components and enhancing the activity of cytokines. Interleukin-4 (IL-4) is incorporated into the coating to be released in a controlled manner upon implantation. In vitro controlled release profiles were assessed to demonstrate efficient and local release of IL-4. Utilizing a New Zealand white rabbit surgical model, we implant mesh using the "gold standard" abdominal sacrocolpopexy procedure and evaluate the changes in the host immunologic response at early (14 d) and tissue remodeling outcomes at late stages (90 and 180 d) of implantation. The mesh-tissue complex was removed from each rabbit and processed for histological staining as well as immunolabeling of immune cells, such as macrophages. Determination of matrix metalloproteinases and fibrotic capsule formation also helps characterize the overall inflammatory response associated with each implant. RESULTS/ANTICIPATED RESULTS: We have developed a clinically relevant rabbit surgical model to implant different conditions of surgical mesh into 2 different sites, including the vagina and the abdomen. The results of this study show that implants into vaginal tissues elicited an increased host inflammatory response at 14 days as compared with those in the abdominal wall. However, at chronic time points the inflammatory response in the vagina was reduced as compared to that in the abdominal cavity. The present study also demonstrates the scale-up of a previous methodology for nano-scale coating. We present a nanometer thickness, tunable, and uniform coating capable of releasing bioactive IL-4. In vitro assays confirm the bioactivity and the controlled local release allowing for shifts in the immune response to promote implant integration. Improved remodeling has been observed to correlate with a shift in the early host response from an M1 to an M2 phenotype, however, there is limited information on the exact mechanism. Our strategy to achieve enhanced tissue remodeling demonstrate outcomes such as minimal changes to the structural properties of the mesh and a controlled release profile to sufficiently polarize macrophages around the mesh to a pro-remodeling state. DISCUSSION/SIGNIFICANCE OF IMPACT: Pelvic organ prolapse is a condition where the pelvic floor muscles weaken over time resulting in the downward shift of the pelvic organs into the vaginal canal. Moreover, factors such as obesity, age, and vaginal birth increase the susceptibility of being diagnosed with pelvic organ prolapse. Direct costs of reconstructive procedures exceed $1 billion each year in the United States. Synthetic mesh has been used to repair abdominal hernias for over half a century. Biomedical companies, through 510k and the 1976 Medical Device Amendments Act, were able to resell their hernia repair mesh as a treatment for pelvic organ prolapse. However, women who have had vaginal mesh implants have reported an increasing number of complications including chronic pain and mesh erosion/exposure at rates as high as 10%–20%. In fact, in 2008 and 2011, the US Food and Drug Administration issued warnings to doctors and patients about the mesh. In January 2016, the FDA officially had to reclassify surgical mesh for transvaginal repair of pelvic organ prolapse from a class II, moderate risk device, to a class III, high-risk device. Presently, data for the use of synthetic mesh has largely derived from abdominal hernia repair, instead of vaginal repair of prolapse. In the rodent model, the vagina is too small to implant mesh in an analogous manner to human implantation. Instead, implantations are done in the abdomen, a different tissue composition and host response profile than the vagina. Primate models of pelvic organ prolapse have been utilized, but are associated with high costs and investigation of acute immune responses are not considered ethical due to the short time of survival. Thus, our presented work will not only show the development of an improved material for implantation, but also the development of an in vivo model clinically relevant to understanding the early host response to mesh.

