SA-OR457

Effect of Recombinant Human Type 1 Pancreatic Elastase (PRT-201) Treatment on Fistula Patency Bradley S. Dixon,[1] Eric K. Peden,[2] David B. Leeser,[3] Mahmoud T. El-Khatib,[4] Prabir Roy-Chaudhury,[4] Jeffrey Lawson,[5] Matthew Menard,[6] Marc H. Glickman,[7] Laura M. Dember,[8] Steven K. Burke.[9] *[1]U Iowa, IA; [2]Weill Cornell MC, NY; [3]Methodist Hospital, TX; [4]U Cincinnati, OH; [5]Duke U, NC; [6]Brigham & Womens' Hospital, MA; [7]Sentara Heart Hosp, VA; [8]Boston U, MA; [9]Proteon Therapeutics, MA.*

Background: Stenosis is a common cause of fistula (AVF) failure. We conducted a phase 1/2 randomized, double-blind, dose-escalation trial to determine if PRT-201 treatment was safe, would promote dilation & prevent failure of newly created AVFs.

Methods: A single dose of PRT-201 (N=45) or placebo (N=21) in 2.5 mL of saline was dripped onto the outside of the AVF over 10 min immediately after creation. Doses were aggregated into low (LD, 0.003, 0.010 & 0.033 mg), medium (MD, 0.1, 0.33 & 1 mg), & high (HD, 3, 6, 9 mg) groups (N=16, 17, 12). Patients were followed for up to 12 mon. Blinded duplex Doppler ultrasound evaluation was done at 6 weeks, & 3 & 6 months. Primary outcomes were safety & immediate change in outflow vein diameter (VD) & blood flow (BF). Secondary efficacy endpoints were AVF maturation (lumen VD ≥4 mm & BF ≥500 ml/min at 6 weeks), & time to primary patency loss (AVF occlusion or procedures required to maintain or restore patency).

Results: No safety concerns occurred. There was a modest but statistically significant immediate change in PRT-201 treated VD (5±6%, p<0.01). Lumen VD and BF increased in all groups with no difference in maturation at 6 weeks. Primary patency at 6 months was not statistically different among groups (Placebo 60%, LD 81%, MD 76%, HD 73%, p=NS). If immediate post-surgical complications that caused patency loss were excluded from the analysis (N=3 patients in LD group) patency loss was reduced in LD versus placebo (HR 0.28, 95% CI=0.08-0.93, p=0.04) and versus HD (HR 0.07, 95% CI=0.01-0.52, p=0.01). Angioplasty was the most common reason for patency loss (placebo 43%, LD 12%, MD 35%, HD 33%), with a trend toward less hemodynamically significant lumen stenosis in LD (placebo 47%, LD 31%, MD 62%, HD 50%).

Conclusions: PRT-201 was safe. At LD, PRT-201 might decrease lumen stenosis & prolong fistula patency but an adequately powered trial is needed.

Funding: Pharmaceutical Company Support

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Far Infrared Therapy Improves Endothelial Function and Access Flow of Newly-Created Arteriovenous Fistula in Patients with Stage 5 Chronic Kidney Disease Chih-Ching Lin.[1,2] *[1]School of Medicine, National Yang-Ming University, Taipei, Taiwan; [2]Divsion of Nephrology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan.*

Background: Endothelial dysfunction plays a significant role in the pathogenesis of malfunction of vascular access. The aim of this study is to evaluate the effect of far infrared (FIR) therapy on endothelial function and access flow (Qa) of newly created AV fistula.

Methods: We enrolled 75 patients (in stage 5 CKD) who were randomly allocated to treatment group (receiving 40 minutes of FIR therapy three times weekly for 3 months postoperatively, N=37) and control group (without FIR therapy, N=38). Access flow of AV fistula was measured by Doppler ultrasonography at 4 timings, including 2 days, 1 month, 2 and 3 months after vascular surgery. Markers of Endothelial function, including asymmetric dimethyl arginine (ADMA) and L-arginine, were measured both immediately before and 3 months after the creation of AV fistula.

Results: Finally, 67 patients completed the study, including 33 in FIR group and 34 controls. In comparison with controls, patients in FIR group had lower values of incremental change of ADMA as well as higher values of Qa at all of the 4 timings and incremental change of L-arginine, thus leading to a higher incremental change in the ratio of L-arginine to ADMA 3 months later (as shown in table 1).

Comparison of the endothelial function and access flow of AVF between HD patients with and without FIR therapy for 3 months

	Control group	FIR group	P value
Case number completing study	34	33	
Qa0 (ml/min)	259.1±85.5	337.9±111.3	0.002
Qa1 (ml/min)	597.9±230.1	805.2±315.7	0.003
Qa2 (ml/min)	681.8±275.2	925.8±354.6	0.002
Qa3(ml/min)	770.6±344.0	987.3±375.1	0.016
Δ L-arginine 3-0 (μM)	-0.7± 2.9	2.2± 5.2	0.007
ΔADMA 3-0 (μM)	0.01±0.05	-0.05±0.07	<0.001
(L-arginine3/ADMA3)/ (L-arginine0/ ADMA0)	0.98± 0.08	1.09±0.12	<0.001

Qa0 /Qa1/ Qa2/ Qa3: Qa measured at 2 days, 1, 2, or 3 months after AVF creation; ADMA0/3 or L-arginine0/3 indicates the concentration measured 1 day before/3 months after AVF creation

Conclusions: In conclusion, 3 months of FIR therapy improves endothelial function and access flow of newly created AVF in patients with stage 5 CKD.

