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Recent Advances in Eisenmenger Syndrome: A Comprehensive Review

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ABSTRACT:

Eisenmenger's syndrome is chronic unrepaired heart related disease present at birth in which there is irregular blood flow in heart and lungs. It can be life threatening as it can cause the blood vessels to become stiff and narrow which results in increase in blood pressure in lung arteries which can be acknowledged as Pulmonary arterial hypertension. As it is chronic slow progressive hypoxia is seen along with central cyanosis.

In adults the complications of multisystemic disorders as such as renal dysfunction, bleeding disorders, heart failure, poor quality of life and premature death. Treatment and therapies are limited to symptomatic options or transplantation of heart and lungs combinedly. For pulmonary arterial hypertension treatment new pulmonary vasodilators are available and proven to be helpful this treatment has been expected to show prompt and good effect in Eisenmenger's patient too.

For such patients a specialized center is required which ensures interdisciplinary management strategies for congenital heart disease & PAH should be warranted. Through the medical updates the recent diagnostic and therapeutic options for such patients are focusing on epidemiology clinical aspect and specific diagnostic option.

KEYWORD:

Pulmonary arterial hypertension (PAH), cyanosis, transplant, surgeries, congenital heart disease, Bosentan

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INTRODUCTION:

In 1897 Victor Eisenmenger described this syndrome by reporting on one patient suffering from dyspnea and cyanosis since childhood who developed subsequently heart failure and stop responding against hemoptysis. On autopsy ventricular septal defect was revealed.

Eisenmenger syndrome is disease develops when there is increase in supply of blood from lungs to heart through arteries which results in pulmonary hypertension. There is high blood pressure in blood vessels of lungs going towards heart and right side of heart which leads to blood shunting between left and right side of heart.

Eisenmenger syndrome is usually result of one or more heart diseases present from birth which overtime leads to permanent damage of lungs and creates more complication. Lastly, due to increased pulmonary vascular resistance the left-right shunt gets changed right-left shunt causing hypoxemia &cyanosis.

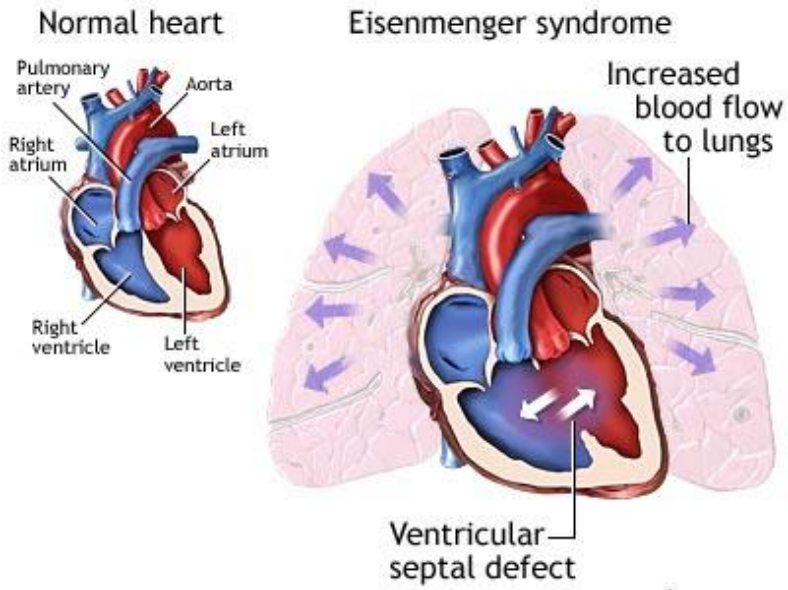
Pulmonary arterial hypertension i.e., PAH is mean while resting is greater than 25mmHg and while exercising is 30mmHg. The development of syndrome at certain point is irreversible pulmonary hypertension which indicates cardiac lesions are inoperable. In last stages the cardiac arrythmias and sudden cardiac death are complications.

For improvement of quality of life of Eisenmenger patient transplants along with medications are approachable.