2519

A quantitative disintegration method to evaluate polymeric films

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OBJECTIVES/SPECIFIC AIMS: To establish an in vitro quantitative method for the evaluation of polymeric film disintegration that can be applied to predict in vivo behavior. METHODS/STUDY POPULATION: Two clinically advanced vaginal microbicide film products containing tenofovir and dapivirine were used as model films throughout this work. Films were made using the solvent cast manufacturing method in which polymers, excipients, plasticizer, and APIs were either dissolved or dispersed in water, mixed, and cast on a heated substrate. The novel, quantitative method was developed using a TA.XT Plus Texture Analyzer® (Texture Technologies) in combination with a TA-108S5 fixture and the TA-8A: 1/8″ diameter rounded end ball probe. Exponent® was used as the data analysis software. In this method, the film was placed and secured in the fixture, the probe applied a constant force to the film product, and a biologically relevant amount of fluid was applied to the film. The probe was able to penetrate the film upon disintegration resulting in an applied force of zero at that point. A curve of force Versus time was plotted, and disintegration time was defined as the time between fluid addition until the probe force reached zero. Test parameters were optimized in order to reduce error. Visual observation of film disintegration was conducted in the in vivo macaque model using films that included a water-soluble blue dye for film visualization. Colpophotography was also used to confirm film disintegration. In vitro results were compared with in vivo findings. RESULTS/ANTICIPATED RESULTS: The Texture Analyzer disintegration method developed provided quantitative disintegration times and did not rely on user defined endpoints which is common in many visual disintegration tests. The disintegration method was able to distinguish differences between the 2 clinical film products and produced reproducible disintegration times for the tenofovir and dapivirine films. The tenofovir film had a shorter disintegration time (41.28 ± 2.85 s) compared with that of the dapivirine film ($88.3\ 6 \pm 9.82$ s). This method was also able to distinguish changes made to these 2 clinical film products in terms of volume and formulation alterations. In vitro and in vivo disintegration times differed by orders of magnitude, with in vitro time being measured in seconds and in vivo time being measured in days, for a variety of factors, mainly the application of constant force to the film product. Regardless of these differences, the rank order of film disintegration remained constant for in vitro and in vivo disintegration and an In Vitro In Vivo Correlation (IVIVC) trend could be seen. DISCUSSION/SIGNIFICANCE OF IMPACT: Standardization of preclinical in vitro assessments which minimize user bias are crucial to the field of pharmaceutical film development. As this field continues to develop and more products advance for pharmaceutical application, this method has the potential to become a standard assessment of film functionality. This study represents a first step in the process of developing an IVIVC. More films will need to be tested using both in vitro and visual methods in order to establish and accurate factor to predict in vivo behavior.

2529

Clinical determinants of clopidogrel responsiveness in a heterogeneous cohort of Caribbean Hispanics

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OBJECTIVES/SPECIFIC AIMS: To determine the association between clinical characteristics and platelet reactivity in Hispanic patients on clopidogrel therapy. METHODS/STUDY POPULATION: A cross-sectional pilot study was performed in 58 Puerto Rican patients diagnosed with any type of vascular disease and actively receiving a maintenance dose of clopidogrel for at least 7 days. The study population was divided into 2 groups: Group I with non-high on-treatment platelet reactivity (TPR); Group II with high TPR. To determine the platelet function, P2Y12 reaction units (PRU) were obtained by VerifyNow® P2Y12 assay (Accumetrics, USA). RESULTS/ANTICIPATED RESULTS: We studied a heterogeneous cohort of patients with coronary artery disease (57%), peripheral artery disease (30%), carotid artery stenosis (7%), cerebral artery aneurysm (3%), and stroke (3%) on clopidogrel therapy for secondary prevention of thromboembolic events. The mean TPR was 205 ± 49 PRU (range: 61–304), with a prevalence of 28% patients with high TPR (PRU $\geq$ 230). No significant clinical differences were found between the non-high TPR and high-TPR groups ($p > 0.05$). However, multivariable logistic regression analysis showed that both diabetes mellitus (OR = 7.5; CI: 1.01–51.9) and proton-pump inhibitors (OR = 13.6; CI: 1.3–142.0) were independently correlated with high TPR ($p < 0.05$) after adjusting for other clinical variables. DISCUSSION/SIGNIFICANCE OF IMPACT: These results provide new insight into the importance of clinical characteristics on platelet reactivity in this Caribbean population. Further studies are warranted to determine whether important clopidogrel pharmacogenes are related with platelet function in Hispanics, as well as the role of TPR in guiding antiplatelet therapy and predicting future adverse cardiovascular events in this population.

OUTCOMES RESEARCH/HEALTH SERVICES RESEARCH/COMPARATIVE EFFECTIVENESS

2025

Institutional and community involvement establishing ARresearch.org and innovative recruitment results in diverse registrants

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OBJECTIVES/SPECIFIC AIMS: To establish a state-wide research registry of diverse participants. METHODS/STUDY POPULATION: We garnered broad institutional and community support by involving TRI's Community Engagement team, its Community Advisory Board (CAB), and 3 UAMS patient CABs in

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