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Comparative study between effect of Milrinone as a positive inotropic agent and Dobutamine in separation from cardiopulmonary bypass in fallot tetralogy repaired by transannualar patch technique

A Thesis

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Sarah Elghareeb

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List of Abbreviations

Abbr.	Full-term
ABG	Arterial blood gases
ACT	Activated clotting time
ASA	American anesthesia association
BF	Blood flow
BF	Blood flow
CABG	Coronary artery bypass graft
CAMP	Cyclic monoamniophosphate
CHD	Congenital heart diseases
CI	Cardiac index
CO	Cardiac output
CPB	Cardiopulmonary bypass
CPB	Cardio pulmonary bypass
CT	Computerized topography
DBP	Diastolic blood pressure
DCM	Dilated cardiomypoathy
DLPA	Diameter of left pulmonary artery
dP/dt);	peak rate of left ventricular pressure rise
DRPA	Diameter of right pulmonary artery
ECG	Electrocadiogram
HR	Heart rate
IV	Intravenous
LPA	left pulmonary artery
LV	Left ventricular
LVEDP	left ventricular end diastolic pressure
LVSP	ventricular systolic pressure
MAP	Mean arterial pressure
MAPCAS	major aortopulmonary collateral arteries
MPAP	mean pulmonary artery pressure
NSVT	Nonsustained ventricular tachycardia
NYHA	New York heart association
PaCO2	Partial arterial carbondioxide tension
PaO2	Partial arterial oxygen tension

PCWP	Pulmonalry capillary wedge pressure
PDE	Phosphodiestraes inhibitor
PR	Pulmonary regurgetation
PS	Pulmonary stenosis
PV	Pulmonary valve
PVC	Premature ventricular contraction
PVR	Pulmonary vascular resistance
RAP	right atrial pressure
RPA	Right pulmonary artery
RV	Right ventricle
RVOT	Right ventricular obstruction outflow
SBP	Systolic blood pressure
SR	Sarcoplasmic reticulum
SVR	systemic vascular resistence
TOF	Teratologhy of fallot
VSD	Ventricular septal defect

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Abstract

Background: Tetralogy of Fallot represents 10% of all congenital heart defects and is the most common form of cyanotic heart disease. **Aim of the Work:** the aim of this work is to compare between effect of Milrinone and dobutamine as positive inotropic agent in separation from cardiopulmonary bypass in fallot tetralogy repaired by transannular patch technique. **Patients and Methods:** After approval of department of anesthesia, faculty of medicine, Ain Shams University, and the medical ethics committee, an informed consent was obtained from all patients' guardian. This study was conducted on 150 pediatric patients of ASA III-IV, admitted to the cardiothoracic surgery unit, Ain Shams university hospital for elective fallot tetralogy total repair. Their age ranged from 12 to 24 months, weight from 6 to 15 kilograms and of both sexes. **Results:** the present study, regarding hemodynamics parameters; there were no significant changes in SBP between both groups, while DBP was higher in dobutamine group rather than milrinone group. **Conclusion:** Both inotropic support milrinone and dobutamine are effective in management of post cardiopulmonary bypass after Fallot repair by transannular patch as inotropic drugs. **Recommendations:** Further studies are needed to confirm the present study results.

Key words: Tetralogy of Fallot, Milrinone, Dobutamine, cardiopulmonary bypass, transannualar patch technique

Introduction

Tetralogy of Fallot represents 10% of all congenital heart defects and is the most common form of cyanotic heart disease. Tetralogy of Fallot comprises four anatomical abnormalities: (i) a large unrestrictive VSD; (ii) ventricular out flow tract obstruction (RVOT); (ill) overriding of the aorta above the ventricular out flow obstruction; and (iv) RV hypertrophy. In reality, there is a spectrum of abnormalities ranging from tetralogy of fallot with pulmonary artery, where there is total obstruction to RV outflow, through TOF with pulmonary stenosis, to TOF with absent PV ***(Van Dongen et al., 2003).***

There are three major goals of the TOF repair: (i) maximal relief of right ventricular out flow obstruction; (ii) separation of the systemic and pulmonary circulation by closure of the VSD; and (iii) preservation of right ventricle function, determine the levels of obstruction of the ventricular out flow obstruction, and continuity of the pulmonary arteries ***(Levy et al., 2002).***

Catecholamines are frequently administered to facilitate separation from CPB and to maintain an adequate CO postoperatively in the cardiac surgical patient. The mechanism of action of catecholamines is stimulation of cAMP production ***(Michelsen and Shanewise, 1995).***

In a study comparing the effects of milrinone and dobutamine, the efficacy of both drugs was observed ***(Duggal et al., 2005).***