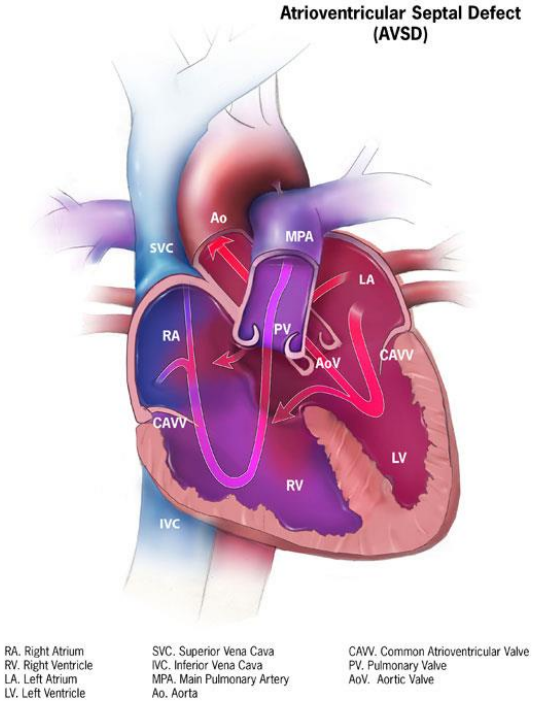
ETIOLOGY:

Eisenmenger syndrome is generally caused when the congenital heart disease is not treated for longer duration. It's usually caused by:

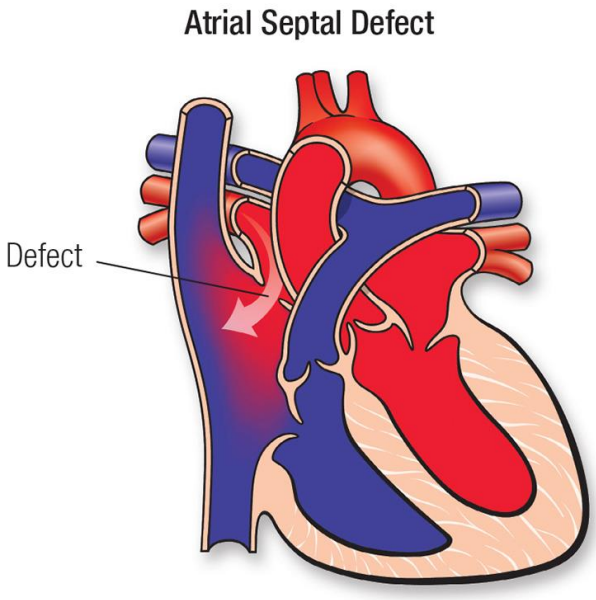
1. **A ventricular septal defect (a hole between right and left ventricles)**



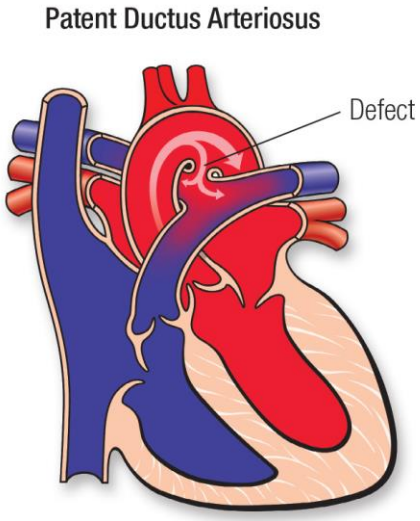
2. **Atrioventricular Canal Effect: (hole between the center of heart and valves doesn't work properly)**



3. **Atrial septal defect (hole in wall of tissue that divides left and right atria):**



4. Patent ductus arteriosus:(opening between pulmonary artery and aorta)



Any of these reasons Eisenmenger syndrome is caused and that leads to irregular flow of blood and subsequently pressure increases on pulmonary artery and which damages small blood vessels in lungs. In these cases, blood pressure increases on sides of heart that contains oxygen poor blood i.e., blue blood which enters or passes through hole to heart or blood vessels and due to this oxygenated and deoxygenated blood mixes now and this decreases the oxygen levels in blood.

EPIDEMILOGY:

It is the rare disorder which is mostly seen in rural or villages area who have poor healthcare access and major defects cannot be detected for many years.

