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Mohammed Mishaal Shareif
Ministry of Health, Nineveh Health Director, Mosul Centre Cardiology and Cardiac surgery, Iraq

Sadiq Mohammed Al Hamash
College of Medicine, Baghdad University, Iraq

Hakam Alsamarrai
Ibn Al-Bitar Specialized Center for Cardiac Surgery, Iraq

Corresponding Author:
Mohammed Mishaal Shareif
Ministry of Health, Nineveh Health Director, Mosul Centre Cardiology and Cardiac Surgery, Iraq

Epidemiological study of pulmonary hypertension and effect of bosentan therapy in specialist Iraqi center

Mohammed Mishaal Shareif, Sadiq Mohammed Al Hamash and Hakam Alsamarrai

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Abstract
Background: Pulmonary hypertension (PH) is a significant health concern in Iraq, known for its high morbidity and mortality rates and commonly associated with structural heart disease. This study aimed to examine the epidemiological characteristics of PH patients and evaluate the effectiveness of bosentan therapy at a specialized Iraqi center.
Method: Conducted at Ibn-Albitar Center for Cardiac Surgery in Baghdad from September 2020 to June 2021, this cross-sectional study involved 244 patients with PH. Data collection involved direct interviews, questionnaires, and reviews of patient files, including detailed histories and laboratory tests such as liver function tests (LFT).
Results: The mean age of the PH patients was 26.17 years, with the majority aged between 6-17 years. Females were more prevalent (74.6%) compared to males (25.4%), with a male to female ratio of 1:2.94. Pulmonary hypertension was classified into five groups, with Group 1 PAH (including 66.9% with congenital heart disease (CHD), 31.7% with idiopathic pulmonary arterial hypertension (IPAH), 0.8% with heritable pulmonary arterial hypertension (HPAH), and 0.4% with connective tissue disease (CTD)) comprising 96.72% of the patients. The study found that bosentan therapy led to an improvement in the 6-minute walk distance (6MWD) and a significant upgrade from functional class III to II in patients with IPAH (p=0.041). However, patients with CHD and those on bosentan for over five years experienced a decline in 6MWD (p=0.024 and p=0.043, respectively).
Conclusion: PH is a prevalent and serious healthcare issue in Iraq, primarily caused by CHD, with large ventricular septal defects being the most common underlying condition. Bosentan therapy, while generally safe and well-tolerated, shows varying efficacy in improving 6MWT performance and functional class in patients with different types of PH.

Keywords: Epidemiological, pulmonary, hypertension, bosentan, therapy, Iraqi, center

Introduction

Pulmonary hypertension (PH) in children is a condition characterized by high blood pressure in the lungs, arising from various diseases and manifesting at any age. Unlike adults, children more commonly have idiopathic pulmonary arterial hypertension (IPAH), pulmonary arterial hypertension associated with congenital heart disease (PAH-CHD), and developmental lung diseases. Pediatric PH demands a unique approach due to differences in aetiology, presentation, and outcomes. Management is challenging as it often relies on evidence from adult studies and pediatric expertise, with limited data on treatment efficacy, dosing, and strategies in children [1].

PH is defined hemodynamically as a mean pulmonary artery pressure (mPAP) of ≥ 25 mm Hg at rest, measured via right heart catheterization. The normal resting mPAP is about 14±3 mmHg. A mPAP between 21 and 24 mmHg has unclear clinical significance. PH is not a diagnosis in itself but a state characterized by elevated mPAP. Pulmonary arterial hypertension (PAH) is a subgroup of PH with precapillary PH and elevated pulmonary vascular resistance (PVR), defined by mPAP ≥ 25 mm Hg, normal pulmonary arterial wedge pressure (PAWP) ≤ 15 mm Hg, and PVR > 3 wood units [2, 3]. Globally, PH affects about 1% of the population, increasing to around 10% in those over 65. Its incidence and prevalence vary by type. For example, in Germany, the incidence of PAH was 3.9 per 1 million adults, and chronic thromboembolic PH was 4 per 1 million adults in 2014 [4].

