency at 14, 21, and 28 days respectively. Patency was classified into the following categories:

Fully Patent: successful blood withdrawal on first attempt.

Patent on Flush: successful blood withdrawal after infusion of saline.

Partially patent: unsuccessful blood withdrawal but patent for infusion.

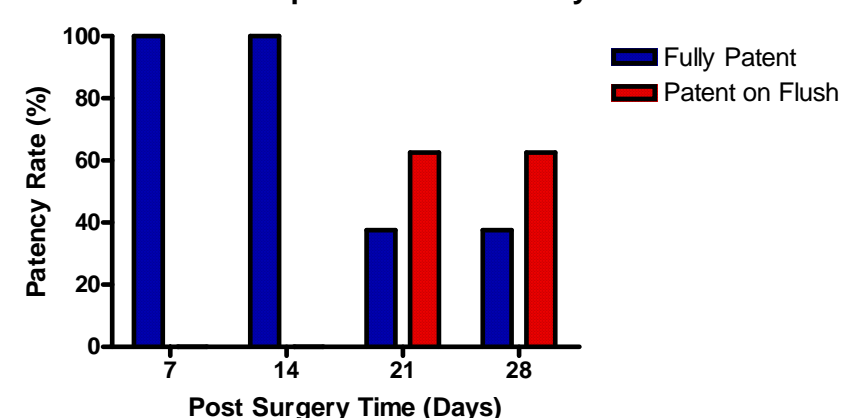
Non-patent: unsuccessful blood withdrawal and infusion.

Catheter patency and animal body weights were assessed during each flushing timepoint.

RESULTS:

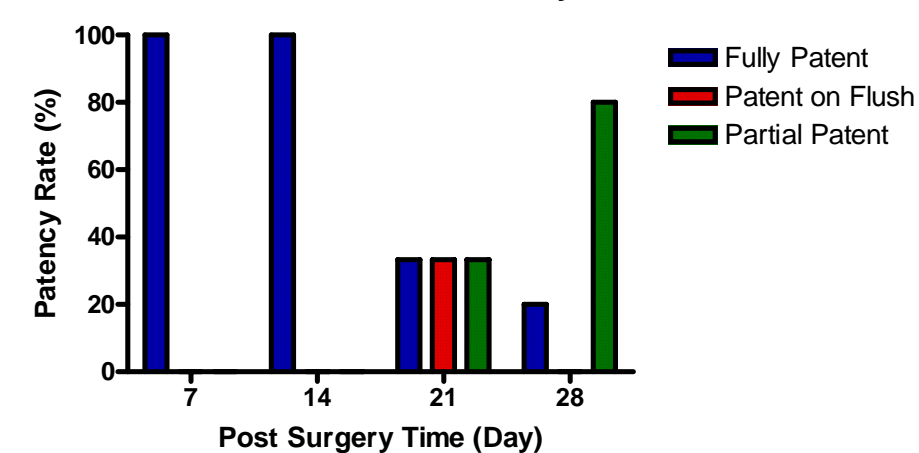
In the non-manipulated groups (2-4), all catheters remained 100% fully patent during the first 14 days. At 21 and 28 days, 37.5% of catheters in these groups were fully patent and 62.5% were patent on flush. (Chart 1).

Chart 1: Non-Manipulated JVC Patency Rate



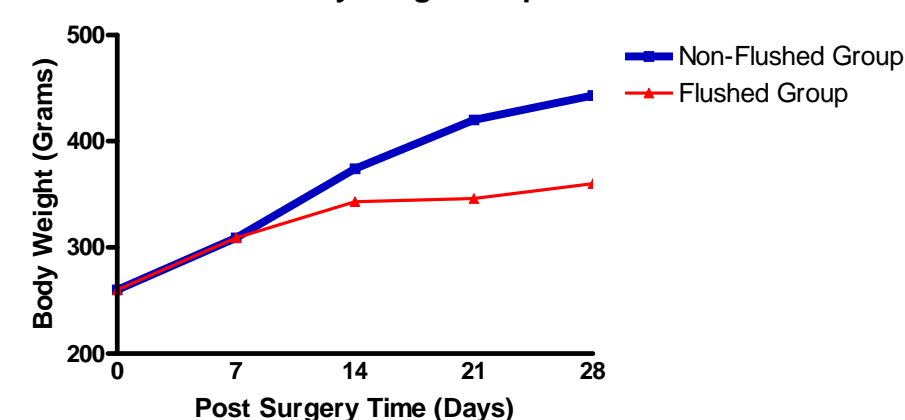
The catheters flushed every 3 days (group 1) also remained 100% fully patent during the first 14 days. At day 21, group 1 catheters were one-third fully patent, one-third patent on flush and one-third partially patent (one animal was removed from the experiment due to surgical complications). At day 28, only 20% of group 1 catheters were fully patent and 80% were partially patent. (Chart 2).

Chart 2: Flushed JVC Patency Rate



Rats in groups 2-4 gained an average of 6.4 grams each day over the 28 day period. The rats in group 1 gained an average of 2.4 grams per day (Chart 3).

Chart 3: Body Weight Graph



DISCUSSION:

The typical flushing procedure for an implanted catheter usually involves withdrawal of the lock solution, infusion of sterile saline and refilling the catheter with fresh lock solution. Fully patent catheters allow removal of the old lock solution, in which occasionally very small clots may be present. Flushing the old lock solution into the vessel may increase the risk of forcing these clots into the general circulation which, depending upon the location of the catheter, could result in renal infarction or embolic showering of other organs (5). Pulmonary embolism is also a possible complication associated with implanted venous catheters.

Using a flushing regimen to maintain catheter patency is a common practice in human and veterinary medicine as well as in the research community. The results from this study indicate that flushing every three days does not necessarily prolong catheter patency. Following surgical implantation, the jugular catheters in this study were more likely to remain fully patent over a 28-day period when no intermittent flushing regimen was used. Moreover, 30% to 80% of flushed catheters became only partially patent (unsuccessful withdrawal but patent for infusion) three weeks after implantation. Partially patent catheters may still be useful for infusion studies, however they are of no value for those studies that require collecting blood samples. There is also an

increased risk of disseminating clots when using a partially blocked catheter.

Catheter flushing can be time consuming, labor intensive, stressful for technicians, and stressful for the animals. Information on how animals react to this process is very limited. The difference in body weight gain between the non-flushing and flushing groups was not apparent from daily observation of the animals. No statistical analysis of the body weight differences was made, however the difference may be significant. Possible explanations for the difference in weight gain include that the flushing process was stressful to the animals or provided an opportunity for contamination at the catheter site leading to a subclinical abnormality or infection.

We conclude that surgically implanted jugular vein catheters made with silicone can remain fully patent without intermittent flushing for at least two weeks. Using a catheter flushing regimen at the frequency of every three days does not necessarily prolong the patency of indwelling catheters.

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