A new Method for Multiple Applications of Cytostatic Drugs in Rats

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Key Words

Intravenous drug application

Microcatheter

Laboratory rat

Summary

The implantation of a small silicon catheter for repeated intravenous applications of drugs in laboratory animals (rats) is described. Under an operation-microscope, the catheter is inserted into the external jugular vein and remains in situ in a skin pocket during the treatment. By dissecting the wound, multiple fractions of drugs can be administered via the catheter at intervals of days or weeks. The method has the advantage that in long-term studies with rats, intravenous injections or infusions of cytostatic drugs are possible with high accuracy.

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Zusammenfassung und Schlüsselwörter

Es wird die Implantation eines Mikrokatheters zur mehrmaligen intra-venösen Injektion von Zytostatika bei Labortieren (Ratten) beschrieben. Der Mikrokatheter wird unter einem Operationsmikroskop in die Vena jugularis externa eingebracht und verbleibt während der Behandlung in situ in einer Hauttasche. Durch Öffnen der Hautwunde können mehrfache Applikationen von Zytostatika über den Katheter im Abstand von Tagen oder Wochen vorgenommen werden. Diese Methode hat den Vorteil, daß bei Ratten in Langzeitstudien intravenöse Injektionen oder Infusionen von Zytostatika mit hoher Genauigkeit durchgeführt werden können.

I.v.-Injektion ■ Mikrokatheter ■ Laborratte

Cytostatic drugs are usually administered in laboratory rats through the tail vein [1, 2] or into the intraperitoneal space [3]. The latter method is not always relevant to the drug application recommended and is, however, more difficult to reproduce with regard to drug uptake and distribution in tumors [4]. For repeated intravenous drug injections, especially in older rats (200 g body weight [b.w.] and more), it is difficult to hit the tail vein accurately through the scaly skin and to inject the drug without extravasation. To overcome these disadvantages, we developed a method for multiple i.v. injections or infusions of cytostatic drugs in rats for long-term studies.

Material and Methods

The method consists of the implantation of a small catheter, which remains in situ during the treatment time into the external jugular vein of the rat. For implantation, female WAG/Rij rats weighing 165 ± 10 g were anesthetized with 6mg/kg b.w. Rompun® (Bayer, FRG) in combination with 50mg/kg Ketavet® (Parke-Davis, FRG). The skin above the left supraclavicular region was shaved and disinfected with Cutasept® (Bode, FRG). The animal

was positioned on its back under an operation microscope (Wild-Leitz, FRG, 16 ×), and the left external jugular vein was prepared by an incision of the skin of about 0.8 cm. The vein was freed from subcutaneous tissue over a small distance (about 0.5 cm) and ligated cranially. A partial incision of the vascular wall was carried out and the sterile silicon catheter (Silastic®, Dow Corning Corp., USA) was inserted. The catheter itself has an outer diameter of 0.64 mm and a length of 40 mm. It was pushed forward until the peripheral end was moved by the heart beats. By pulling it back for a few millimeters, the tip of the catheter was located

Fig. 1. Implanted silicon catheter in the left external jugular vein of the rat. v = v. jugularis ext. sin., c = catheter, p = metal pin, a = a. carotis communis sin.

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Results and Conclusion

Side effects, e.g. catheter occlusions or subcutaneous abscesses were not observed. Loss of implanted catheters occurs in less than 6 out of 100 implantations. The behavior and mobility of the rats with the implanted catheter was not restricted. Besides minor microsurgical preparation, this method is regarded to be suitable for repeated intravenous applications of drugs with high accuracy in rats. It was used for i.v. applications of cytostatic drugs in more than 100 tumor-bearing rats [5] and can be recommended for future trials.

Fig. 2. X-ray picture of the implanted catheter visualized by injecting a contrast solution. c = catheter, k = cannula, s = syringe.

in its correct position. Then the catheter was fixed to the vein by a ligature. Figure 1 shows the implanted catheter in the vena jugularis sinistra of the rat.

The function of the catheter was verified by aspiration of blood. This was performed by a 1 ml single-use syringe which was connected to the silicone catheter by a blunt-edged cannula of 27G^{3/4}. The open end of the catheter was closed by inserting a bended metal pin with a diameter of 0.6 mm and a total length of 12 mm. Figure 2 demonstrates the correct position of the catheter, which was controlled by injecting a contrast solution (Conray®, Byk-Gulden, FRG) and taking an X-ray picture. The catheter was placed in a pocket under the skin. A small amount of Terramycin® (Pfizer, FRG) was given into the operation area to avoid local infections. The incision of the skin was closed by three 9 mm metal clamps (Autoclip®, Clay Adams, USA). By removing the clamps or by a new incision, repeated injections or infusions of drugs via the catheter at intervals of days or weeks are possible.

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M. Mit Hilfe der quantitativen Immunzytologie als nicht invasivem Untersuchungsverfahren werden Fortschritte in der Verlaufskontrolle von Patienten mit Harnblasentumorerkrankungen erreicht.

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