Left heart disease is a common cause, with about 50% developing PH, and lung diseases like chronic obstructive and fibrotic disease also contribute significantly to PH prevalence [4]. Symptoms of PH include progressive exercise dyspnea, fatigue, exhaustion, bendopnea, and syncope, often leading to a delay in diagnosis. Physical examination may reveal cyanosis, a pronounced pulmonary valve component of the second heart sound, and a systolic flow murmur in tricuspid valve insufficiency [5]. Early detection and classification are crucial, with basic diagnostic tests including ECG and BNP or NT-proBNP levels. Further investigations are needed if these tests are abnormal or clinical suspicion is high. Echocardiography is a key noninvasive tool, often raising the first suspicion of PH or right heart overload. The definitive diagnosis of PH is confirmed by right heart catheterization, though not indicated in all suspected cases, especially in chronic left heart or lung disease. It is crucial for suspected PAH or chronic thromboembolic PH cases [2, 3]. Vasoreactivity testing during catheterization identifies candidates for calcium antagonist treatment in idiopathic, hereditary, or drug-related PAH [2, 3]. Perfusion scintigraphy is important to detect chronic thromboembolic PH [2, 3]. Treatment for PH is mostly symptomatic, depending on disease type and severity. Oxygen therapy is recommended for hypoxemia, and diuretics are used for hyperhydration. Anticoagulation is specific to certain PH types and comorbidities [2, 3, 6]. Rehabilitation and physiotherapy improve exercise capacity, quality of life, and cardiac function [7]. Bosentan, an oral dual antagonist of endothelin receptors (ETRs), inhibits the function of Endothelin-1 (ET-1), a key isoform in pulmonary vascular regulation. ET-1, consisting of 21 amino acids, is produced in endothelial cells and regulates vasomotor tone through a multi-step synthesis process. It acts on ET-A receptors on smooth muscle to cause vasoconstriction, while ET-B receptors help maintain vascular homeostasis by releasing vasodilators like nitric oxide under normal physiological conditions [8]. Aim of study to study the epidemiological characteristics of patients with pulmonary hypertension and assess the effect of bosentan therapy in specialist Iraqi center.

Method

The study on pulmonary hypertension (PH) involved direct interviews and questionnaires with patients registered at Ibn-Albitar specialized center. Data were collected from patients and/or their parents, as well as patient files. The questionnaire, designed by the researcher and supervisor, included sociodemographic details, PH causes, family history, treatment history (Focusing on Bosentan and phosphodiesterase 5 inhibitors), treatment compliance and duration, side effects of Bosentan therapy, pulmonary artery and systemic pressure measurements from catheterization, right ventricular pressure and mean pulmonary artery pressure from echo studies, and blood tests including liver enzymes and complete blood count. Inclusion criteria were PH diagnosis by echo and/or catheterization, with specific criteria for congenital heart disease (CHD) and idiopathic pulmonary arterial hypertension (IPAH). All age groups were included. The study also examined the prevalence of certain variables using the 6-Minute Walk Test (6MWT) and functional classification (FC) to identify responders to endothelin receptor antagonists (ERA), specifically Bosentan. Patients were included if Bosentan was their first-line therapy, with at least 6 months of follow-up. The study involved retrospective selection of 60 patients from 244 consecutive IPAH and CHD-associated PAH patients. The 6MWT, conducted before the first dose of Bosentan and during the research period, measured exercise capacity. The New York Heart Association (NYHA) functional classification was used to assess patients' physical limitations. Patients and/or their parents' consent was required for participation in the 6MWT. Exclusion criteria for the 6MWT included refusal to participate, pre-existing severe medical conditions, and NYHA functional class IV. The 6MWT protocol involved standardized conditions and instructions, with measurements of heart rate, oxygen saturation, and walking distance before and after the test. Anthropometric variables like age, height, weight, and gender were significant predictors of 6MWT performance, with weight having the greatest impact. Predictive 6MWD equations were used for men and women to calculate the percentage of predicted value. Ethical considerations included approvals from Ibn-Albitar specialized center and patients or their parents, confidentiality, and informing physicians about any deteriorated cases. Statistical analysis was conducted using SPSS version 26, presenting data as mean, standard deviation, and ranges. Categorical data were represented by frequencies and percentages. A paired t-test compared the predictive distance percentage between the first and second 6-minute walk tests, with a P-value of less than 0.05 indicating significant statistical analysis.

