SUMMARY
Patent Ductus Arteriosus Post NICU Discharge in Premature Infants: A Prospective Registry (PDX-002-15)

Sponsor
MEDNAX Center for Research, Education and Quality

Steering Committee
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Study type - Prospective Registry Study
Multicenter study - Number of sites – 10-12
Study enrollment goal - 200
Site enrollment goal - 20

Purpose
The purpose of this study is to track post-discharge outcomes on prematurely born infants who are discharged from the NICU with a patent ductus arteriosus (PDA). We plan to report on the spontaneous closure rate as well as the incidence of pulmonary and/or cardiac events in these infants. Our goal is to identify risk factors associated with adverse outcomes in prematurely born infants who are sent home with a PDA.

Background
Patent ductus arteriosus (PDA) is a common finding in premature infants.1 Multiple therapies can be utilized to promote closure of the PDA, though there remains considerable controversy regarding optimal treatment of the ductus.2 After failure of pharmacologic management (such as use of indomethacin and ibuprofen) some infants undergo surgical ductal ligation while still in the NICU.3 Recent reports have identified an association between either medical4 or surgical5 closure and poor outcomes.

The conundrum has been expressed by Clyman et al6 who stated, “… there is great uncertainty about whether a PDA needs to be closed during the neonatal period. While 95% neonatologists believe that a moderate-size PDA should be closed if it persists in infants (born before 28 weeks) who still require mechanical ventilation, the number that treat a PDA when it occurs in infants that do not require mechanical ventilation varies widely. Both the high likelihood of spontaneous ductal closure and the absence of RCTs, specifically addressing the risks and benefits of neonatal ductal closure, add to the current uncertainty. New information suggests that early pharmacologic treatment has several important short-term benefits for the preterm newborn. On the other hand, ductal ligation, while eliminating the detrimental effects of a PDA on lung development, may create its own set of morbidities that counteract many of the benefits derived from ductus closure.6

In this context, clinicians have shifted their practice to include discharge of these premature infants with their ductus still patent.5,6 Data from the Pediatrix Medical Group, Inc. clinical data warehouse (CDW) shows ductal ligation is decreasing in this population. However, studies of post-discharge outcomes for these infants are lacking, limited to one retrospective report of a small sample of infants from a single center.6
Study Population

This is a prospective multicenter descriptive study to collect data on neonatal outcomes and treatment modalities of neonates diagnosed with a patent ductus arteriosus by echocardiogram and have an active diagnosis of a PDA at discharge from the hospital. Potential study candidates will be identified by the Investigator, study coordinator, or other research personnel based on whether or not the infant has had one echocardiogram obtained during their hospital stay documenting/confirming PDA diagnosis. The parent(s) will need to consent to provide contact information in order to collect up to one year of follow-up outcome data on their child.

Once informed consent is obtained, a member of the research team will generate a study code from the MDXPLORE™ electronic data system. The study code is used to facilitate the de-identification of the subject and data collected specifically for the study. Outcome data will be collected while the neonate is hospitalized and up to one year post birth date for the follow-up information.

Inclusion Criteria

1. Documentation of informed consent and authorization for participation.
2. Estimated gestational age of 32 weeks or less.
3. Active diagnosis of a PDA at discharge.
4. At least one echocardiogram obtained during hospital stay documenting/confirming PDA diagnosis.
5. Parental agreement to provide follow-up information on their child.
6. Cardiologist and/or Pediatrician willing to provide follow-up information on enrolled infants.

Exclusion Criteria

1. No known major congenital anomalies (inborn error of metabolism, cyanotic congenital heart disease, gastrochisis, omphalocele, diaphragmatic hernia or other major gastrointestinal anomalies, major neurological injury or anomaly, multiple congenital abnormalities).
2. Chromosomal / genetic disorders – Inherited metabolic disorders (Aa, fat or carbohydrate), Trisomies, Turner’s syndrome, Vater’s syndrome, CHARGE, DiGeorge or other 22q11 deletions, Major chromosomal duplications, deletions detectable on high resolution karyotype (not microarray).
3. Parent(s) unwilling to participate in follow-up.

*For infants < 32 weeks gestation who survive to discharge with a PDA, all of the above exclusions will be rare.

Outcome Measures

1. Spontaneous closure of PDA.
2. Post NICU discharge intervention on the PDA.
   a. Ligation.
   b. Cardiac catheterization based occlusion.
   c. Complications associated with treatment to include: death, pneumothorax, chylothorax, vocal cord paresis, occlusion of a vessel other than the PDA, infection, pulmonary hypertension, heart failure and bleeding.
3. Use of medications typically associated with treatment of ductal shunting (digoxin, furosemide, other diuretics, ACE inhibitors).
4. Re-admission to hospital.
   a. Respiratory problems.
   b. Cardiac problems including heart failure and pulmonary hypertension.
5. Death and if death, primary cause will be reported.
6. Echocardiographic/clinical signs consistent with cardiac volume overload and
   heart failure.
7. Echocardiographic/clinical signs consistent with pulmonary arterial hypertension.
8. Continued need for respiratory support.
9. De-identified data on general incidences of PDA and PDA treatment in each
   center. This data will be collected at the initial site visit and will be based on
   review of the Pedriatrix Medical Group, Inc. clinical data warehouse.

**Follow-up**
The follow-up plan will include follow-up calls with the subjects’ parent(s) or legal
 guardian, cardiologist and/or pediatrician at approximately six (6), and twelve (12)
 months of age to determine if the infant experienced any of the outcome measures
 listed in section 9.3. An additional eighteen-month follow-up call will occur for those
 subjects that have a report of an open PDA at the 12-month follow-up.

**Follow-up plan**
Follow-up will be coordinated by the MEDNAX research staff in collaboration with the
 site principal investigator and study coordinator. The parent(s) will need to provide
 contact information including telephone number(s), cellular phone number(s), and
 address in order for the study team to contact them to obtain the follow-up information
 on their child. This will be completed at the time informed consent and authorization is
 obtained. Follow-up with the cardiologist and/or pediatrician may also take place if an
 authorization has been signed by the parent to release their child’s records.

Follow-up will be completed on all enrolled subjects. Follow-up phone calls to the
 parents and cardiologist will occur at approximately six and twelve months of age. An
 additional eighteen-month follow-up call will occur for those subjects that have a report
 of an open PDA at the 12-month follow-up. The site PI/Study Coordinator will assist
 with cardiology follow-up phone calls at the designated study time points. A cardiology
 follow-up case report form will be completed and the findings recorded for the outcome
 measures listed in section 9.3.

The MEDNAX research team will conduct follow-up phone calls to the study participant’s
 parents or legal guardian at the designated time points. An Outcome at Follow-up Case
 Report Form will be completed by the MEDNAX research team and the findings
 recorded for the outcome measures listed in section 9.3. The investigator at the site will
 be required to review the data and finalize these case report forms in the MDXPLORE™
 system.
References


