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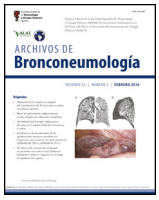

Original Article

Tracheal Self-Expandable Metallic Stents: A Comparative Study of Three Different Stents in a Rabbit Model☆

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ABSTRACT

Introduction: The objective of this study was to assess tracheal reactivity after the deployment of different self-expandable metal stents (SEMS).

Material and methods: Forty female New Zealand rabbits were divided into four groups. Three groups received three different SEMS: steel (ST), nitinol (NiTi), or nitinol drug-eluting stent (DES); the fourth group was the control group (no stent).

Stents were deployed percutaneously under fluoroscopic guidance. Animals were assessed by multislice, computed tomography (CT) scans, and tracheas were collected for anatomical pathology (AP) study. Data from CT and AP were statistically analyzed and correlated.

Results: The DES group had the longest stenosis (20.51 ± 14.08 mm vs 5.84 ± 12.43 and 6.57 ± 6.54 mm in NiTi and ST, respectively, day 30; $P<.05$), and higher granuloma formation on CT (50% of cases). The NiTi group showed the lowest grade of stenosis (2.86 ± 6.91% vs 11.28 ± 13.98 and 15.54 ± 25.95% in DES and ST, respectively; $P<.05$).

The AP study revealed that the ST group developed intense proliferative reactivity compared to the other groups. In the DES group, a destructive response was observed in 70% of the animals, while the NiTi was the least reactive stent.

CT was more effective in detecting wall thickening (positive correlation of 68.9%; $P<.001$) than granuloma (not significant).

Conclusions: The ST group developed granulomas and significant stenosis. NiTi was the least reactive stent, while DES caused significant lesions that may be related to drug dosage. This type of DES stent is therefore not recommended for the treatment of tracheobronchial stenosis.

Stents traqueales metálicos autoexpandibles. Estudio comparativo de 3 tipos diferentes de stents en un modelo animal

Palabras clave:
Stents
Stents liberadores de fármacos
Estenosis traqueal
Obstrucción de la vía aérea
Experimentación animal

RESUMEN

Introducción: El objetivo de este estudio es evaluar la reactividad traqueal tras la implantación de distintos stents metálicos autoexpandibles (SMAE).

Material y métodos: Se utilizaron 40 conejos hembra de raza neozelandesa, que se dividieron en 4 grupos. En 3 grupos se implantaron SMAE: de acero (SA), de nitinol (NiTi) o stents liberadores de nitinol (SLF). El cuarto grupo fue el grupo de control (sin stent).

Los stents se implantaron por vía percutánea bajo control fluoroscópico. Los animales se evaluaron mediante tomografía axial computarizada (TAC) multicorte y las tráqueas se extirparon para su estudio anatomopatológico (EAP). Los datos de la TAC y el EAP se analizaron estadísticamente y se correlacionaron.

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Resultados: El grupo que recibió SLF presentaba la mayor longitud de estenosis (20,51 ± 14,08 mm frente a 5,84 ± 12,43 y 6,57 ± 6,54 mm en los grupos NiTi y SA, día 30; p < 0,05) y el mayor índice de formación de granulomas evidenciados mediante TAC (50% de los casos). El grupo al que se implantaron stents NiTi mostró el menor grado de estenosis (2,86 ± 6,91% frente a 11,28 ± 13,98 y 15,54 ± 25,95% en los grupos SLF y SA; p < 0,05).

En el estudio AP, el grupo SA presentó reactividad proliferativa intensa en comparación con los otros 2 grupos. En el grupo SLF se observó una respuesta destructiva en el 70% de animales, mientras que el stent NiTi fue el que menos reacción provocó.

La TAC resultó ser superior para detectar el engrosamiento (correlación positiva de un 68,9%; p < 0,001) que para la observación de granulomas (n.s.).

Conclusiones: El grupo SA desarrolló granulomas y estenosis significativas. El stent NiTi fue el que menos reacción indujo, mientras que el SLN provocó lesiones importantes que podrían estar relacionadas con la dosis de fármaco. Por consiguiente, este tipo de SLF no se recomienda para el tratamiento de la estenosis traqueobronquial.

