Journal of Surgery: Open Access
ISSN 2470-0991 | Open Access

RESEARCH ARTICLE

Volume 4 - Issue 1 | DOI: http://dx.doi.org/10.16966/2470-0991.163

Use of Enalapril to Prevent Myointimal Hyperplasia in Arm's Arteriovenous Fistula for Hemodialysis Access

Héctor Bizueto-Rosas[1]*, Javier Ismael Hernández-Vázquez[1], Hugo Alonso Pérez-González[2], Carlos Daniel Gómez-Calvo[3], Carla Isabel Moreno-Ramírez[1], Rodrigo Marcelo Maitret-Velázquez[1], Perla Elín Leyva-Rivera[1], Nayeli Leticia Jiménez-Tejada[1], Martha Carolina Rosales-Ramos[1], Delio Felipe Martínez-Blanco[1], Noemí Antonia Hernández-Pérez[4], Sofía Muñoz-Vega[5], Rafael Mejía-Espinosa[5], Armando Guzmán-Caballero[5] and Jesús Herminio Rivera-Bañuelos[5]

[1]Vascular Surgery and Angiology Department, Specialties Hospital, "La Raza" National Medical Center, Mexican Institute of Social Security, México City, México

[2]Vascular Surgery and Angiology Department, General Hospital, Institute of Security and Social Services of State Workers, Querétaro, México

[3]Vascular Surgery and Angiology Department, General Hospital, Institute of Public Health Services of Baja California State, Ensenada, México

[4]Family and Work Physician, Mexican Institute of Social Security, Mexico City, Mexico

[5]Surgery Department, General Hospital "Darío Fernández Fierro", Institute of Security and Social Services of State Workers, México City, México

***Corresponding author:** Héctor Bizueto-Rosas, *Vascular Surgery and Angiology Department, Specialties Hospital, "La Raza" National Medical Center, Mexican Institute of Social Security, México City, México*, Tel: (+52 55) 3599 0728; **E-mail:** dr_bizueto_h@yahoo.com

Received: 04 Jan, 2018 | **Accepted:** 07 Feb, 2018 | **Published:** 15 Feb, 2018

Citation: Bizueto-Rosas H, Hernández-Vázquez JI, Pérez-González HA, Gómez-Calvo CD, Moreno-Ramírez CI, et al. (2018) Use of Enalapril to Prevent Myointimal Hyperplasia in Arm's Arteriovenous Fistula for Hemodialysis Access. J Surg Open Access 4(1): dx.doi.org/10.16966/2470-0991.163

Abstract

End-point: Evaluate the effect of Enalapril in preventing Myointimal Hyperplasia (MIH) in arm's arteriovenous fistula (AVF) for hemodialysis access.

Method: Inclusion criteria consisted on patients with no ACEI, or angiotensin II receptor blockers (ARB) treatment, or no intake up to 3 months before procedure, declared suitable for AVF access, and having thrill and bruit after AVF construction procedure. Under these criteria, we selected eighty-eight patients and assigned them randomly in case group and control group.

Case group received Enalapril 48 hours before AVF construction procedure and during study. We did evaluations of efferent vein diameter, myointimal complex, and flow velocities with Doppler Ultrasound (DU) during six weeks after procedure. MIH risk factors according to medical history and obtained data analysis were performed using student test.

Results: After medical history analysis, the main MIH risk factors presented were diabetes, hypertension and active smoking p=0.05. Within control group, MIH was higher as three patients had AVF failure *vs* one patient in case group, the Enalapril group.

Conclusion: We found no statistical difference in both groups (p=0.637).

Keywords: Myointimal hyperplasia; Arteriovenous fistula; Enalapril; Hemodialysis

Abbreviations: End-Stage Renal Disease (ESRD); Arteriovenous Fistula (AVF); Myointimal Hyperplasia (MIH): Angiotensin-Converting Enzyme Inhibitors (ACEI); Angiotensin II Receptor Blockers (ARB); Doppler Ultrasound (DU)

Introduction

The end-stage renal disease (ESRD) has a high morbid-mortality in Mexico and other countries [1]. In the United States 62% of the patients receiving hemodialysis uses an arteriovenous fistula (AVF) as vascular access, having a 60% primary patency [2]. Myointimal Hyperplasia (MIH) is one of the main causes of complications, presented in 30-50% of the cases and it has been demonstrated that steroids, calcium antagonists and angiotensin-converting enzyme inhibitors (ACEI) can diminish it [2-3].

In Mexico, ESRD has a prevalence of 337 per 1,000,000 habitants per year, and 1,142 per 1,000,000 habitants, of which 40% are under treatment and 16% receive hemodialysis as regular treatment at the Mexican Institute of Social Security [1].