Results

Comprehensive clinical classification of pulmonary hypertension divided into 5 groups as shown in the figure 1: Group 1 PAH including (96.72%) from patients, it is consisting of 66.94% CHD, 31.77% IPAH, 0.85% HPAH, and 0.42% CTD as shown in the figure 2 Note: About PH One hundred seventy seven patients confirmed by catheterization ((152 patient of CHD and 25 patient of IPAH)) Group 2 comprises PH caused by left heart diseases, including (0.82%), one patient has COA, and another one has mitral valve disease, Group 3 PH include lung disease representing only (0.41%), one patient with chronic obstructive pulmonary disease, Group 4 Chronic thromboembolic PH representing (2%), two patient with pulmonary embolism and three patient with deep vein thrombosis.

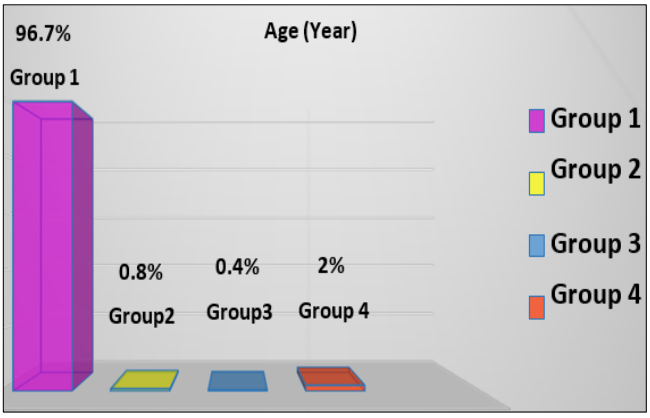

Fig 1: Clinical classification of pulmonary hypertension.

Table 1 shows the distribution of study patients by classification. The most common associated condition was

CHD (66.9%), and the most common CHD detected was VSD (56.52%).

Table 1: Classification of CHD patients

Classification		No. (n= 161)	Percentage (%)
Classi-fication CHD	CHD	No. (n= 161)	Percentage (%)
	VSD	91	56.52
	AVC	16	9.9
	ASDII	15	9.32
	PDA	13	8.07
	Single ventricle	7	4.3
	LTGA	6	3.72
	AP	3	1.86
	DORV	5	3.1
	TOF+PA+ Collatral	2	1.24
	TA	2	1.24
	DTGA	1	0.62

In this study, there was 29.5% has history of CHD with left to right shunt, but now has right to left shunt due to severe PH ((Eisenmenger patients)). The most common CHD associated with Eisenmenger is VSD as shown in table 2.

Table 2: Classification of CHD in Eisenmenger syndrome.

Classification		No. (n= 72)	Percentage (%)
Eisenmenger syndrome	VSD	46	63.9
	PDA	11	15.3
	AVC	10	13.9
	DORV/PH	3	4.2
	AP window	2	2.7

Family history: CHD and HPAH was positive in 3.27%: as shown in table 3.

1. 2.45% from study patient has 1st degree relative of CHD (VSD and PH)
2. 0.82% from study patient has 1st degree relative of HPAH

We noticed that more than half of study patients (53.3%) were treated by dual therapy (Bosentan + PDE5I). Regarding compliance ((obeying to treatment)) of patients, 70.9% of them were compliant with bosentan and 76.4% were compliant with sildenafil as shown in table 3.

Table 3: Distribution of study patients by treatment options

Treatment	No. (n= 244)	Percentage (%)
Treatment option		
Mono therapy	104	42.6
Dual therapy	130	53.3
Triple therapy	10	4.1
Compliance to bosentan		
Yes	173	70.9
No	71	29.1
Compliance to Sildenafil		n= 140
Yes	107	76.4
No	33	23.6
Duration of bosentan treatment (Month)		
< 24	96	39.3
24 - 60	106	43.4
> 60	42	17.2

Table 4 shows the side effect of bosentan (symptoms starting after bosentan treatment. The most common side effect was headache (21.3%) especially in adults (14.3%).

