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Protocol: AAAR5436

Principal Investigator: Liberman, Leonardo

Title: Comparison of Holter with Leadless Patch Ambulatory Electrocardiographic Monitoring in Children

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Study Purpose and Rationale:

The utility of ambulatory electrocardiography has been reported using a variety of devices, including the short-term (24- to 48-hour) Holter monitor and the longer term event monitor (7-30 days). Each monitoring modality has its strengths and limitations. The Holter monitor can detect asymptomatic arrhythmias by continuously recording, however the multiple leads are cumbersome and it is not ideal for capturing infrequent arrhythmias because of the short wear time. The Holter monitor's ability to detect an arrhythmia, or diagnostic yield, was 10% in a retrospective study of 1319 children. The event monitor is preferred for infrequent arrhythmias, however it requires cognitive capacity to press a trigger button, and patient compliance may be difficult in the pediatric population. The adhesive patch monitor (Zio Patch; iRhythm Technologies, San Francisco, California) is a single-lead, intermediate-duration, water-resistant adhesive patch monitoring device that can continuously record for up to 14 days. The Zio patch has demonstrated great utility in the adult population as it detected more arrhythmias in the first 24 hours as compared with the Holter monitor when worn simultaneously. In a retrospective study of 3,209 pediatric patients across the United States who used the Zio patch, the diagnostic yield was 12%.While both the Holter and the Zio patch are continuously recording and are able to detect asymptomatic arrhythmias, to date there has been no direct comparisons of the diagnostic yield (ability to detect an arrhythmia) of the Holter monitor versus the Zio patch in the pediatric population.

Study Design:

Pediatric patients less than or equal to 21 years at Children's Hospital of New York (CHONY) who are referred for ambulatory ECG monitoring will be consented and enrolled prospectively to have the Holter monitor and the Zio patch placed simultaneously in the pediatric cardiology clinic. Patients will be instructed to wear both devices for 48 hours. Demographic data will be collected, including date of birth, age, gender, weight, height, chest circumference, body surface area, indication for ambulatory ECG monitoring, prior congenital heart disease, prior cardiac surgery, and prior Holter or Zio patch use. A one page patient satisfaction survey will be given to the patient and parent/guardian after completion of the study to compare the comfort, interference with daily activities, adverse events (such as skin irritation or if either device fell off), and preference for each device. Holter monitors will be returned to the clinic along with the patient satisfaction survey, and the Zio patch will be mailed back to manufacturer headquarters and the report will be returned to us. Primary Objective: This prospective study aims to compare the diagnostic yield of the Holter monitor versus the Zio patch in children by having patients wear both devices simultaneously for 48 hours. We will compare the incidence of specific abnormal heart rhythms using each device, specifically supraventricular tachycardia 4 beats (SVT), ventricular tachycardia 4 beats (VT), advanced second degree or complete heart block, atrial flutter or fibrillation (AF), pause > 3 seconds, premature ventricular contractions (PVCs) > 5%, premature atrial contraction (PACs) > 5%, and presence of preexcitation suggestive of Wolff-Parkinson-White syndrome (WPW).Secondary objective: We will compare the minimum, maximum, and average heart rates, as well as the percent analyzable data for each device over the 48 hours.Tertiary objective: To determine if age, weight, gender, presence of congenital heart disease, or prior cardiac surgery had an effect on diagnostic yield of Holter monitor versus the Zio patch.Quaternary objective: To compare the patient and/or parental satisfaction for the Holter monitor versus the Zio patch using a one page survey at the end of the 48 hour study.

Statistical Procedures:

Descriptive statistics will be used for patient demographics and survey results. To compare presence or absence of any of the clinically significant arrhythmias (SVT > 4 beats, VT > 4 beats, advanced second degree or complete AV block, atrial fibrillation or flutter, pause > 2 seconds, PVCs > 5%) over 48 hours, McNemar's test will be used. Further subgroup analysis of each of the arrhythmia types can be done between the 2 devices using McNemar's test again. Logistic regression will be used to determine if age, weight, gender, presence of congenital heart disease, or prior cardiac surgery has an effect on diagnostic yield of Holter monitor versus the Zio patch. Using a power of 80% and allowing for 25% variability, the number of patients needed for the study was determined to be 255 using McNemar's test. We anticipate enrolling about 260 patients in this study.

Study Procedures:

Informed consent will be obtained in a private room in the pediatric cardiology clinic. If the patient agrees to participate in the research, the Holter monitor and the Zio patch will be placed on the patient in that private room. The Holter monitor will be returned to the clinic and the Zio patch will be returned in the mail, per protocol from the manufacturers. The results of both ambulatory ECG monitors will become part of the patient's confidential medical record.

After the data is collected, it will be de-identified and stored in a password protected electronic database on an encrypted endpoint (desktop and labtop computer). The patient satisfaction survey will be a hardcopy that will be stored in a binder locked inside the filing cabinet of the study coordinator. Only research investigators will have access to the electronic database or the binder of patient satisfaction surveys.

Study Devices:

Device name: Holter
Device description: Traditional ambulatory electrocardiographic monitor
Device Model/Version #: H3+ Digital Holter Recorder
Already approved by FDA and used as gold standard

Device name: Zio Patch
Device description: Leadless ambulatory patch electrocardiographic monitor
Device Model/Version #: Zio XT
FDA approved in adults, off-label use in children. This is a Nonsignificant Risk device (21 CFR 812.2(b)); no more than Minimal Risk (45 CFR 46.404/21 CFR 50.51; i.e., 'Section 404').