On 1966, Drs. Brescia and Cimino described the arteriovenous internal fistula as vascular access [4-6] and today is considered the access of choice, associated with a low-rate infection, low–rate complications and high patency, on comparison with the other types of vascular access. [2,4-6] In order to have a functional AVF, it has to complete a process of growth and vein wall thickening also known as maturation. Other maturation targets are parameters such as, 6mm vein diameter minimum, 6mm below skin location maximum, and over 600ml/min flow [4-6].

The construction of an arterial-venous abnormal shunt, (meaning from a high speed and high pressure system to a low pressure and capacitance system), originates changes at the vein wall, such as vascular smooth muscle cells proliferation and medial thickening. These due to high shear stress and flow dynamics, that tend to continue until vein lumen is reduced, and eventually thrombosis occurs [5-6].

Between 55 to 65% of AVF do not complete a successful maturation process and up to 50% of those are due to obliterative processes [7]. AVF access have a primary patency of 60% in the first year, [3-5] and it is strictly related to factors such as age, diabetes, hypertension, arterial disease, active smoking and surgical technique, nevertheless, all these have similar molecular physiopathology [3].

Animal models and vein analysis have shown that the pro-inflammation response has a marked wall migration of macrophage, lymphocyte and cytokines and this exaggerated response has an inversely proportional relation to a successful maturation [4-7]. Experimental studies showed that using substances such as angiotensin-converting enzyme inhibitors (ACEI), angiotensin II receptor blockers (ARB) and calcium-antagonists (CA) could diminish MIH due to trauma or endothelial stress by blocking vasoconstrictors and releasing bradykinin [7-10].

Genes that encode Beta transformation growth factor (TGF-B) and platelet derivative growth factor (PDGF) are induced by angiotensin II to activate mRNA that cause cell proliferation, therefore can be suppressed by ACEIs and this reduction seems to be dose-dependent, with a maximum effect of Enalapril calculated at 0.07 mg per kg [9]. There are other medications, such as corticosteroids, that decrease MIH by attenuating inflammatory response, however, its combined use with ACEIs does not potentiate the protective effect, so to achieve the maximum effect of suppressing the MIH response, only one medication is required [8-9].

In our hospital, we perform an average of 150-240 AVF access construction procedures each year and we have a short-term follow-up program of 10-12 weeks to supervise reached maturation targets before sending the patient to start HD therapy through AVF access.

Material and Method

The present descriptive, longitudinal, cross-sectional of case and control study was performed in our hospital at the vascular surgery service in collaboration with the radiology service from January to May of 2017. Patients were randomized in 2 groups, *case group* where Enalapril oral intake of 10mg daily, starting 2 days prior to AVF construction procedure and continued for 6 weeks and *control group* with no Enalapril intake.

Patients were at least 18y old, with ESRD requiring HD continuous therapy, declared suitable for AVF access, having no previous AVF and no ACEIs or ARBs intake within at least 3 months. Only patients that had immediate bruit and thrill after surgery and had agreed to informed consent were included. Excluded patients were those with ACEI allergy or contraindication for it, and those lost in follow-up.

Doppler ultrasound of AVF was performed on all patients 6 weeks after procedure, in order to evaluate the myointimal complex of the efferent vein, diameter and flow velocity.

To diminish variation, all AVF were performed by the same vascular surgeon and all DU studies by the same radiologist using Toshiba Xario XG equipment and being blind to which study group each patient belonged to.

Data regarding medical history and non-pathological background that could affect AVF maturation process was collected and statistical analysis using standard deviation, interquartile range, Student's T and Shapiro-Wilk tests was made with Stata13® (StataCorp, college station, Texas, USA).

Results

Both groups were homogeneous. During the study, one patient of the Enalapril group and three patients of the control group were excluded due to early AVF thrombosis.

Enalapril group (n=43) characteristics are listed in table 1. Patient excluded for AVF thrombosis kept an active smoking habit. Twenty-seven patients were over the limit of 1.0mm at vein intimal-media complex, of those 27 patients, 16 of them (59%) had a complex over 1.6mm associated with having diabetes, hypertension, renal polycystosis or active smoking. MIH predominate with humerus median and radio cephalic configurations.

Control group (n=45) characteristics are listed in table 1. Two patients had AVF dysfunction associated with active smoking. Thirty-one patients were over the limit of 1.0 at vein intimal-media complex, of those 31 patients, 27 of them (87%) had a significant increase in that measure, with 1.7mm associated with diabetes, renal hypoplasia and 11 patients had active smoking. MIH predominate with radio median configuration.

In 50% of patients at Enalapril group, myointimal complex basal measure, prior to surgery, was of 0.06mm and 1.16 after AVF procedure; at control group basal measure was 0.09 and 1.7 after (Figure 1).