Table 4: Side effect of bosentan therapy

Side effect		No. (n= 244)	Percentage (%)
Headache	< 6 (Year)	5	2.1
	6-17 (Year)	12	4.9
	18-29 (Year)	35	14.3
Edema(leg)	6-17 (Year)	3	1.2
	≥ 18 (Year)	10	4.1
Recurrent chest infection	< 18 (Year)	7	2.9
	≥ 18 (Year)	5	2.1
Arthralgia	6-17 (Year)	4	1.6
	18-29 (Year)	26	10.7
Flush	6-17 (Year)	2	0.8
	18-29 (Year)	6	2.5

By comparison in percentage of predictive distance between 1st and 2nd six mints.' walk test, no statistical significant change (P= 0.11) in percentage of predictive distance at 2nd six mints.' walk test compared to that at 1st six mints.' walk test, as shown in table 5.

Table 5: Comparison in percentage of predictive distance between 1st and 2nd six mints.' walk test

Percentage of predictive distance (%)	Six mints.' walk test		P - Value
	First Mean ± SD	Second Mean ± SD	
	45.29±30.2	39.14±19.8	0.11

Table 6 shows the comparison in percentage of predictive distance between 1st and 2nd six mints.' walk test according certain characteristics. Among patients with CHD and among those who received bosentan for more than 5 years, percentage of predictive distance at 2nd six mints.' walk test was significantly decreased (51.95 versus 34.21%, P= 0.024; and 45 versus 32.25%, P= 0.043 respectively); while it significantly increased among patients with IPAH (37.78 versus 44.39%, P= 0.041) compared to that at 1st six mints.' walk test. No statistical significant differences detected (P ≥ 0.05) among all other characteristics.

Table 6: Comparison in percentage of predictive distance between 1st and 2nd six mints' walk test according certain characteristics

Percentage of predictive distance (%)	Six mints.' walk test		P - Value
	First Mean ± SD	Second Mean ± SD	
Age (Year)			
6–17	35.67±24.3	31.17±15.5	0.599
18– 47	52.95±34.6	41.32±19.8	0.082
Gender			
Male	46.67±22.1	51.33±26.1	0.644
Female	45.06±31.7	35.94±18.1	0.055
Classification			
CHD	51.95±35.5	34.21±18.1	0.024
IPAH	37.78±24.53	44.39±21.0	0.041
Treatment option			
Mono therapy	40.05±22.4	41.05±19.9	0.761
Dual and triple therapy	49.61±35.4	35.74±19.8	0.058
Compliance to bosentan			
Yes	47.71±32.7	38.23±21.5	0.085
No	38.45±21.8	37.91±14.7	0.92
Duration of bosentan treatment (month)			
< 24	46.71±26.1	43.35±19.4	0.593
24 – 60	38.8±25.6	39.6±21.5	0.917
> 60	45.0±22.0	32.25±22.2	0.043

Discussion: Pulmonary arterial hypertension (PAH) is a severe lung disease characterized by increased pulmonary

vascular resistance and arterial pressure, leading to right ventricular (RV) failure and premature death. RV function is a critical predictor of morbidity and mortality, underscoring the importance of quantifying RV function for treatment response assessment [9, 10]. Exercise intolerance, a primary symptom of PAH, necessitates evaluating exercise capacity, commonly measured by the six-minute walk test (6MWT). The 6MWT is a central component in PAH assessment, reflecting RV performance under stress and providing a non-invasive, inexpensive, and repeatable measure of exercise capacity. However, it is influenced by non-cardiopulmonary factors like age, height, weight, and musculoskeletal disease [11, 12]. European guidelines recommend performing the 6MWT at baseline, every 3-4 months after treatment initiation or modification, and regularly every 3-6 months in stable patients [13]. Socio-demographic characteristics of PAH patients vary, with a higher prevalence among females and a wide age range, suggesting influences from genetic factors, different causative diseases, and socioeconomic factors affecting follow-up attendance [14-16]. PAH trends show varying patterns across studies, likely due to differences in study designs, geographic locations, healthcare systems, and the disease's nature. Early diagnosis and management of congenital heart disease (CHD), a common cause of PAH, are crucial, particularly in developing countries [17]. Classification of PAH patients varies, with a significant proportion having CHD and a smaller percentage with idiopathic PAH (IPAH). Differences in patient characteristics across studies might be due to the timing of diagnosis and intervention for CHD, socioeconomic status, and educational levels [18-20]. Regarding the 6MWT, findings are mixed. Some studies show improvements in walk distance and functional class after treatment, while others report no significant changes. These discrepancies could be due to sample size, study design, geographic variations, differences in clinical presentations, treatment types, disease severity, and comorbid conditions [21, 22]. Treatment response varies among patients, with some showing significant improvements in 6MWT performance and others experiencing little change. This variability might be influenced by factors like the type of PAH, treatment regimen, and presence of comorbidities. Bosentan, a common PAH treatment, has shown mixed results in different studies, with some patients experiencing significant improvements and others showing no change or even decline in 6MWT performance [23-25]. Side effects of PAH treatments like bosentan include headache, liver function abnormalities, and other systemic vasodilatation symptoms. Hepatotoxicity is a concern, requiring regular monitoring of liver function. The severity and frequency of side effects vary among studies and patient populations [26, 27]. In summary, PAH is a complex disease with varying presentations and responses to treatment. The 6MWT is a valuable tool for assessing PAH, but its results can be influenced by many factors. Treatment strategies need to consider individual patient characteristics, and side effects should be closely monitored. The management of PAH requires a comprehensive approach, considering the multifaceted nature of the disease and the diverse patient population it affects.