The size of shunt plays important role in epidemiology of syndrome 3% of patients with small ventricular septal defect (<1.5cm) and 50% of patient with large ventricular septal defect (>1.5cm) further develops Eisenmenger syndrome. This syndrome develops before puberty. Approx. 8% of patients with congenital heart diseases develops Eisenmenger syndrome.

PATHOPYSIOLOGY:

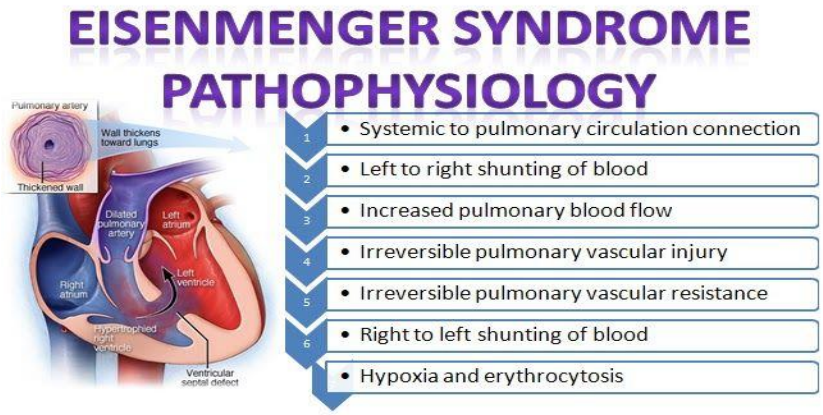
The common defects that lead to Eisenmenger syndrome are

a. Arterial septal defect (ASD)
b. Ventricular septal defect (VSD)
c. Patent ductus arteriosus (PDA)

By three processes this syndrome progresses:

A. VASOCONSTRICTION: It is caused by imbalance in pulmonary vascular tone
B. VASCULAR REMODELING: It is second stage in which proliferation of pulmonary vascular smooth muscles takes place.

C. THROMBOSIS: It is the last stage or process caused due to increased blood flow resistance.



CLINICAL PRESENTATION:

The symptoms vary from person to person. Some common symptoms of Eisenmenger syndrome are as follows:

- Headache
- Fatigue
- Chest pain
- Shortness of breath at rest
- Hypoxemia
- Cyanosis
- Heart palpitation
- Blurred vision
- Syncope
- DOE (dyspnea on exertion)
- Blue color near lips toes and finger tips
- Erythrocytosis
- Clubbing (rounding of tips and toes)
- At high risk the signs like hemoptysis or gout can be observed.

COMPLICATIONS:

- Thrombosis can be found in deep veins.
- Gout
- Hemoptysis
- Stroke
- Hemorrhage
- Brain swelling

RISK FACTORS:

In Eisenmenger syndrome there are risk factors that can worsen the condition. Having a genetic mutation has more risk of carrying and expressing the trait. Complex and large defects can increase the risk and can be proven life threating. Exposure to rubella viruses during pregnancy increase chances of child to suffer from this syndrome. Drug or alcohol consumption during pregnancy also leads to chances of acquiring this syndrome to the infant.

DIAGNOSIS:

