Histologic Inflammatory Response to Transvaginal Polypropylene Mesh: A Systematic Review

Dominique Thomas, Michelle Demetres, Jennifer T. Anger, and Bilal Chughtai

To evaluate the inflammatory response following transvaginal implantation of polypropylene (PP) mesh. A comprehensive literature search was performed in the following databases from inception in April 2017: Ovid MEDLINE, Ovid EMBASE, and The Cochrane Library (Wiley). The studies retrieved were screened for eligibility against predefined inclusion and exclusion criteria. Twenty-three articles were included in this review. Following the implantation of PP mesh, there are immediate and local inflammatory responses. PP mesh elicits an inflammatory response that decreases over time; however, no studies documented a complete resolution. Further studies are needed to determine if there is a complete resolution of inflammation or if it persists. UROLOGY 111: 11–22, 2018. © 2017 Elsevier Inc.

The implantation of synthetic mesh has been used to repair weak tissue since its introduction in the 1940s.[1] Beginning in the early 1990s the implantation of surgical mesh was used to reinforce the weak pelvic floor tissue for both stress urinary incontinence (SUI) and pelvic organ prolapse (POP).[2] Since this time, the use of mesh has been the gold standard for these conditions. The most commonly used type of mesh is polypropylene (PP) because of its nonabsorbable properties and tensile strength.

Furthermore, PP mesh use for transvaginal surgery gained rapid popularity after its introduction because of its ease of use and decrease in morbidity.[3] However, immediate complications included mesh erosion into the urinary tract, sexual dysfunction, bleeding, pelvic pain, urinary tract infections, and vaginal extrusion.[4] Following the discovery of these complications, the Food and Drug Administration released multiple communications regarding the consequences of transvaginal mesh.[3]

Apart from the well-known risks of PP mesh, a myriad of patient advocacy groups have implicated its use with the subsequent development of systemic conditions, such as autoimmune diseases and carcinogenesis.[5] Although the data have not been substantiated in the medical literature, these claims have been a key element of mesh litigation lawsuits.[6] To date, there is a wealth of studies detailing how PP mesh reacts after being placed transvaginally. This systematic review will examine the available data in the literature on the inflammatory response of PP mesh placement on its host. Furthermore, it will detail when the inflammatory response subsides in animals and humans who have been implanted with PP mesh transvaginally.

METHODS

The present study was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[7]

Search Strategy

A medical librarian performed comprehensive searches to identify studies that evaluated the host response to PP surgical mesh in female animal and human models vaginally. Searches were run in April 27, 2017, in the following databases: Ovid MEDLINE (in-process and other nonindexed citations and Ovid MEDLINE from 1946 to present); Ovid EMBASE (from 1974 to present); and the Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials [CENTRAL], and Cochrane Methodology Register). The full search strategy for Ovid MEDLINE is available in Table 1. There were no language restrictions, publication date restrictions, or article type restrictions on the search strategy.

Study Selection

The searches across the chosen databases retrieved 1194 results. After the results were de-duplicated, 2 independent reviewers screened a total of 749 citations. Discrepancies were resolved by consensus. Titles and abstracts were reviewed against predefined inclusion and exclusion criteria. Articles considered for inclusion involved randomized controlled trials, controlled trials, and cohort studies

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From the Department of Urology, Weill Cornell Medical College/New York Presbyterian Hospital, New York, NY; Samuel J. Wood & C.V. Starr Biomedical Information Center, Weill Cornell Medical, College/New York Presbyterian Hospital, New York, NY; and the Department of Surgery, Division of Urology, Cedars-Sinai Medical Center, Los Angeles, CA

Address correspondence to: Bilal Chughtai, M.D., Department of Urology, Weill Cornell Medicine, 425 East 61st Street, 12th Floor, New York, NY 10065. E-mail: bic9008@med.cornell.edu

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Table 1. Ovid MEDLINE epub ahead of print, in-process and other nonindexed citations, Ovid MEDLINE daily, and Ovid MEDLINE from 1946 to the present