Conclusion: In Iraq, pulmonary hypertension (PH) is a significant health issue, often caused by congenital heart diseases like large ventricular septal defects. Early diagnosis and management of these conditions are crucial to reduce PH prevalence. The 6-minute walk test is a practical, safe, and reliable method for assessing exercise capacity and monitoring treatment effects in PH patients. Bosentan therapy improves functional class in idiopathic pulmonary arterial hypertension but may lead to declining exercise capacity over time in congenital heart disease patients. Regular monitoring of liver function and complete blood count is essential for patients on bosentan therapy.

Conflict of Interest
Not available

Financial Support
Not available

References

1. Rosenzweig EB, Abman SH, Adatia I, Beghetti M, Bonnet D, Haworth S, *et al*. Paediatric pulmonary arterial hypertension: updates on definition, classification, diagnostics and management. Eur Respir J. 2019;53(1):1801916.
2. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, *et al*, ESC Scientific Document Group. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J. 2016;37(1):67-119.
3. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, *et al*. ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Respir J. 2015 Oct;46(4):903-75. DOI: 10.1183/13993003.01032-2015. Epub 2015 Aug 29. Erratum in: Eur Respir J 2015; 46(6):1855-1856.
4. Hoeper MM, Humbert M, Souza R, Idrees M, Kawut SM, Sliwa- Hahnle K, *et al*. A global view of pulmonary hypertension. Lancet Respir Med. 2016;4(4):306-322.
5. Hoeper MM, Ghofrani HA, Grünig E, Klose H, Olschewski H, Rosenkranz S. Pulmonary Hypertension. Dtsch Arztebl Int. 2017;114(5):73-84.
6. Olsson KM, Delcroix M, Ghofrani HA, Tiede H, Huscher D, Speich R, *et al*. Anticoagulation and survival in pulmonary arterial hypertension: results from the Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension (COMPERA). Circulation. 2014;129(1):57-65.
7. Ehlken N, Lichtblau M, Klose H, Weidenhammer J, Fischer C, Nechwatal R, *et al*. Exercise training improves peak oxygen consumption and haemodynamics in patients with severe pulmonary