Within Enalapril group, 60% of patients (n=26) passed the 1.0mm myointimal complex limit and within control group, 75.6% (n=31) were over the limit.

No significant statistical difference was found regarding percentage of patients with MIH (*P value: 0.137) or at the myointimal complex measurement increase between before and after AVF procedure between the 2 groups (*P value 0.579) (Table 1 and Figure 1).

Table 2 resumes patients and characteristics with MIH. No difference was observed between the 2 groups regarding age, number of patients with diabetes and active smoking, AVF configuration or ESRD etiology, although, a tendency was observed involving more patients with active smoking and hypertension within MIH group. Statistical difference regarding years of ESRD between the 2 groups.

Table1: Patient characteristics, vascular access configuration and risk factors by group.

	Enalapril group N=43	Control group N=41	P Value
Gender n (%)			
Female	24 (55.8)	18 (43.9)	0.275
Male	19 (44.2)	23 (56.1)	
Age			
Mean ± SD	39.0 ± 14.0	43.8 ± 14.3	0.13
Diabetes n (%)	18 (41.9)	15 (36.6)	0.621
Hypertension n (%)	23 (53.5)	24 (58.5)	0.641
Smoker n (%)	16 (37.2)	14 (34.1)	0.908
Years w/ ESRD			
Mean	6 (3;9)	9 (4;14.5)	0.023*
AVF configuration n (%)			
Humerus median	12 (27.9)	14 (34.1)	0.826
Humerobasilic	6 (13.9)	3 (7.3)	
Humerus perforation	6 (13.9)	6 (14.6)	
Humero cephalic	4 (9.3)	3 (7.3)	
Radio cephalic	10 (23.3)	8 (19.5)	
Radio median	4 (9.3)	7 (17.1)	
Radio perforation	1 (2.3)	0 (0.0)	
ESRD etiology n (%)			
Renal hypoplasia	11 (25.6)	13 (31.7)	0.762
Diabetes	11 (25.6)	12 (29.3)	
Hypertension	9 (20.9)	4 (9.8)	
Polycystosis	3 (7.0)	5 (12.2)	
Infectious	4 (9.3)	3 (7.3)	
Preclampsia	4 (9.3)	4 (9.8)	
Lupus disease	1 (2.3)	0 (0.0)	

Table2: Patient characteristics with and without myointimal hyperplasia.

	With MIH N=57	No MIH N=27	P Value
Group n (%)			
Enalapril	26 (45.6)	17 (63.0)	0.137
Control	31 (54.4)	10 (37.0)	
Age			
Mean ± SD	40.6 ± 13.4	43.0 ± 16.1	0.462
Diabetes n (%)	22 (38.6)	11 (40.7)	0.851
Hypertension n (%)	28 (49.1)	19 (70.4)	0.067
Smoker n (%)	23 (40.4)	7 (25.9)	0.198
Years w/ ESRD			
Mean	8 (5-13)	5 (2-8)	0.003
AVF configuration n (%)			
Humerus median	17 (29.8)	9 (33.3)	0.621
Humerobasilic	5 (8.8)	4 (14.8)	
Humerus perforation	10 (17.5)	2 (7.4)	
Humero cephalic	5 (8.8)	2 (7.4)	
Radio cephalic	13 (22.8)	5 (18.5)	
Radio median	7 (12.3)	4 (14.8)	
Radio perforation	0 (0.0)	1 (3.7)	
ESRD etiology n (%)			
Renal hypoplasia	16 (28.1)	8 (29.6)	0.857
Infectious	5 (8.8)	2 (7.4)	
Polycystosis	6 (10.5)	2 (7.4)	
Preclampsia	5 (8.8)	3 (11.1)	
Lupus disease	1 (1.7)	0 (0.0)	
Diabetes	15 (26.3)	8 (29.6)	
Hypertension	9 (15.8)	4 (14.8)	

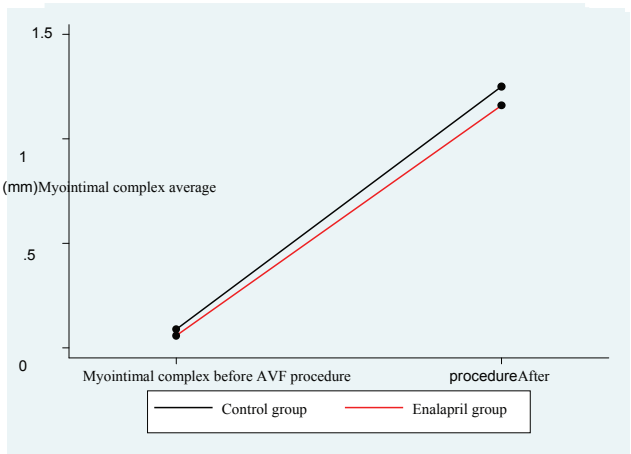

Figure 1: Myointimal complex before and after AVF procedure.

