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A newly designed total implantable venous access device in rats for research with high efficiency and low cost

Hsin-Lin Tsai, MD, PhD,[a,b] *Jei-Wen Chang, MD, PhD,*[b,c,*] *Chin-Su Liu, MD, PhD,*[a,b] *Tai-Wai Chin, MD,*[a,b] *Chou-Fu Wei, MD,*[d] *Oscar Kuang-Sheng Lee, MD, PhD,*[b,e,f] *and Shyh-Jen Wang, PhD*[b,g]

[a] *Division of Pediatric Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, Republic of China*

[b] *School of Medicine, National Yang-Ming University, Taipei, Taiwan, Republic of China*

[c] *Department of Pediatrics, Taipei Veterans General Hospital, Taipei, Taiwan, Republic of China*

[d] *Department of Surgery, Taipei Medical University Hospital, Taipei, Taiwan, Republic of China*

[e] *Department of Medical Research and Education, Taipei Veterans General Hospital, Taipei, Taiwan, Republic of China*

[f] *Stem Cell Research Center, National Yang-Ming University, Taipei, Taiwan, Republic of China*

[g] *Division of Experimental Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, Republic of China*

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ABSTRACT

Background: In this study, we introduced a newly designed totally implantable device for long-term vascular access in rats and compared its efficacy, related complications, and cost-effectiveness with conventional exteriorized jugular vein catheters.

Methods: Forty adult male Sprague-Dawley rats, weighing 250–300 g, were equally divided into two groups (I and II) and all underwent jugular vein catheterization surgery. The totally implanted device was used in group I and conventional exteriorized catheters were used in group II. The functionality of each catheter was checked every 3 d and evaluation included vascular accessibility, patency, and infection. The weight of the animal and microbial culture from the wound and tube were also monitored. We analyzed the cause of vascular access failure and complications, both mechanical and infectious, and compared related variables.

Results: The proportions of 9-d patency and 30-d patency in group I were 90% (18/20) and 75% (15/20), respectively, and in group II 80% (16/20) and 35% (7/20), respectively. There was a statistically significant difference in 30-d patency. The rats in group II were more liable to involve vascular access failure because of catheter dislodgment and had a higher infection rate ($P = 0.001$). Daily body weight gain was also greater in group I than in group II (2.46 ± 0.59 g/d *versus* 1.84 ± 0.96 g/d; $P = 0.02$).

Conclusions: This newly designed and totally implanted device substantially increases the success rate of long-term venous access compared with conventional methods. It reinforces the merits of the subcutaneous port and a tethered swivel system and overall has

* *Corresponding author*. Department of Pediatrics, Taipei Veterans General Hospital, No. 201, Section 2, Shih-Pai Road, Beitou District, Taipei 11221, Taiwan. Tel.: +886 2 2875 7484; fax: +886 2 2875 7537.

E-mail address: hsinlintsai@gmail.com (J.-W. Chang).

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better performance and reliability. Furthermore, given its low cost and the high level of effectiveness offered, this technology could be a powerful tool to be used in future translational medicine research, especially in cases of long-term intravascular administration.

1. Introduction

Rats are commonly used for experiments especially in preclinical research. Depending on the demands of different investigations, protocols use several time points to efficiently deliver drugs and cells as well as involving blood sample collection, where the key to success is a reliable venous route. Generally, investigators choose the most convenient method that meets their specific requirements. One common method is the implantation of indwelling catheters, usually in the jugular vein as it offers safe and effective access in rats. Traditionally, the catheter tip is placed in the atrium *via* the jugular vein and exits in the mid-scapular space through a subcutaneous tunnel [1,2]. However, the exteriorized nature of the catheter raises several concerns for their long-term use, including difficultly in maintenance, catheter-related infection, complications, and overall costs.

In humans, total implantable venous access ports have been clinically applied for decades. They enable comfortable and convenient access for hemato-oncologic patients. In addition, they have fewer complications with regard to the long-term use as compared with the Broviac catheter or the Hickman catheter (Bard, NJ), which are both exteriorized [3]. Although many subcutaneous access ports for rodents also known as vascular access ports (VAPs) are available on the market, there are still several readily apparent drawbacks, in particular the high cost and the maintenance of the system during study periods.

This study introduced a new totally implantable device and analyzed related complications and the overall cost-effectiveness compared with conventional exteriorized catheters.

2. Methods

2.1. Animals

Adult male Sprague-Dawley rats (weight ranging from 250–300 g) were purchased from the National Yang-Ming University Laboratory Animal Center (Taipei, Taiwan). All animal experiments were performed with the approval and guidance of the Animal Care Committee of the Taipei Veterans General Hospital.

The experimental animals were divided into two groups I and II of 20 rats each. The totally implantable device was placed in group I, whereas group II had the exteriorized catheters.

2.2. Assembly of total implantable device

A piece of Silastic catheter (I.D. 0.5 mm × O.D. 0.9 mm; Harvard Apparatus, MA), a 23-G injection needle (Terumo, Tokyo, Japan), and an intermittent injection cap were used in the preparation of the catheter. The 23-G injection needle was cut into 5-mm length and its stinging tip was blunted to be flat using a fine grit polishing paper. The flattened tip was then gently inserted into the Silastic catheter to avoid tube fracture at the junction. Instant glue was applied for added security. The intermittent injection cap was then tightly connected to the needle connector (Fig. 1).

The length of the tube was determined based on the sum of the planned intravascular distance (from the insertion point to the right atrium, 2.5 cm) and the subcutaneous tunnel distance (from the insertion point to the mid-scapular space, 5 cm). To prevent the restriction of movement or catheter kinking at the needle tip, the proper length used was on average 8 cm.

2.3. Exteriorized catheter assembly

An 8-cm long piece of Silastic catheter (I.D. 0.5 mm × O.D. 0.9 mm; Harvard Apparatus, MA) and a 23-G butterfly puncture needle (Terumo, Tokyo, Japan) were used in the preparation of the catheter. The assembly procedures were in the same manner (Fig. 1).

2.4. Lock solution

Cefuroxime (10 mg/mL) with heparinized dextrose (500 IU/mL) was used as a lock solution.

2.5. Ligature thread

Two pieces of 6-0 silk free tie thread about 7 cm in length were required. One was for the distal jugular vein hemostat and the other was tied on the proximal vein and catheter.

2.6. Catheter placement

The animals were anesthetized *via* intraperitoneal injection of ketamine (80 mg/kg of body weight) and xylazine (8 mg/kg). The operation was performed under sterile conditions on a warm pad.

Each rat was initially placed in a prone position (Fig. 2). A 1-cm transverse dorsal incision was made at the mid-scapular area to create a subcutaneous pocket caudally for the injection cap implantation. The rat was then placed in a supine position. A 2-cm ventral vertical neck incision was made right of the midline, and the underlying salivary and lymphatic tissue was separated by blunt dissection to identify the right common jugular vein. The right common jugular vein was isolated from the adjacent tissue by about 5 mm and the vessel was looped with ligature silk thread. The Silastic catheter was pulled through a subcutaneous tunnel from the dorsal pocket, where the indwelling injection cap