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Case Report

ADMINISTRATION OF NITRATES AFTER SPONTANEOUS DELIVERY IN RHEUMATIC HEART DISEASE

Mirza Koeshardiandi[1a], Muhammad Wildan Afif Himawan[1], Fajar Perdhana[2], Zulfikar Loka Wicaksana[2]

[1] Department of Anaesthesiology and Reanimation, dr. Soedono General Hospital, Madiun, Indonesia
[2] Department of Anesthesiology and Reanimation, Faculty of Medicine, Universitas Airlangga/dr. Soetomo General Academic Hospital, Surabaya, Indonesia
[a] Corresponding author: mirzakoes@gmail.com

ABSTRACT

Introduction: Heart disease is one of the most common causes of maternal death. The incidence has increased since women with congenital and acquired heart disease reached fertile age. The circulation system changes during pregnancy which are induced by changes in the progesterone. The changes in progesterone levels increase heart work and cause death in pregnant women. **Objective:** This report aims to elaborate on the administration of nitrates as the management of labor in rheumatic heart disease (RHD). **Case Report:** A 27-year-old woman complained of shortness of breath and wanted to give birth. The patient was 38 weeks pregnant and had a history of heart disease. Antero-posterior chest radiography examination showed pulmonary edema and cardiomegaly. The patient was examined using echocardiography before spontaneous labor and was diagnosed as pregnant with rheumatic heart disease. As an emergency management, the patient was given painless spontaneous labor. The patient was given nitrates on the first day after delivery as a treatment for progesterone withdrawal syndrome in this case. After the delivery process was completed, the patient was admitted to the Intensive Care Unit (ICU). Progesterone hormone produced by the corpus luteum and the placenta until the eighth week of pregnancy and before delivery, respectively, can reduce systemic vascular resistance. Progesterone hormone increase causes peripheral vasodilation by affecting the function of endothelial nitric oxide synthase (eNOS) and nitrite oxide (NO) production. **Conclusion:** A pregnant woman with rheumatic heart disease can be given exogenous nitrate. Administration of exogenous nitrates in this patient successfully prevent the reduction of peripheral vascular resistance and postpartum hemodynamic instability because it can replace the reduction in nitric oxide caused by progesterone withdrawal.

Keywords: Cardiovascular Disease; Maternal Health; Preventable Death; Progesterone; Rheumatic Heart Disease

ABSTRAK

Pendahuluan: Penyakit jantung merupakan salah satu penyebab kematian pada ibu hamil yang paling sering terjadi. Kejadian penyakit tersebut meningkat sejak wanita dengan riwayat penyakit jantung bawaan dan dapatan mencapai usia subur. Selama masa kehamilan terjadi perubahan sistem kardiovaskuler yang diinduksi oleh perubahan hormon progesteron. Perubahan hormon progesteron saat melahirkan dapat meningkatkan kerja jantung dan menyebabkan kematian pada ibu hamil. **Tujuan**: Laporan kasus ini bertujuan untuk menjelaskan manfaat pemberian nitrat sebagai tatalaksana persalinan pada *rheumatic heart disease*. **Laporan Kasus:** Seorang perempuan hamil berusia 27 tahun mengeluhkan sesak napas dan menunjukan tanda-tanda persalinan. Pasien hamil 38 minggu dengan riwayat penyakit jantung. Pemeriksaan penunjang foto radiologi *thorax anteroposterior* menunjukkan gambaran edema paru dan kardiomegali. Pemeriksaan ekokardiografi dilakukan pada pasien sebelum partus spontan dan pasien terdiagnosis sebagai *rheumatic heart disease (RHD)*. Pasien diberikan tatalaksana dengan persalinan tanpa nyeri. Pasien diberikan nitrat pada hari pertama setelah melahirkan sebagai terapi *progesterone withdrawal syndrome* pada kasus tersebut. Setelah proses persalinan selesai, pasien dirawat di ruang *Intensive Care Unit (ICU)*. Hormon progesteron yang dihasilkan oleh korpus luteum hingga minggu kedelapan dan plasenta hingga menjelang persalinan dapat menurunkan resistensi sistemik vaskular. Kejadian tersebut menyebabkan vasodilatasi perifer yang diperantarai oleh fungsi *endotel nitric oxide synthase* (eNOS) dan produksi Nitrit Oxide (NO). **Kesimpulan:** Pasien wanita hamil dengan *rheumatic heart disease* dapat diberikan nitrat eksogen. Pemberian nitrat eksogen pada pasien ini berhasil mencegah penurunan resistensi pembuluh darah perifer dan ketidakstabilan hemodinamik setelah melahirkan karena dapat menggantikan penurunan *nitic oxide* yang disebabkan oleh *progesterone withdrawal*.