Discussion

ESRD is a serious public health care problem in Mexico and several other countries [1]. It has a very high morbidity and mortality rate in our country [1] and has a strong association with diabetes, with a prevalence of up to 7.2%, is considered the first cause of ESRD. Even when guidelines stipulate that between 65 to 85% patients with ESRD must be with continuous hemodialysis treatment, according to WHO, in Latin America only 15% are under hemodialysis.

Mexico occupies the 6th place of countries with people with diabetes, and according to the National Health and Nutrition Enquiry (ENSAUT) and WHO, Mexico is also the 6th place with male active smokers and the 2nd with female active smokers [14,15].

As AVF is considered the access of choice for under hemodialysis patients [2,4-6], primary patency is an important issue, considered up to 60% at first year of procedure, MIH is presented as reason of early failure in between 30 to 50% of patients.

In our study main causes of early AVF thrombosis, were diabetes and active smoking; also presenting higher MIH within those patients. Our results are non-conclusive regarding Enalapril as a protection factor against MIH, but in general, patients in Enalapril group developed lower myointimal complex measures and less AVF early failure. That, among other experimental studies, stands up for using medication against MIH in order to improve AVF useful life [2-3].

Conclusion

Active smoking and diabetes have an important role at MIH ($^{*}P=0.05$).

No statistical difference was found ($^{*}P=0.637$), associated to the number of cases.

Authors declare no interest conflict.

Special thanks to the technical assistance provided for Dr. Alexander Maximiliano Martínez Blanco, MD, MSc. Universidad del Valle, Cali, Colombia.

References

1. Méndez A, Méndez JF, Tapia T, Muñoz A, Aguilar L (2010) Epidemiología de la insuficiencia renal crónica en México. Dial Traspl 31: 7-11.
2. Sgroi MD, Patel MS, Wilson SE, Tenning WC, Blebea J, et al. (2013) The optimal inicial choice for permanent arteriovenous hemodialysis access. J Vasc Surg 58: 539-548.
3. Brahmbhatt A, Remuzzi A, Franzoni M, Misra S (2016) The molecular mechanisms of hemodialysis vascular access failure. Kidney Int 89: 303-316.
4. Browne LD, Bashar K, Griffin P, Kavanagh EG, Walsh SR, et al. (2015) The Role of Shear Stress in Arteriovenous Fistula Maturation and Failure: a systematic review. PLoS One 10: e0144297.
5. Lazich I, Chang A, Watson S, Dhar P, Madhurapantula RS, et al. (2015). Morphometric and histological parameters in veins of diabetic patients undergoing brachiocephalic fistula placement. Hemodial Int 19: 490-498.
6. Huber TS (2014) Hemodialysis Access: General Considerations. In: Cronenwett JL, Johnston KW, editors: Rutherford's Vascular Surgery, 8th ed. Philadelphia: Saunders, 1082-1098.
7. Mudoni A, Caccetta F, Caroppo M, Musio F, Accogli A, et al. (2016) Echo color Doppler ultrasound: a valuable diagnostic tool in the assessment of arteriovenous fistula in hemodialysis patients. J Vasc Access 17: 446-452.
8. Powell JS, Muller RK, Baumgartner HR (1991) Supression of the vascular response to injury: the role of angiotensin-converting enzyme inhibitors. J Am Coll Cardiol 17: 137B-142B.
9. Petrik P, Law MM, Moore WS, Colburn MD, Quinones-Baldrich W, et al. (1998) Dexamethasone and Enalapril Suppress Intirnal Hyperplasia Individually but Have No Synergistic Effect. Ann Vasc Surg 12: 216-220.
10. Jiang Z, Ozaki CK (2014) Intimal Hyperplasia. In: Cronenwett JL, Johnston KW, editors: Rutherford's Vascular Surgery, 8th ed. Philadelphia: Saunders, 78-86.
11. Tabbara M, Duque JC, Martínez L, Escobar LA, Wu W, et al. (2016) Pre-existing and Postoperative Intimal Hyperplasia and Arteriovenous Fistula Outcomes. Am J Kidney Dis 68: 455-464.
12. Model LS, Dardik A (2012) Neointimal Hyperplasia Disponible en: Haimovici's Vascular Surgery, 6th Edition.
13. Instituto Mexicano del Seguro Social (2008) Dirección de Prestaciones Médicas. Informe de Productividad. México, Distrito Federal.
14. American Diabetes Association (ADA) Guía de diabetes 2017. Hacia una visión más integral?
15. Estepa Misael. Situación actual del tabaquismo en México. Cardia Academic.