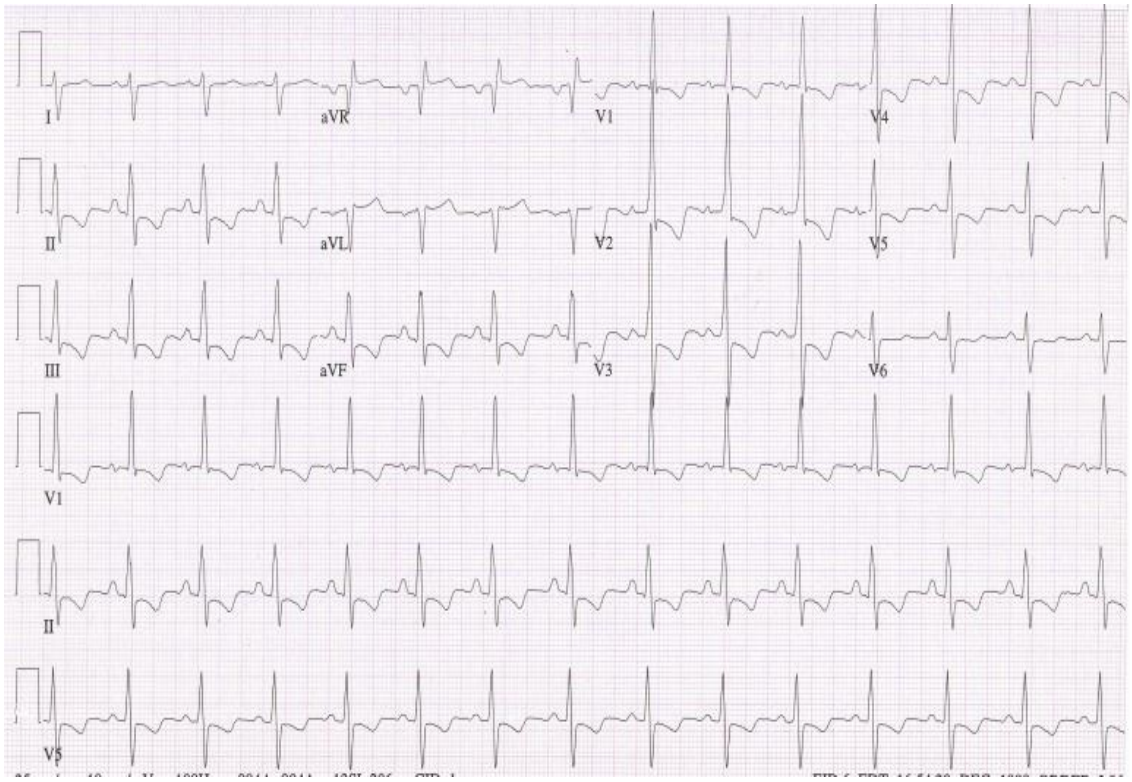
To do diagnosis of Eisenmenger syndrome some tests are done on basis of provisional clinical presentation to detect final diagnosis which of them are mentioned below:

1. Blood test
2. Electrocardiogram (ECG)
3. Chest X-ray
4. Echocardiogram
5. Computerized tomography (CT) scan
6. Magnetic resonance imaging (MRI) -lungs
7. Cardiac catheterization
8. Walking test

1. Blood test:

The CBC (complete blood count) is done to detect the erythrocytes count a it may increase in this case. It shows liver and kidney function test. Iron levels are also determined by blood tests.

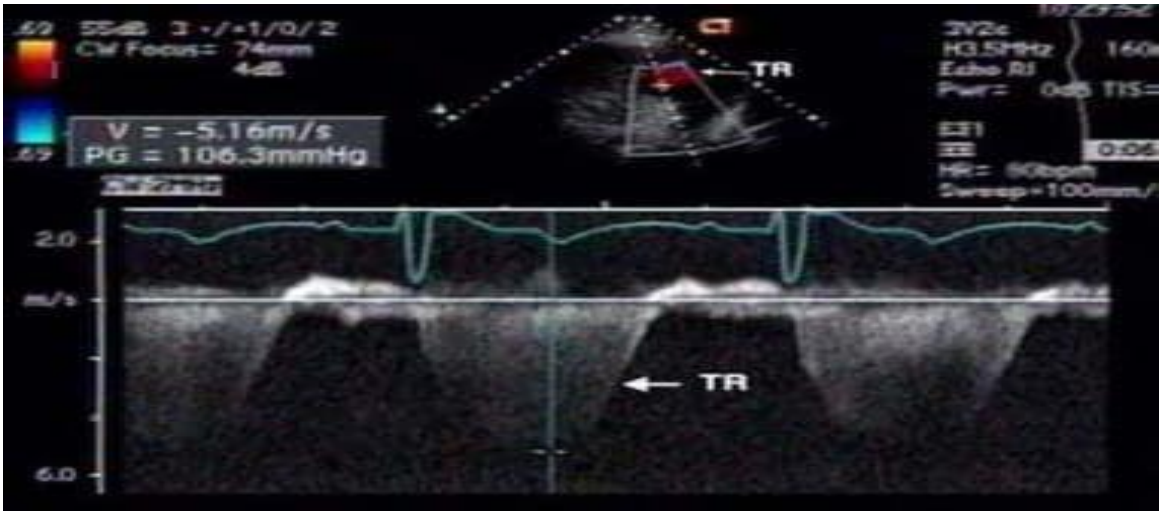
2. ECG (electrocardiogram):



ECG is a method of measuring the electrical activity of heart in which the electrodes are attached or placed on chest, arm, legs.