Kata kunci: Penyakit Kardiovaskular; Kesehatan Ibu Hamil; Kematian yang dapat dicegah; Progesteron; *Rheumatic Heart Disease*

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INTRODUCTION

Heart disease is one of the most common causes of maternal death. Heart disease is usually not identified at the time of delivery. The event occurred after the gestational age of more than 20 weeks. Fifteen percent of maternal deaths are related to heart disease during pregnancy (1). Cardiovascular disease can occur in 1-3% of pregnancies. The incidence has increased since women with congenital and acquired heart disease reached fertile age (2). Women with congenital heart disease may have congestive heart failure and arrhythmias during pregnancy (3).

The circulation system can change during pregnancy. The peripheral vasodilatation triggers a decrease in systemic resistance. This process occurs due to the induction of progesterone during pregnancy (3). Progesterone level increases with gestational age. Increased hormones can indirectly reduce the work of the heart by lowering systemic resistance (4). Decreased systemic resistance can increase cardiac output by 30% to 60% more than pre-pregnancy levels during pregnancy, and the cardiac output continues to rise during labor due to sympathetic stimulation and autotransfusion from uterine contractions (3).

There are several dangerous periods during pregnancy with heart disease, the first is between 12-16 weeks. Second, the critical period is between 28-32 weeks of gestation, and the third is during the delivery process. The last one is on 4-5 days postpartum (1). Overall perinatal mortality for pregnant patients with heart disease is as high as 20% (1).

We reported the case of a pregnant patient with a diagnosis of G1P0A0, 38 weeks pregnant, stage 1, with rheumatic heart disease (RHD). In this case, emergency and intensive care management were needed to help the mother give birth so that the baby could be born alive. This report explains about the administration of nitrates as the management of labor in RHD.

CASE REPORT

A 27-year-old pregnant woman with a gestational age of 38 weeks came to the emergency department of Dr. Soedono Madiun General Hospital. The patient complained of shortness of breath one month ago and had worsened three days before being admitted to the hospital. The complaint accompanied by discharge from the birth canal and an increase in heart palpitations. The patient explained that the heart palpitations had been felt since the patient was young and had never been to a doctor.

The physical examination of the general condition was good and fully conscious. Vital signs obtained were blood pressure of 142/100 mmHg, pulse of 160 beats per minute, lung respiratory rate of 20 times per minute, and temperature of 36.5 ℃. Upon obstetrical and gynecological examination, the uterine fundus height was 25 cm, the fetal heart rate was 140 beats per minute, and uterus contraction was palpable once in ten minutes which lasted for ten seconds. Speculum examination found 1 cm opening, 25% effacement, amniotic skin not palpable, head on Hodge 1. Anteroposterior chest x-ray examination revealed pulmonary edema and cardiomegaly (Figure 1).

