Medical Management Of Hypercyanotic Spells In Fallot's Tetrology

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Paroxysmal hypercyanotic spells in Fallot's Tetrology (TOF) are due to intermittent spasm of the right ventricular out flow tract. The spells are characterised by intense cyanosis, persistent crying, irritability and hyperventilation culminating into deep sleep or continuing into unconsciousness or convulsions[1-2]. These spells are life threatening and necessitate corrective or palliative surgery.

The treatment of cyanotic spell is to place the patient in knee chest position, administer Oxygen, Morphia and Propranolol. Most spells would subside with the above management, however, occasionally prolonged spell may require correction of metabolic acidosis with Sodium Bicarbonate. Recent reports have shown that recurrence of cyanotic spells can be safely and effectively achieved by continuous oral administration of propranolol[3-7]. Present study was undertaken to prospectively evaluate (i) the effectiveness of propranolol in preventing recurrence of the cyanotic spells; (ii) to determine the maximum period of palliative effectiveness of propranolol; and (iii) to evaluate the safety of prolonged propranolol administration.

Material and Methods:

The study includes 45 patients with TOF who presented with cyanotic spells from amongst 142 TOF patients seen at the Congenital Heart Clinic at National Institute of Cardiovascular Diseases, Karachi, during one year period between October, 1980 to October, 1981. The diagnosis was made on clinical grounds, confirmed by Echocardiography and Cardiac Catheterization and Angiocardiography.

M-mode Echocardiograms were obtained in supine position with or without sedation of Chloryl Hydras, using commercially available EKoline Echocardiograph (Smith, Kline). The recordings were made on light sensitive paper or Polaroid film. A 3.5, 5.00 or 2.25 HZ transducer was used. Haemodynamic and Cardiac Catheterization studies were performed under sedation with Morphia or Pethidine and Promethazine mixture. Angiograms were obtained in each patient. Propranolol was given in Tablet form in initial daily dose of greater than 1 mg/Kg in two divided doses.

In patients with no response or incomplete response the dose of Propranolol was increased in increments upto 3 mg/kg. The incremental increase of Propranolol was obtained by increasing the daily frequency to three or four times a day with subsequent increases in individual doses. Parents were instructed to crush the tablet portion in powder form and administer with milk or liquids. Infants less than three months of age were admitted in the hospital during initial phase of Propranolol therapy. All children with inadequate response to Propranolol were studied by Cardiac Catheterization and subjected to either corrective surgery or aorto-pulmonary shunt.

Results:

Tetrology of Fallot was present in 142 of 814 new patients seen at the National Institute of Cardiovascular Diseases, Karachi between October, 1980 to October, 1981. Forty -five patients, mean age 3.4±2.9 years (Range 0.3—10 years) presented with hypercyanotic spells. Nine patients were older than five years of age (Table I).

Table I: Clinical Data of 45 TOF Patients on Propranolol

Age (Year)	3.4±2.9 (Range 0.3±10)
Wt. (Kg)	9.7±6.0 (Range 4.5—17.7)
Initial Dose (mg/kg)	1.19±0.64

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The clinical diagnosis of Fallot's Tetrology was confirmed on M-mode Echocardiography by demonstrating aortic ride above the ventricular septum and hypertrophied right ventricle in 19/45 patients and by Haemodynamic and angiocardiographic studies in 8/45. Starting daily dose of Propranolol was 1.2± 0.6 mg/K g administered in 2 divided doses. Adequate response, defined as complete cessation of cyanotic spells, was noted in 34/45 patients. The initial dose was 1.2±0.5 mg/Kg, and mean age of these patients was 3.6±2.9 years. Inadequate response, defined as recurrence of milder and less frequent cyanotic spells, was noted in 9/45. The mean age in this group was 3.0±2.9 years and the initial dose of Propranolol was 0.9±0.3 mg/Kg. Complete remission of the spells occurred on increasing the Propranolol dose to 1.6 mg/Kg per day. One patient in this group discontinued the drug and was brought to the hospital in severe prolonged spell and died. Two of the 45 patients failed to respond to Propranolol with daily doses in excess of 3.0 mg/Kg administered at six hourly intervals. The age of these patients as 1.5 and 3.5 years (Table II). Eight of 45 patients with either no response or inadequate response underwent surgery. Six patients underwent palliative surgery, either a Waterston-Cooley shunt or Gortex grafting between the subclavian and pulmonary artery, with one death due to a non functioning Waterston-Cooley shunt. Two patients had complete correction with one death due to respiratory insufficiency (Table III). Propranolol was continued till the day of surgery in all patients. Thirty -four of 45 patients with adequate response remained on Propranolol taking a mean daily dose of 1.2±0.5 mg/Kg and have been followed for a mean period of 7.2 months (Range 0.5—12) (Table IV) No adverse effects to Propranolol were noted. Few of the infants had bradycardia with heart rates in 80 to 90 beats/min. range without an adverse hemodynamic effects.

Table II: Response to Propranolol in 45 TOF Patients

	No.	*Age (years) ± SD*	*Starting daily dose ± mg/kg (SD)*
Adequate	34	3.6±2.9	1.2±0.5
Inadequate	9	3.0±2.9	0.9±0.3
None	2	2.5±1.4	3.0
Total		45	

* One patient died after discontinuation of Propranolol by parents.