The wires connected to the sensors are attached to monitor which shows a graph as shown above which indicates the fast or slow beating of heart.

3. **Chest X-ray:** Chest X-ray indicates the condition of heart and lungs in this type of syndrome
4. **Echocardiogram:**It is a process of ultrasound of heart in which the soundwaves are used to detect the motion of heart and get an image of blood through heart.



5. **CT scan**

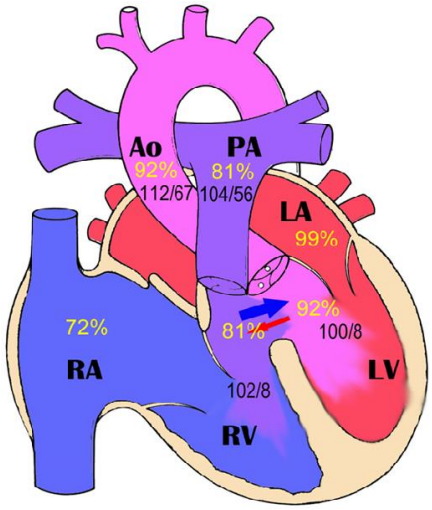
The CT scan id done to get detailed image and information of lungs and its arteries by using X-rays which create a cross section of organ. Dye is administered through IV prior to test which improves the opacity of blood vessels.

6. MRI of lungs:

Radio waves and magnetic field is used to carry out this test and getting a detailed image of lung blood vessels.

7. Cardiac catheterization:

The catheter (thin flexible tube) is inserted through wrist and guided towards heart in which dye flows in arteries making it more visible on Xray image or video. It also shows the size of hole and blood flow through blood vessels.



8. Walking test:

It's done to know your capacity to tolerate mild exercise by 6 min walk.

TREATMEANT:

In this syndrome we can aim to controlling the damage of lungs and hear. Certain therapies ca be used which include:

- **Antibiotics:** it can prevent bacterial infection in heart and lungs.
- **Anticoagulants:** these are used to prevent clot formation.
- **Diuretics:** they are given to reduce the fluid retention in body
- **Dual endothelin receptor antagonist:** reduces blood pressure in lungs.
- **Iron supplement:** it is given to treat anemia
- **Supplemental oxygen:** it is given to ease the breathing of patient.
- **Heart rhythms drugs:** these help to control irregular heart rhythms.
- **Blood thinners:** aspirin warfarin such blood thinner is prescribed to prevent blood clot.
- **Drugs for PAH:** Bosentan used to increase supply of blood to lungs an also precaution is to be taken by doing monthly liver test as it can damage liver.
- **Sildenafil and tadalafil:** these ae used to treat high blood pressure caused by Eisenmenger syndrome.

This all help in early diagnosis and treatment. As the time passes and there is development of syndrome doing surgery and transplants is the only option to be considered. Detection in early stage and solving heart defects is the one of the ways to control and prevent Eisenmenger syndrome.

- **Surgeries and other procedures:**

Surgeries are recommended at early stage to repair shunt only it is not recommended after the Eisenmenger syndrome is developed. Following are the surgeries or procedure carried out:

1. **Phlebotomy (Blood withdrawal):** This is recommended or prescribed when the blood cell count is high and causing problems like headache, vision problems, difficulty in concentrating. This procedure should only be preferred if CHD expert recommends it and patient should be treated through IV to recover loss of fluid,
2. **Transplants:** when other any treatment doesn't work transplant of heart and lungs is mandatory.