	Searched on 04/27/2017
1	Polypropylenes/
2	polypropylene.tw.
3	polypropylenes.tw.
4	propylene polymer.tw.
5	propylene polymers.tw.
6	prolene.tw.
7	polypro.tw.
8	Hostalen.tw.
9	Marlex.tw.
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11	Surgical Mesh/
12	mesh.tw.
13	meshes.tw.
14	4DDOME.tw.
15	AIGISRx.tw.
16	AlloDerm.tw.
17	AlloMax.tw.
18	Bard Composix EX.tw.
19	BIO-A Tissue Reinforcement prosthesis.tw.
20	CollaMend.tw.
21	DermaMatrix.tw.
22	DualMesh.tw.
23	Evolution P3EM.tw.
24	FasLata.tw.
25	FlexHD.tw.
26	FortaGen.tw.
27	IntePro Lite.tw.
28	InteXen.tw.
29	NEOVEIL.tw.
30	Parietex composite.tw.
31	Pelvicol.tw.
32	Pelvisoft.tw.
33	Pelvitex.tw.
34	PerFix.tw.
35	Peri-Strips Dry.tw.
36	PeriGuard.tw.
37	Permacol.tw.
38	Physiomesh.tw.
39	SeamGuard.tw.
40	SoftMesh.tw.
41	Strattice.tw.
42	Surgisis.tw.
43	TIGR.tw.
44	TiLoop Bra.tw.
45	Timesh.tw.
46	Tutomesh.tw.
47	Tutopatch.tw.
48	Ultrapro.tw.
49	Ventralex.tw.
50	Veritas.tw.
51	Vivosorb.tw.
52	Vypro.tw.
53	X-repair.tw.
54	XenMatrix.tw.
55	or/11-54
56	10 and 55
57	Autoimmune Diseases/
58	(autoimmune disease or autoimmune diseases).tw.
59	Carcinogenesis/
60	(carcinogenesis or carcinogeneses or carcinogenicity or tumorigenesis or tumorigeneses or oncogenesis or oncogeneses).tw.
61	(systemic effect or systemic effects or systemic reaction or systemic response or local effect or local effects or local reaction or local response or host response or host reaction or host tissue reaction or host tissue response or host responses or long-term behavior).tw.
62	(degradation or deterioration or degeneration).tw.
63	Inflammation/
64	(inflammation or inflammatory or inflamed).tw.
65	or/57-64
66	56 and 65

conducted with animal or female humans, with PP surgical mesh for vaginal repair. Excluded studies were those that focused only on animal or male humans, those that used a non-PP surgical mesh, or those that used a nonvaginal repair (eg, abdominal wall, hernia, and bowel).

Full text was then pulled for selected studies for a second round of eligibility screening. Reference lists for articles selected for inclusion in the study were also searched; from these, an additional 62 unique, relevant articles were screened. A total of 23 articles were selected for inclusion in this review. The full PRISMA flow diagram outlining the study selection process is available in Figure 1.

RESULTS

A total of 547 animals were used in this review (rabbits, n = 183; ewes, n = 114; rats, n = 202; mice, n = 48), with a total of 625 females receiving reinforcement with transvaginal mesh because of POP and SUI. Results were divided based on the type of PP mesh, a comparison of PP to different mesh types, and environmental factors affecting mesh and explanted mesh. Inflammatory biomarkers were described as macrophages, neovascularization, matrix metalloproteinase 2 (MMP2) and MMP9 cells (proinflammatory cells), foreign body giant cells, lymphocytes, necrosis, fibrin, cell density percentages, and so on. For a complete description of all studies including mesh type, placement and outcomes, please refer to Table 2.

Zhang et al compared macropore (type I) vs micropore (type II) GYNEMESH in 24 adult New Zealand rabbits.[8] Mesh was implanted in the vesicovaginal space. Mesh was explanted at days 7 and 60. At day 7, the inflammatory response was more pronounced, resulting in a number of inflammatory markers such as FBGCs and poly- and mononuclear cells, which were statistically significant ($P < .05$).[8] Type I mesh had a stronger inflammatory response at day 7 ($P < .05$), but by day 60, the inflammatory response was similar in both groups.

When comparing 17 female White New Zealand implanted with PP and poly(L-lactic) acid in comparison to a control implant (macroporous PP monofilament), Bader et al found there was no significant difference noted between the 3 groups. PP and poly(L-lactic) acid was comparable