Introduction

Although surgical resection is the primary procedure for the treatment of tracheobronchial stenosis,[1] tracheal stenting, along with other minimally invasive techniques, such as radiofrequency, laser ablation, and cryotherapy, provides satisfactory management of central airway obstruction in non-surgical patients.[2] Silicone prostheses are the most commonly used, but these require the use of a rigid bronchoscope with general anesthesia for implantation. In contrast, metal stents can be deployed using fluoroscopy or through a flexible fiberoptic bronchoscope or endotracheal tube under light sedation, providing immediate symptomatic relief.[3] Other advantages of metal stents over silicone models are their higher radial force, better internal to external diameter ratio, lower incidence of migration, and decreased risk of mucus obstruction and bacterial colonization.[4] However, these important advantages have been clouded by long-term complications (such as restenosis due to granuloma formation or tumor growth), and difficulties involved in their removal.[5] These issues led the Food and Drug Administration (FDA) in 2005 to advise against the use of metal stents in benign lesions.[6]

Nevertheless, since then, studies have reported that metal stents are safe for the treatment of benign and malignant tracheobronchial stenosis.[6–9] Restenosis due to intraluminal overgrowth has been described mainly for steel stents.[10] Studies with laser cut, self-expandable nitinol stents have had better results. However, these nitinol stents are mostly used for other territories such as cardiovascular and biliary tree indications. Antiproliferative drugs are used in cardiovascular indications to avoid restenosis,[11,12] but experience in airway disease is limited.

We hypothesized that DES may combine the advantages of the metal stents in tracheal stenosis management, while avoiding or attenuating restenosis from intraluminal overgrowth through the mesh and over the ends. Therefore, the purpose of this study was to assess the tracheal responses to three different SEMS (drug-eluting nitinol, nitinol, and stainless steel bare metal stents) in an animal model.

Methods

Animals and Stents

Forty adult female New Zealand rabbits (3.95 ± 0.48 kg) were used in this study. The care and use of animals complied with the European Communities Council Directive (86/609/EEC) and local animal welfare laws, guidelines and policies, and was approved by the University of Zaragoza ethics committee. Animals were randomly distributed into four groups: ST (n=10), steel stent (Wallstent™, Boston Scientific, Natick, MA. USA); NiTi (n=10), nitinol stent (Zilver®Flex™ Vascular Stent, Cook Medical, Bjaeverskov, Denmark); DES (n=10), paclitaxel-eluting nitinol stent (Zilver®PTX® Drug Eluting Peripheral Stent, Cook Medical, Bjaeverskov, Denmark); and control (n=10), with no stent. Both nitinol stents are laser-cut and have exactly the same pattern design, whereas the steel stent is braided wire. All stents were self-expandable and measured 8 mm × 40 mm, at a 1:1 ratio to the trachea of the animal model. The stents were deployed percutaneously under general anesthesia and fluoroscopic guidance. Animals were followed for 90 days.

Stenting Technique

Before stent implantation, all rabbits were examined to ensure that they were healthy, and fasted for 8 h. They were medicated intramuscularly with 0.5 mg/kg medetomidine (Sedator®, Eurovet Animal Health, Netherlands) and 25 mg/kg ketamine (Imalgene 1000®, Merial, Barcelona, Spain). Anesthesia was maintained with 1%–2% isofluorane (Isovet, Braun, Barcelona, Spain) by inhalation. Animals were monitored throughout the procedure (Samurai anesthetic equipment, La Bouvet, Madrid, Spain and Dash 3000 monitor, General Electric Company, Helsinki, Finland).

After positioning animals in supine recumbency with neck hyperextension, and administering 50 mg/kg of oxytetracycline (Terramicina LA, Pfizer, Madrid, Spain), a straight 5F centimeter sizing catheter (Aurous®, Cook Medical, Bjaeverskov, Denmark) was introduced into the esophagus to obtain a reference measurement. Tracheal access was gained by puncturing between the two most cranial tracheal rings using an 18 G catheter-over-needle (Introcan®, Braun, Germany), then 0.15 ml lidocaine (Braun, Barcelona, Spain), was introduced into the trachea. A 0.035 inch hydrophilic guide wire (Radifocus® Guide Wire M Standard type, Terumo, Leuven, Belgium), soaked in lidocaine, was advanced into the trachea, and the catheter was removed. The stent delivery system was inserted directly over the guide wire and placed at a defined position (distal mark of the stent, 1 cm cranial to the tracheal carina) where the stent was deployed under fluoroscopic guidance (C-arm system BV Endura, Philips, Eindhoven, Netherlands). Once placed, the delivery system, guide wire, and centimeter catheter were removed, and the animal was supervised until recovery (Fig. 1).

All procedures were performed in the same way for the control group, using a stent delivery system without a stent.

Follow-Up and CT Study

After stent placement, all animals were observed for any sign of respiratory tract obstruction and surgical wound infection. The