Blood examinations of the patient in the emergency department were hemoglobin 11.2 g/dL, platelets 168x103/µL, hematocrit 33.2%, leukocyte count 9.9x103/µL, erythrocyte number 4.07 million/cm, MCV 89.8 fL, MCH 30.4 pg, MCHC 33.8 g/dl. Coagulation physiology showed PT and APTT of 8.7 and

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APTT 28.5 seconds, respectively. Clinical chemistry examination of liver function revealed albumin of 3.6 g/dl, SGOT of 21 U/L and SGPT of 18 U/L. Clinical examination of kidney function revealed BUN of 6 mg/dl, creatinine of 0.42 mg/dl, and carbohydrate metabolism blood glucose of 100 mg/dl. Blood electrolyte examination revealed blood sodium of 138 mmol/L, blood potassium of 3.74 mmol/L, and blood chloride of 108 mmol/L. Anti-HIV immunological examination was Non-reactive and HBsAg was Negative. Urinalysis examination found glucose, bilirubin, ketone, protein, urobilinogen, leukocytes were all negative while epithelium was positive. Furthermore, the urinalysis showed urine pH of 7 as well as urine sediment consisting of erythrocytes and leukocytes were 6-8/LPB and 4-6/LPB, respectively.

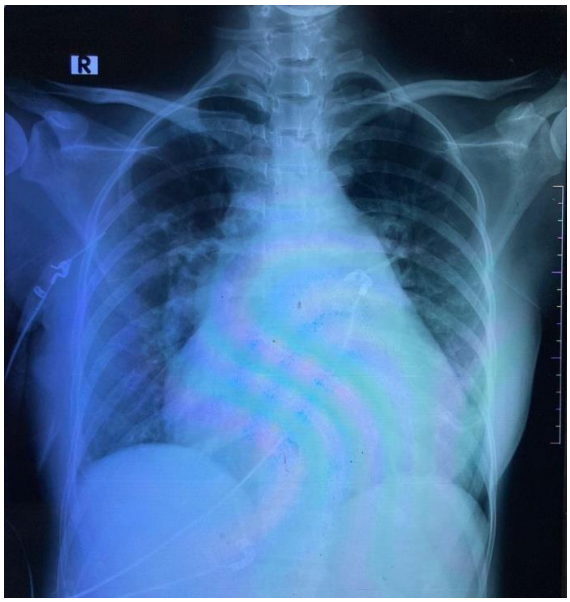

Figure 1. The Image of The Thorax Before Giving Birth

Blood gas analysis examination with a momentary arterial blood sample showed pH of 7.41, pCO_2 of 34 mmHg, pO_2 of 149 mmHg, NA^+ of 135 mmol/L, K^+ of 3.7 mmol/L, glucose of 77 mg/dl, lactate of 0.8 mmol/L, HCT of 34% and derived parameters consisting of Ca^{2+} (7.4) of 1.1 mmol/L, HCO_3^- of 21.6 mmol/L, HCO_3^- standard of 23.0 mmol/L, TCO_2 of 22.6 mmol/L, BEEcf of - 3 mmol/L, BE(B) of -2.5 mmol/L, SO2c of 99%, THbc of 10.5 g/dl, A-aDO_2 of 243 mmHg and PAO_2 of 392 mmHg.

The patient was examined using echocardiography with the results of heart chamber dimensions of left ventricle dilatation (EDD = 6.35 cm), left atrium dilatation (LAD = 4.17 cm), and right atrium and right ventricle were within normal limits. The patient also had normal left ventricular systolic function (EF Teich 64.9%), pseudonormal left ventricular diastolic function (E/A 1.06, DT 253 ms), and normal right ventricular systolic function (TAPSE 2.88 cm). Segmental analysis revealed normokinetic basal, middle, and apex. Examination of heart valves and volume revealed severe mitral regurgitation, prolapse of the anterior mitral leaflet, 3-layer aortic calcification, severe tricuspid regurgitation (est PASP 132 mmHg), mild pulmonary regurgitation, severe probability pulmonary hypertension, and eccentric left ventricular hypertrophy (LVMI 193.28 g/m^2).