Milrinone produce positive inotropic effects by slowing the hydrolysis of cyclic adenosine monophosphate in the myocardium.This may be particularly important in patients who were in CHF prior to operation, as 1-adrenergic receptors can be downregulated in this population. Therefore, when ventricular dysfunction occurs despite standard catecholamine therapy, milrinone can provide additional and effective inotropic support. Milrinone is a potent pulmonary vasodilator for patients with right ventricular dysfunction and pulmonary vasoconstriction. Low-dose milrinone may have antiinflammatory properties and potentially can improve splanchnic perfusion ***(Bailey et al., 1999).***

Dobutamine is a direct-acting inotropic agent whose activity results from stimulation of the ß receptors of the heart while producing comparatively mild chronotropic, hypertensive, arrhythmogenic, and vasodilative effects. In patients with depressed cardiac function, both Dobutamine and isoproterenol increase the cardiac output to a similar degree. In the case of Dobutamine, this increase is usually not accompanied by marked increases in heart rate (although tachycardia is occasionally observed), and the cardiac stroke volume is usually increased ***(Choudhury and Saxena, 2003).***

Aim of the work

The aim of this work is to compare between effect of Milrinone and dobutamine as positive inotropic agent in separation from cardiopulmonary bypass in fallot tetralogy repaired by transannular patch technique.

Chapter (1)
Anatomical and pathophysiological considerations of fallot tetralogy

Congenital heart disease has been recognized for many centuries, few or no treatments were available until the twentieth century. Most children with congenital heart disease (CHD) were consigned to a life of invalidism ***(Maeda et al., 2000).***

Congenital heart disease (CHD) affects approximately 1% of children through worldwide. Fortunate children will be born in an economically developed countries, politically stable country with a health care system capable of providing the most up-to-date treatments for all its citizens. For many children, however, the luxury of cardiac surgery is available only to the richest members ***(Maeda et al., 2000).***

Tetralogy of Fallot (TOF) represents 10% of all congenital heart anamolies, and the most common form of cyanotic heart disease, it refers to a spectrum of heart defects that includes:

(i) right ventricular outflow tract (RVOT) obstruction
(ii) a large unrestrictive ventricular septal defect (VSD)
(iii) overriding of the aorta above the RVOT
(iv) Right ventricle (RV) hypertrophy

(Murphy et al., 1993).

The etiology of TOF is unknown for most cases, but chromosome 22 microdeletions has been found in 15.9% of patients ***(Pizzuti et al., 2003).***

Although Mendelian inheritance pattern is not present, but The recurrence risk in siblings is approximately 3%,, and this recurrence is considered greater in the general population (table 1) ***(Kohli et al., 2008).***

Table (1): Genetic distribution of TOF ***(Eldadah et al., 2001).***

	Tropical Areas (%)			**Temperate Areas**
	Africa	South Africa	Singapore	United Kingdom
Tetralogy of Fallot	14.9	16.1	8	9.5

I. Embryological background:

The embryological basis of the combination of this anamoliess is antero-cephalad deviation of the developing outlet ventricular septum, or its fibrous remnant should this septum fail to muscularise. Such deviation, however, can be found in the absence of subpulmonary obstruction, so called Eisenmenger ventricular septal defect. So as to produce the features of the Fallot, The septoparietal trabeculations abnormal morphology necessary have to be found, so that it encircle the subpulmonary outflow tract. The combination of both deviated outlet septum and hypertrophied septoparietal

trabeculations, produce the characteristic right ventricular outflow tract obstruction of the tetralogy. The malalignment type ventricular septal defect is crearted by deviation of the muscular outlet septum, and also results in the aortic override. The associated hypertrophy of the right ventricular myocardium is the hemodynamic consequence of the anatomical lesions created by the deviated outlet septum ***(Oppenheimer-Dekker et al., 1985).***

The ventricular septal defect

The interventricular communication found in the tetralogy exists because of the anterior and cephalad malalignment of the outlet portion of the muscular ventricular septum, or of its fibrous remnant should the outflow cushions fail to muscularise during embryonic development. The resulting hole is one of a number of those appropriately described as a malalignment defect. In four-fifths of Caucasians with such a defect, the postero-inferior margin of the hole between the ventricles is formed by an area of fibrous continuity between the leaflets of the aortic and tricuspid valves, also involving the remnant of the interventricular portion of the membranous septum. In these patients, therefore, the defect is also appropriately classified as being perimembranous, the interventricular communication is unrestrictive, which is allowing for bidirectional shunting ***(Anderson and Weinberg, 2005).***