Table III: Surgical Correction on Inderal

	No.	*Dead*
Waterston-Cooley Shunt	6	1
Total Correction	2	1

Table IV: Data on Patients with Adequate Response

Number	34/45
Dose Propranolol (mg/kg)	1.2±0.5
Duration (Month)	7.2±5.0 (0.5—12)

Discussion:

The management alternatives of patients with Tetrology of Fallot depends upon the individual institution's surgical expertise[8-9]. There are a few Centres in the World where surgical correction of infants with TOF can be safely undertaken under 1 year of age[10-11]. At our Institute complete repair of Tetrology of Fallot can be taken at 3-4 years of age. For the smaller children we have performed Aorto-Pulmonary shunt surgery. However, shunt surgery under 6 months of age carries significant mortality in our experience. Therefore medical means of preventing the recurrence of cyanotic spells have a definite significance for us. This study shows that recurrence of spells can be effectively prevented in majority of patients with oral Propranolol. The success rate of Propranolol Therapy is higher in our study than the reported experience. This may be due to shorter follow-up period and that recurrence rate would be higher with continued follow-up. There are, however problems with which one needs to be aware of in treating infants with propranolol. Non compliance of the drug is a real hazard of Propranolol therapy in our environment and one death in our study was due to discontinuation of Propranolol. The parents need to be repeatedly reminded about the need for continuing Propranolol particularly when spells are controlled. The tendency for the parents is to discontinue the drug once the spells no longer recur. Repeated clinic visits can ensure that non compliance is effectively prevented, our own and reported experience suggests that inadequate response to Propranolol is dose related and is unrelated to the age of the patient[7]. All patients with inadequate response should be admitted to the Hospital and dose of

Propranolol should be increased incrementally till complete remission of the spells is achieved. We have administered Propranolol upto 3 mg/kg/day in our study. There is evidence to suggest that larger dosage upto 5 mg/kg can be safely tolerated[7]. No side effects due to the Propranolol were noted in our study. Few infants showed heart rate as low as 80 beats per minute without adverse haemodynamic effects. We did not observe Congestive Cardiac failure in any of our patients[7]. Since only some of our patients were studied by Cardiac Catheterization, the adequacy of response vis-a-vis the severity of Cardiac abnormalities cannot be commented here. A recent study, however, suggests that the response to Propranolol is unrelated to the severity of Cardiac anatomy[7]. The Plasma level of Propranolol is not available so that determination of drug compliance and of the adequacy of response to the plasma concentration of Propranolol could not be documented[7]. We have no reason to believe that the continuation of Propranolol upto the day of surgery adversely effects the surgical outcome and the reported experience is consistent with this view[7].

Although 34/45 patients in our study showed adequate response to 1.2 mg/kg/day dose of Propranolol significant number did require increased amount of Propranolol. We now employ 2 mg/kg as starting dose preferably four times a day. The liquid suspension of Propranolol is not available locally, which would allow the administration of smaller doses more frequently during the day, however our study shows that the 2 daily doses are quite adequate. Presently we increase the dose of Propranolol by increasing the daily frequency of administration to six hourly schedule and when this is achieved individual doses are increased in accordance with the period of the day the spells occur. Our follow-up period is short and the study is continuing to determine as to the maximum period of palliation with Propranolol.

Starting daily dose of Propranolol was $1.2 + 0.6^2$ mg/K_2g administered in 2 divided doses. Adequate

Summary

It is concluded that Propranolol can be safely administered and that majority of patients with TOF will show remission of cyanotic spells.

References:

1. Johnson A.M.: Norepinephrine and cyanotic attacks in Fallot's Tetrology: Brit Heart J. 21:429, 1959.
2. Wood P.: Attacks of deeper Cyanosis and loss of consciousness (Syncope) in Fallot's Tetrology: Brit. H.J. 20:282, 1958.
3. Cumming G.R.: Propranolol in Tetrology of Fallot: Circulation, 41:9, 1970.
4. Honey M., Chamberlain D.A., Howard J.: The effect of beta sympathetic blockade on arterial oxygen saturation in Fallot's Tetrology, Circulation: 30:501, 1964.
5. Eriksson B.O., Thoren C., Zetterqvist O.: Long term management with Propranolol in selected cases of Fallot's Tetrology: Bri. H. J. 31:37, 1969.
6. Ponce F.E., Williams L.C., Webb H., Riopel D.A. Hohn A.R.: Propranolol palliation of Tetrology of Fallot. Experience with long term treatment of Paediatric patient. Paediatrics 52:100-100, 1973.
7. Garson A., Gillet P.C., McNammara D.G.: Propranolol: The preferred palliation for Tetrology of Fallot. Amer. J. Card. 47: 1098, 1981.
8. Garson A., Gorry G.A., McNammara D.G., Cooley D.A.: The Surgical decision in Tetrology of Fallot weighing risks and benefits with decision analysis. Am. J. Cardiol 45:108, 1980.
9. Kirklin J.W., Blackston E.H., Pacifico A.D., Brown R.N., Bargeron M.J.R.: Routine Primary repair vs. Two stage repair of Tetrology of Fallot. Circulation 60:373, 1979.
10. Castaneda A.R., Freed M.D., William R.G., Norwood W.I.: Repair of Tetrology of Fallot in infancy. Early and late results. J. Thorac. Cardiovasc. Surgery 74:372, 1972.