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Improved Arteriovenous Fistula Maturation with Intra-Operative Implant of a Perianastomotic Sirolimus Eluting Collagen Membrane (Coll-R) Maria V. DeVita,[1] Eric S. Chemla,[4] Kipshidze Nickolas,[2] Surendra Shenoy,[3] Sriram Iyer.[1] *[1]Lenox Hill Hospital, New York, NY; [2]Center of Angiology and Vascular Surgery, Tbilisi, Georgia; [3]Washington U School of Medicine, St Louis, MO; [4]St. George's Healthcare NHS Trust, London.*

Background: Nonmaturation of arteriovenous fistulae (AVF) remains a major limiting factor for their use in hemodialysis patients(pts). Etiologies include perianastomotic stenosis and neointimal hyperplasia of the draining vein. Since there is no proven solution, novel approaches are needed. The Coll-R, an investigational product (Vascular Therapies, NJ, USA) is indicated and designed for perivascular implantation. It consists of collagen, a topical hemostat and sirolimus, an anti-proliferative agent with proven efficacy for suppressing neointimal tissue growth when delivered locally to the vascular wall. The goal of this study was to evaluate the performance and safety of the Coll-R when applied around the anastomotic site and outflow vein during creation of AVF. In this first in human study, endpoints were freedom from Coll-R related adverse effects and time to maturation.

Methods: Pts. from 2 hospitals inTbilisi, Georgia, scheduled for AVF creation were invited to participate. Venous mapping was performed to assure suitable vascular anatomy. The Coll-R was implanted intra-operatively during AVFcreation. Data collected included technical success of the implantation, wound healing, time to unassisted maturation and whole blood sirolimus levels.

Results: Thirty pts, 17 male, mean age 51 years (range 25-77) underwent radiocephalic (n=22) or brachiocephalic(n =8) AVF creation with implantation of the Coll-R (675μg of sirolimus). All completed a minimum of 11 weeks of follow up. There were no Coll-R related technical failures or adverse events. AVF matured in 26 pts. (87%); mean maturation time was 27±18 days; 4 pts thrombosed in <4 weeks; mean peak sirolimus level was 4.13 ng/ml seen 6 hr post-op. Two late AVF failures occurred at 119 and 170 days respectively.

Conclusions: Coll-R implantation during AVF creation does not cause systemic immunosuppression and improves fistula maturation. Use of this novel therapy may provide an unmet clinical need.

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Frequent Hemodialysis Fistula Infectious Complications Charmaine E. Lok,[1] Sarah Daisy Kosa,[1] Christopher T. Chan,[1] Deborah Lynn Zimmerman.[2] *[1]Toronto General Hospital, Toronto, ON, Canada; [2]Ottawa Hospital, Ottawa, ON, Canada.*

Background: Frequent hemodialysis (FHD) is associated with many beneficial clinical outcomes. Fistulas (AVF) are the preferred access for FHD; however there is a paucity of data on the impact of frequent cannulation and infectious complications. We compared the rate of infections in patients on FHD who cannulated their AVF using buttonhole (BH) vs. stepladder (SL) techniques. A second comparison was made with conventional intermittent HD (CIHD) patients using SL cannulation.

Methods: Patients who received short daily hemodialysis (SDH)(≥5x/wk) and nocturnal hemodialysis (NHD) (≥3 x/week, ≥5 hrs/session) who were dialyzed with an AVF were prospectively followed for infectious complications between Jan 2001-Dec 2010. Rates of bacteremia and BH site infections were compared using the exact binomial test.

Results: Forty-six patients had SDH and 128 had NHD. For self cannualtion, 50% of SDH and 72% of NHD used BH technique. In total, the BH technique was used on 198,910 fistula days while SL cannulation was performed on 99,681 fistula days. There were 39 BH-related bacteremias and at least 2 local BH-site infections (BHI). The BH bacteremia rate was 0.196/1000 fistula days. Staphylococcus aureus accounted for 85% of bacteremias. There were 5 related hospitalizations, and 3 metastatic infections (endocarditis, septic arthrisit, mycotic aneurysim and loss of fistula). In comparison, there was 1 possible fistula related infection in CIHD between Jan 1 2000-dec 31 2010 (rate of 0.002/1000 fistula days).

Conclusions: The rate of BH related infection is high in patients who self cannulate on FHD. The rate of bacteremia is >50 times that on CIHD. The majority of bacteremias are due to s. aureus and the consequences are serious with 13% requiring hospitalization and 10% with metastic spread or loss of access. The risks and benefits of BH cannulation require individual consideration with careful monitoring, prophylaxis and management.

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