arterial hypertension and inoperable chronic thrombo-embolic pulmonary hypertension: a prospective, randomized, controlled trial. Eur Heart J. 2016;37(1):35-44.
8. Wang Y, Chen S, Du J. Bosentan for Treatment of Pediatric Idiopathic Pulmonary Arterial Hypertension: State-of-the-Art. Front Pediatr. 2019;7:302.
9. Guillevin L, Armstrong I, Aldrighetti R, Howard LS, Ryftenius H, Fischer A, *et al*. Understanding the impact of pulmonary arterial hypertension on patients' and carers' lives. European Respiratory Review. 2013;22(130):535-42.
10. Badagliacca R, Poscia R, Pezzuto B, Papa S, Reali M, Pesce F, *et al*. Prognostic relevance of right heart reverse remodeling in idiopathic pulmonary arterial hypertension. The Journal of Heart and Lung Transplantation. 2018;37(2):195-205.
11. Humbert M, Sitbon O, Chaouat A, Bertocchi M, Habib G, Gressin V, *et al*. Survival in patients with idiopathic, familial, and anorexigen- associated pulmonary arterial hypertension in the modern management era. Circulation. 2010;122(2):156-63.
12. Halliday SJ, Wang L, Yu C, Vickers BP, Newman JH, Fremont RD, *et al*. Six-minute walk distance in healthy young adults. Respiratory medicine. 2020;165:105933.
13. Galie N, Hoeper MM, Humbert M, Torbicki A, Vachiery JL, Barbera JA, *et al*. Guidelines for the diagnosis and treatment of pulmonary hypertension: the Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). European heart journal. 2009;30(20):2493-537.
14. Halliday SJ, Wang L, Yu C, Vickers BP, Newman JH, Fremont RD, *et al*. Six-minute walk distance in healthy young adults. Respiratory medicine. 2020;165:105933-.
15. Verlinden NJ, Benza RL, Raina A. Safety and efficacy of transitioning from the combination of bosentan and sildenafil to alternative therapy in patients with pulmonary arterial hypertension. Pulm Circ. 2020;10(4):2045894020945523-.
16. AL-Kinani AAA. Clinical study of patients with primary pulmonary hypertension (PPH). Journal of the Faculty of Medicine Baghdad. 2018;60(2):80-4.
17. Anand V, Roy SS, Archer SL, Weir EK, Garg SK, Duval S, *et al*. Trends and Outcomes of Pulmonary Arterial Hypertension–Related Hospitalizations in the United States: Analysis of the Nationwide Inpatient Sample Database From 2001 Through 2012. JAMA Cardiology. 2016;1(9):1021-9.
18. Loaiza CAQ, Martín MTV, López-Guarch CJ, Cano MJR, Tejedor PN, Carreira PE, *et al*. Trends in pulmonary hypertension over a period of 30 years: Experience from a single referral centre. Revista Española de Cardiología (English Edition). 2017;70(11):915-23.
19. Güngör H, Ertugay S, Ayık MF, Demir E, Engin C, Yağdı T, *et al*. [Clinical and hemodynamic features of Eisenmenger syndrome patients at the time of first admission: a tertiary referral-center experience]. Anadolu kardiyoloji dergisi: AKD = the Anatolian journal of cardiology. 2012;12(1):11-5.
20. D'Alto M, Romeo E, Argiento P, Sarubbi B, Santoro G, Grimaldi N, *et al*. Bosentan-sildenafil association in patients with congenital heart disease-related pulmonary arterial hypertension and Eisenmenger physiology. International Journal of Cardiology. 2012;155(3):378-82.
21. Degano B, Sitbon O, Savale L, Garcia G, O'Callaghan DS, Jaïs X, *et al*. Characterization of pulmonary arterial hypertension patients walking more than 450 m in 6 min at diagnosis. Chest. 2010;137(6):1297-303.
22. Gabler NB, French B, Strom BL, Palevsky HI, Taichman DB, Kawut SM, *et al*. Validation of 6-Minute Walk Distance as a Surrogate End Point in Pulmonary Arterial Hypertension Trials. Circulation. 2012;126(3):349-56.
23. Girgis RE, Mathai SC, Krishnan JA, Wigley FM, Hassoun PM. Long-term outcome of bosentan treatment in idiopathic pulmonary arterial hypertension and pulmonary arterial hypertension associated with the scleroderma spectrum of diseases. The Journal of heart and lung transplantation: the official publication of the International Society for Heart Transplantation. 2005;24(10):1626-31.
24. Rubin LJ, Badesch DB, Barst RJ, Galie N, Black CM, Keogh A, *et al*. Bosentan therapy for pulmonary arterial hypertension. The New England journal of medicine. 2002;346(12):896-903.
25. Tokgözoğlu L, Akdoğan A, Okutucu S, Kaya EB, Aytemir K, Ozkutlu H. [Two years of multidisciplinary diagnostic and therapeutic experience in patients with pulmonary arterial hypertension]. Turk Kardiyoloji Dernegi arsivi: Turk Kardiyoloji Derneginin yayin organidir. 2009;37(6):378-83.
26. Sohn DW, Kim HK, Kim MA, Song YW, Noh CI, Kim DK *et al*. Beneficial and adverse effects of bosentan treatment in korean patients with pulmonary artery hypertension. Korean Circ J. 2009;39(3):105-10.
27. Stamm JA, Risbano MG, Mathier MA. Overview of current therapeutic approaches for pulmonary hypertension. Pulm Circ. 2011;1(2):138-59.

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