There are some approaches that can be considered for treatment:

- Oxygen therapy
- Pulmonary vasodilator therapy
- Endocarditis
- Contraception pregnancy and genetics counselling
- Corrective surgery

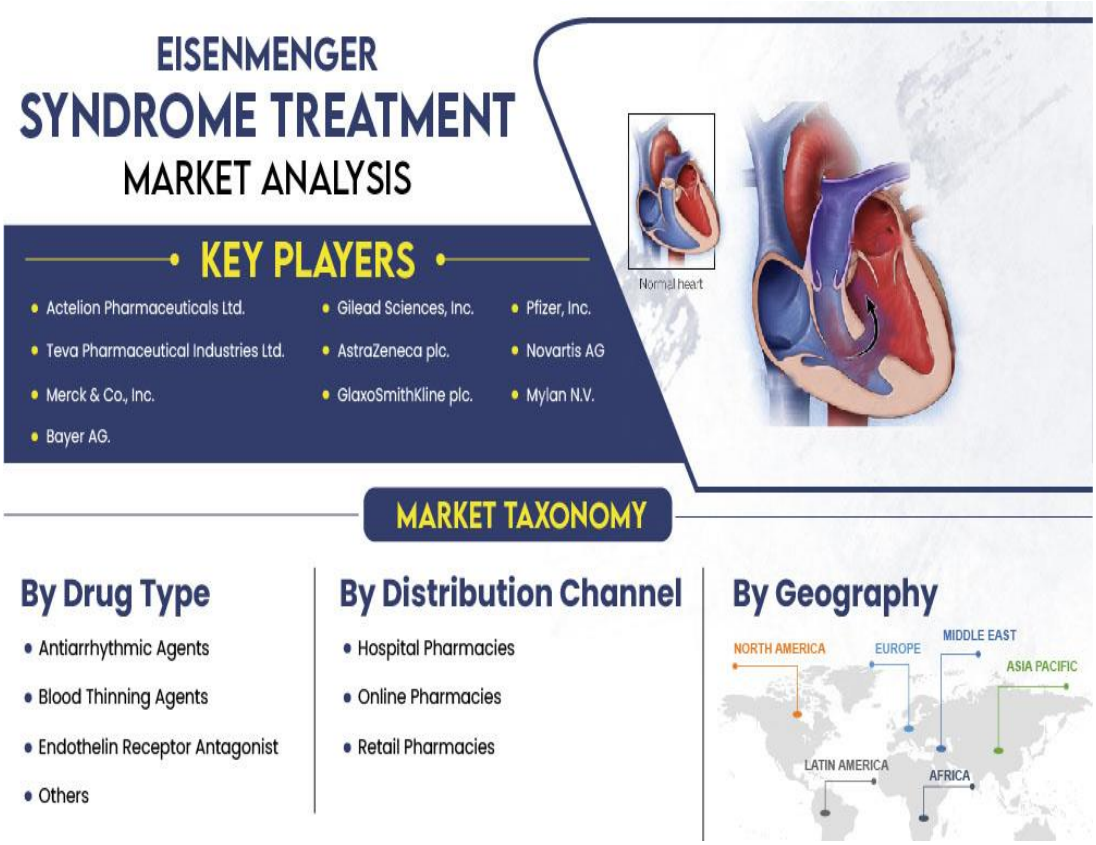
This medical condition of patient should be handled by a team of expertise in CHD and pulmonary hypertension and approaching help of another specialist like radiologist, hematologist, anesthetist etc. In

such cases beta blockers and calcium channel blockers are avoided to be prescribed to patient as they show negative effect on right ventricle.

Drugs having anesthetic and sedation effect should be avoided as they have a risk. By any chance the patient has to undergo unavoidable surgery, careful monitoring should be done during anesthesia.

Women's having Eisenmenger syndrome should avoid pregnancy as it can be life threating for both mother and developing fetus. Hence the counselling is mandatory to such women by the physicians.

Such patients should avoid high altitudes, dehydration, activities that cause sudden drop in blood pressure such as hot tubs, steam room etc. Physical exercise should be done in limit or avoid it.