Treatment

A pregnant patient with a diagnosis of G1P0A0, 38 weeks, latent phase 1 *inpartu* with RHD underwent spontaneous labor without pain. Postpartum therapy was given oxygen 8-10 lpm, Asering infusion 7 dpm, IV paracetamol injection 1 gram/8 hours, ondansetron injection 4 mg/8 hours, esomeprazole injection 40 mg/12 hours, injection of furosemide 1 mg/hour using pump and nitroglycerin 1 mg/hour using syringe Pumps.

Result and Follow-Up

Spontaneous labor without pain gave good results. After the delivery process was completed, the patient was admitted to the

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Intensive Care Unit (ICU). The patient was given therapy in the form of D10% infusion 8 dpm, ceftriaxone injection 1 gram/12 hours (H7), esomeprazole injection 40 mg/12 hours, paracetamol injection 1000 mg K/p, nitroglycerin injection 1 mg/hour using syringe pump, furosemide injection 5 mg/hour, peroral captopril 12.5 mg 2 times, spironolactone 25 mg 1 time, digoxin 0.25 mg 1 time, and 1 tablet VIP Albumin 3 times. Complaints of shortness of breath and chest palpitations decreased after one day of ICU treatment. After that, the patient underwent an antero-posterior chest x-ray examination which aimed to evaluate the cardiac features and pulmonary edema (Figure 2).

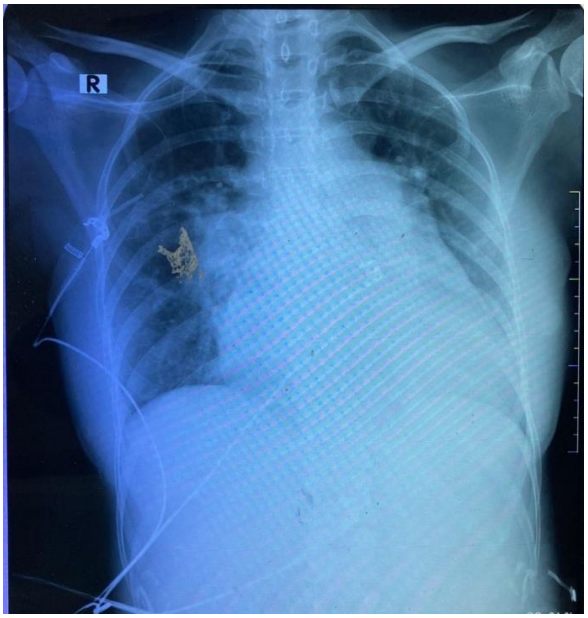

Figure 2. The image of the thorax after giving birth

The patient was re-x-rayed to determine the patient's progress after four days post-treatment in the ICU. The patient's complaints decreased, and the chest X-ray indicated that the pulmonary edema also subsided (Figure 3).