Research Question(s)/Hypothesis(es):

Primary objective: This prospective study aims to compare the diagnostic yield (ability to detect an arrhythmia) of the Holter monitor versus the Zio patch in children by having patients wear both devices simultaneously for 48 hours. We will compare the incidence of specific abnormal heart rhythms in children using each device, specifically supraventricular tachycardia 4 beats (SVT), ventricular tachycardia 4 beats (VT), advanced second degree or complete heart block, atrial flutter or fibrillation (AF), pause > 3 seconds, premature ventricular contractions (PVCs) > 5%, premature atrial contractions (PACs) > 5%, and presence of preexcitation suggestive of Wolf Parkinson White syndrome (WPW).

Secondary objective: We will compare the minimum, maximum, and average heart rates, as well as the percent analyzable data for each device over the 48 hours. Tertiary objective: To determine if age, weight, gender, presence of congenital heart disease, or prior cardiac surgery had an effect on diagnostic yield of Holter monitor versus the Zio patch.Quaternary objective: To compare the patient and/or parental satisfaction for the Holter monitor versus the Zio patch using a one page survey at the end of the 48 hour study. Hypotheses:1. There will be no difference in the diagnostic yield or the heart rate parameters (maximum, minimum, or average heart rate, percent analyzable data) of the Zio patch compared to the Holter monitor during the 48 hours of monitoring2. Age, weight, gender, presence of congenital heart disease, or prior cardiac surgery will not affect diagnostic yield of the Holter versus the Zio patch.3. Patients will prefer the Zio patch over the Holter monitor based on the patient satisfaction survey.

Scientific Abstract:

Ambulatory electrocardiographic (ECG) monitoring is common diagnostic tool used to detect arrhythmias in the outpatient setting. The traditional Holter monitor is the gold standard ambulatory ECG monitoring device that is commonly used in children. However, it has multiple leads and can be cumbersome. The Zio patch is a new single□lead patch ECG monitor that has been FDA approved for use in adults and has been used off-label in children for several years. While both the Holter and the Zio patch are continuously recording and are able to detect asymptomatic arrhythmias, to date there has been no direct comparisons of the diagnostic yield (ability to detect an arrhythmia) of the Holter monitor versus the Zio patch in the pediatric population. This prospective study aims to compare the diagnostic yield, heart rate parameters, and patient satisfaction of the Holter versus the Zio patch in pediatrics. Patients less than or equal to 21 years of age referred for ambulatory ECG monitoring at the pediatric cardiology clinic at Children's Hospital of New York (CHONY) will be recruited to participate in the study. ECG technicians will obtain informed consent and place the Holter monitor and Zio patch simultaneously on the patient. After 48 hours of monitoring, the patient will mail the Zio patch to the manufacturer and the return the Holter monitor to the clinic. The patient satisfaction survey will be submitted to the researchers in clinic upon completion of the study. Descriptive statistics will be used for patient demographics and survey results. To compare presence or absence of any of the clinically significant arrhythmias (supraventricular tachycardia (SVT) > 4 beats, ventricular tachycardia (VT) > 4 beats, advanced second degree or complete atrioventricular block, atrial fibrillation or flutter, pause > 2 seconds, premature ventricular contractions (PVCs) > 5%) over 48 hours, McNemar's test will be used. Further subgroup analysis of each of the arrhythmia types will be done using McNemar's test again. Logistic regression will be used to determine if age, weight, gender, presence of congenital heart disease, or prior cardiac surgery has an effect on diagnostic yield of Holter monitor versus the Zio patch.

Lay Abstract:

Ambulatory electrocardiographic (ECG) monitoring is common diagnostic tool used to detect arrhythmias in the outpatient setting. The traditional Holter monitor is the gold standard ambulatory ECG monitoring device that is commonly used in children. However, it has multiple leads and can be cumbersome. The Zio patch is a new singl lead patch ECG monitor that has been FDA approved for use in adults and has been used off-label in children for several years. While both the Holter and the Zio patch are continuously recording and are able to detect asymptomatic arrhythmias, to date there has been no direct comparisons of the diagnostic yield (ability to detect an arrhythmia) of the Holter

monitor versus the Zio patch in the pediatric population. This prospective study aims to compare the diagnostic yield, heart rate parameters, and patient satisfaction of the Holter versus the Zio patch in pediatrics. Patients less than or equal to 21 years of age referred for ambulatory ECG monitoring at the pediatric cardiology clinic at Children's Hospital of New York (CHONY) will simultaneously wear both the Holter and the Zio for 48 hours. Data parameters will be compared using descriptive statistics, McNemar's test, and logistic regression.

Subject Population Justification:

Any patient from birth through 21 years of age who is referred for ambulatory ECG monitoring at CHONY will be recruited for participation in this study. In a large retrospective study using the Zio patch, neonates (under 1 month of age) have used the Zio patch off label, therefore this study will prospectively study the device in all ages from birth through 21 years. We will obtain informed consent in English or in Spanish. Target enrollment is 260 participants.