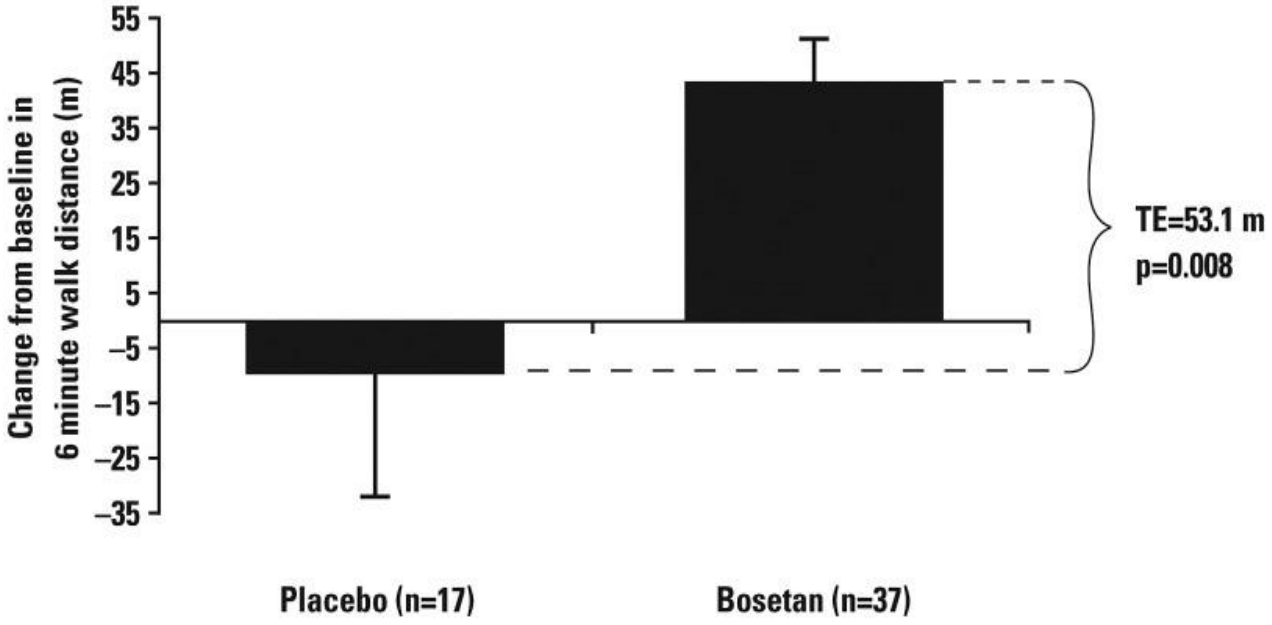


BOSENTAN: A NEW THERAPY FOR EISENMENGER SYNDROME:

Bosentan is a dual endothelin receptor antagonist that is used to treat effectively idiopathic PAH and PAH related connective tissue disease. To confirm the drugs efficacy and safety the Bosentan randomized trial of endothelin antagonist therapy-5 (BREATH-5) was carried out.

Therapy of bosentan (n=37) or placebo (n=17) was randomized trial on 54 patients with WHO functional class III Eisenmenger syndrome. The results of this therapy after 16 weeks were checked which showed that bosentan doesn't compromises oxygen saturation (levels). Bosentan therapy decreases pulmonary vascular resistance index. Mean pulmonary arterial pressure was reduced among patient treated with Bosentan while subsequently their capacity to do exercise was increased.

From about total 18% patients in placebo group and 14% patients from Bosentan group had at least one serious adverse event or effects. This finding shows that bosentan improves hemodynamics and exercise capacity of Eisenmenger syndrome patient peripheral levels of oxygen are not worsen by Bosentan therapy and doesn't show any adverse side effects



CONCLUSION:

Eisenmenger syndrome is chronic and severe medical condition which is permanent unless and untill it is diagnosed at early stage and treated immediately. It is a life threatning syndrome and counselling about it in rural areas in mandatory and imporatant to control its genetic mutation which increases chances of carrying its trait to next generation. High intake of drugs alcohol during pregnancy should be avoided my the mother and also should precautions that she don't get nfected by rubella virus during pregnancy.

Endothelin receptor antagonists, phosphodiesterase type -5, prostacyclin analogs are used in ES patient and this improves the exercise capacity, hemodynamics, functional class using this all ES has become a stable disease in nation. Now researches are done to detect ES early, combined regimens of targeted therapies, and potensial to reverse Pulmonanry vascular remodeling.life expectancy is significantly reduced in affected individual.

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