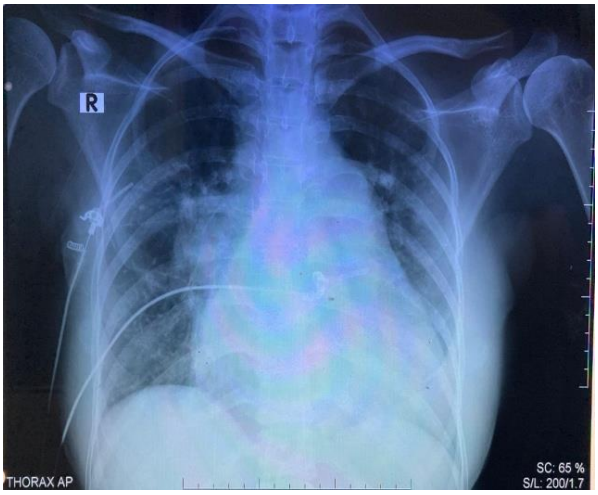

Figure 3. The image of the thorax four days after treatment

The patient was re-examined 14 days postpartum. This examination was aimed to assess heart function during the treatment process. The results of the echocardiography examination showed that the dimensions of the heart chambers were left ventricle dilated (EDD 5.66 cm), left atrium dilated (LAD 4.17 cm), and right atrium, and right ventricle within normal limits. The patient also had normal left ventricular systolic function (EF Teich 54.4%), pseudonormal left ventricular diastolic function (E/A 1.07, DT 159 ms), and normal right ventricular systolic function (TAPSE 3.12 cm). Segmental analysis revealed normokinetic basal, middle and apex. Examination of the valves and heart volume revealed severe mitral regurgitation, prolapse of the anterior mitral leaflet, 3 layers of aortic calcification, severe tricuspid regurgitation (est PASP 93 mmHg), mild pulmonary regurgitation, severe probability pulmonary hypertension and eccentric left ventricular hypertrophy (LVMI 181.48 g/m^2).

DISCUSSION

The diagnosis of RHD can be divided into three categories, namely the diagnosis of rheumatic fever (RF), the presence of active vs. inactive disease with recurrent RF, and the

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identification of carditis due to valve damage in RHD (4). Identification of carditis due to valve damage is the main goal in establishing the diagnosis and therapy in these cases. Rheumatic endocarditis can be described as damage to the heart valves. The disease can occur as a result of permanent RF damage to the heart valves (4). Based on the results of the history, physical examination, and supporting examinations that have been mentioned, the patient was pregnant with a diagnosis of G1P0A0, 38 weeks, latent phase 1 labor with RHD.

Spontaneous delivery is the first choice for pregnant women with heart disease. Spontaneous delivery and low-dose regional anesthesia are the best options. Regional anesthesia is highly recommended to reduce the increase in cardiac output and oxygen demand of the heart muscle during labor (5). Therefore, pregnancy with RHD is not an absolute indication of a caesarean section.

RHD disease or sub-clinic carditis can affect the cardiovascular system during pregnancy. This process occurs due to disturbances in the heart valves and can be a pathological stimulus due to excessive pressure. This occurs due to an increase in cardiac afterload volume and causes concentric and eccentric hypertrophy. These events can lead to cardiomyopathy and heart failure (6).

The progesterone hormone produced by the corpus luteum until the eighth week and the placenta until before delivery can reduce systemic vascular resistance (6). The progesterone hormone causes peripheral vasodilation by affecting the function of endothelial nitric oxide synthase (eNOS), a process known as the genomic and non-Genomic mechanism (6). Progesterone activates phosphoinositide/AKT (P13T/AKT) and an increase in eNOS leads in an increase of nitric oxide (NO) production. The results of cellular studies in animals suggest that the generation of NO and prostacycline has potential benefits on endothelial vasodilation and promotes endothelial repair and regeneration, with anti-inflammatory and antioxidant effects (6). Progesterone levels peak at the time of delivery and decrease drastically shortly after delivery which is also known as progesterone withdrawal. Progesterone withdrawal causes NO production to decrease (7).

Patients with heart failure should be placed on medical therapy such as angiotensin-converting enzyme (ACE) inhibitors, diuretics, and beta-blockers (8). Nitrates can significantly reduce vascular resistance in heart failure patients due to heart valve disorders. Nitrates are one of the drugs commonly used for patients with heart failure (9,10). These drugs can be used to reduce afterload in patients with systolic dysfunction (11). These effects can generally increase cardiac output (10,12).

CONCLUSION

A pregnant woman with rheumatic heart disease can be given exogenous nitrate. Administration of exogenous nitrates in this patient successfully prevent the reduction of peripheral vascular resistance and postpartum hemodynamic instability because it can replace the reduction in nitric oxide caused by progesterone withdrawal.

Acknowledgment
None.

Conflict of Interest
The authors declare no conflict of interest.

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Authors' Contributors

All authors have contributed to all processes in this research.

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