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HISTOPATHOLOGICAL EFFECTS OF THREE MID-URETHRAL TAPE BRANDS: AN ANIMAL STUDY ON FEMALE RATS

Hypothesis / aims of study

The use of sub-urethral slings in treating urinary incontinence dates back to 1900s. However tension-free mid urethral tapes are substantially new in medicine. Different tapes have been produced, used and investigated during the recent decade. Two groups of studies can be retrieved in literature reading these products; efficacy studies mainly being human studies and mechanistic-histological studies mainly being animal studies. Regardless of study populations, most of these have been short-mid-term studies with very few of them conducted for a long-term evaluation. Other features of interest in the available literature is that most of the major studies have been initiated by industry rather than being researcher-initiated. Also most of the animal histological studies have solely used photo-microscopic methods. The aim of this study was to assess biomechanical and histopathologic effects of some midurethral tapes on Rat model using photo- electron-microscopy.

Study design, materials and methods

Thirty female Wistar rats, aged 10 weeks, with an average weight of 220 g, were randomly allocated into five groups (A, B, C, D, E) of 6 animals each. Groups A to E were assigned to receive one of the four brands of tapes designed to be used in anti-incontinence surgery as follows: A: Intravaginal slingplasty(IVS), B: Transobturator vaginal tape (TOT), C: Tension-free vaginal tape (TVT), D: Mersilene ,E: Control(Sham), without mesh placement.

The tapes in a length of 1cm were implanted sub-dermally in paravertebral area on the studied rats. Experimental groups were euthanized and tissue specimens collected from tape implanted regions of skin as well as the intact samples from control group, were fixed in 10% buffered formalin, embedded in paraffin and 5 µm thick microscopic sections were prepared through hematoxykin-eosin staining method.

Inflammatory infiltrate and fibrosis assessed and subjectively graded as low, moderate and extensive. In addition, collagen filling of the tapes was subjectively classified as good (> 50%), partial (25-50), or minimal (<25%). For each group, a score for biocompatibility potential was developed, consisting of the summation of grades (1–3) respectively assigned to inflammatory infiltrate, fibrosis, and collagen filling. With an ocular micrometer, the size of the tissue reaction around the tapes was evaluated. The average measurement for each tape was calculated. This parameter was also assigned a grade from 1 to 3. A thickness of 0.05-0.1 mm was considered as grade 1, 0.11-0.2 as grade 2 and above 0.21mm as grade 3.Grades were inversely proportional to the severity of inflammatory infiltrate and fibrosis as well as thickness of tissue reaction and directly proportional to collagen filling. Tapes shrinkage was assessed by measuring the average width of the tapes implanted into the rat skin using an ocular micrometer and calculating the percent of differences between the data's obtained and primary size of the tapes investigated. Electron microscopy: Small pieces of 2–3 mm size were immersed in the Karnovsky's fixative (0.1 M paraformaldehyde and glutaraldehyde solution in cocodylate buffer, pH 7.3) for 4 h, and thereafter washed with 0.1 M cacodylate buffer (pH 7.3). The samples were post fixed for 3 h at 4 °C in 1% osmium tertraoxide prepared in 0.1 M cacodylate buffer. The specimens were washed with distilled water and left in 1% aqueous uranyl acetate overnight. Subsequently, dehydration was carried out in ascending grades of alcohol, acetone and in pure acetone. Following dehydration, the specimens were embedded in Epon 812 at room temperature. Sections were cut on an LKB-Ultramicrotome with a glass knife. Thereafter, sections were mounted on 300 mesh copper grids, stained with 1% uranyl acetate and lead citrate and examined with a Phillips (FEI Tecnai 12 twin) Transmission Electron Microscope.

Results

Tissue reaction thicknesses are given in table 1 , scores for biocompatibility potential of different tapes 6 weeks post implantation into the rat skin in table 2 and Shrinkage rate in table 3.

Table 1. Tissue reaction thickness around the tapes implanted into rat skin (mm)

	A	B	C	D
6 weeks	0.2878	0.2675	0.2980	0.2852
12 weeks	0.1071	0.1315	0.2875	0.2380

Table 2. Scores for biocompatibility potential of different tapes 6-12 weeks post implantation into rat skin

	A		B		C		D	
	6 wks	12 wks	6 wks	12 wks	6 wks	12 wks	6 wks	12 wks
Inflammatory infiltrate	1	2	2	2	2	2	1	2
Fibrosis	3	3	1	2	1	1	2	2
Tissue reaction thickness	1	2	1	2	1	1	1	1
Collagen filling	1	1	2	2	2	3	1	1
Biocompatibility potential	6	8	6	8	6	7	5	6

Table 3. Shrinkage rate of the tapes implanted into rat skin

	A	B	C	D
6 weeks	54/77	52.90	67/94	38/74

12 weeks	60.44	56.59	68/42	50.18

Interpretation of results

In our study TVT showed slightly higher compatibility compared to IVS or TOT; and in both photomicroscopy and electron microscopy collagen bundles orderly surrounded the tapes. This can be a clue for its stability and effect in treatment of incontinence. However, higher degree of fibrosis in this brand may explain the findings regarding its slightly lower tissue compatibility after 12 weeks compared to IVS and TOT. Although IVS is multi-filament poly propylene, in current study biocompatibility potential of multi and mono filements are almost same.

Concluding message

Overall it may be concluded that regarding tissue compatibility and shrinkage rate in 12 weeks is almost same. Mersilene as a positive control showed lower compatibility and stability, according photo and electron microscopic data, TOT had base stability higher than other types, but no major deference observed.

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Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
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