Early Enteral Nutrition and Aggressive Fluid Resuscitation are Associated with Improved Clinical Outcomes in Acute Pancreatitis

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Objectives To determine whether recommendations for treatment of acute pancreatitis (AP) in adults impact the outcomes of pediatric AP.

Study design Adult guidelines regarding early management of AP were implemented through an admission order set at Cincinnati Children's Hospital Medical Center at the beginning of the year 2014. Recommendations included administering high rates of intravenous fluid (IVF) within 24 hours of admission and enteral nutrition within 48 hours of admission. A retrospective chart review of AP admissions before and after the implementation of the recommendations was undertaken. Outcomes studied were: hospital length of stay, intensive care unit transfer rates, development of severe AP, pulmonary complications, and readmission rates post discharge from the hospital.

Results The study included 201 patients. Children who received feeds within the first 48 hours and received greater than maintenance IVF within 24 hours had a shorter length of stay, less intensive care unit admissions and severe AP rates compared with the patients who remained nil per os during the first 48 hours and received lower rates of IVF.

Conclusion Our data support that early enteral nutrition and early aggressive IVF improve outcomes of pediatric AP. *(J Pediatr 2015;167:397-402)*.

The incidence of acute pancreatitis (AP) in the pediatric population has increased in the past 2 decades and is estimated to be around 3.6-13.2/100 000 annually.[1-4] The management of AP in pediatric patients varies greatly, and current strategies are derived from adult guidelines. The adult literature suggests that early aggressive fluid management and early enteral nutrition (EN) are associated with better outcomes, decreased hospital length of stay (LOS), and less likelihood of developing severe AP (SAP).[5-7] Pediatric patients are still managed with complete bowel rest and varying rates and types of intravenous fluids (IVFs) or parenteral nutrition. A recent survey within our institution found that the majority of pediatric providers taking care of patients with AP delay starting EN until the patient's pain or narcotic use has subsided.[8] Early nutrition has not yet been embraced in the management of children in part because the pediatric population is "different" from the adult population and given the lack of data in children.

Data from adult studies suggest that early aggressive IVF administration results in decreased systemic inflammatory response (SIRS) and organ failure, length of hospitalization, and mortality.[6,7] However, there is no agreement on what the exact volume or type of fluid to be used in adult patients should be, and there is even less guidance for the pediatric population. Based on our survey results, fluid management in AP varies between providers.[8]

Standardizing care has been shown to improve patient outcomes in different medical conditions and would facilitate comparative effectiveness studies.[9,10] Our survey results[8] demonstrated that standardizing management as a quality improvement measure for inpatient admissions with AP in pediatrics was needed; hence, we implemented a "standard of care" as an admission order set through our electronic medical record system. The order set was based on available adult literature, and order set was made available hospital-wide to be used at the time of admission for patients with mild AP. Mild AP was defined by the Atlanta criteria[11] as no evidence of complications or SAP as defined by the following: multisystem organ failure, progressive SIRS requiring intensive care unit (ICU) admission, local pancreatic complications (such as necrosis, hemorrhage, or pseudocyst formation), or respiratory complications (pulmonary edema or pleural effusion).

We sought to determine whether the outcomes of AP were different in patients managed according to these new recommendations compared with those who were not.

AP	Acute pancreatitis
EN	Enteral nutrition
GI	Gastroenterology
ICU	Intensive care unit
IVF	Intravenous fluid
LOS	Length of stay
NPO	Nil per os
PO	Per os
SAP	Severe acute pancreatitis
SIRS	Systemic inflammatory response

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Methods

Beginning in January 2014, hospital-wide education on current available literature and adult data in AP management was conducted, as was the implementation of the admission order set in our electronic medical record system as a quality improvement measure to improve outcomes by standardization of care.

Specific recommendations on the timing of EN, as well as timing, type, and rate of IVF, were provided through the order set. Recommendations included: (1) initiation of enteral feeds upon admission (clears with progression to general age-appropriate diet within 6 hours if tolerated); and (2) initiation of IVF at 1.5-2 times the maintenance rate of dextrose 5% normal saline on admission.

A retrospective review of admissions of children with AP from November 30, 2009, to September 30, 2014, at Cincinnati Children's Hospital Medical Center was conducted. The study was approved by the institutional review board committee (no. 2014-8246). Identification of cases of AP based on *International Classification of Diseases, 9th Revision* codes that started with 577 (AP). The cohort was narrowed to include only children who had elevated lipase levels ≥ 3 times the upper limit of normal, and who were admitted to the general pediatric services (hospitalist medicine service, adolescent medicine, community pediatrics), and the gastroenterology (GI) service. Patients with other comorbidities such as oncologic disease and cardiac, diabetes, kidney, or acute surgical conditions were excluded.

Inclusion criteria were: (1) admitted to one of the above mentioned services (general pediatrics or GI); and (2) mild AP as defined by the Atlanta criteria[11] (meeting 2 of 3 criteria: symptoms of pain, vomiting; elevated lipase and or amylase at ≥3 times the upper limit of normal; imaging findings of AP), or (3) 0-21 years old at the time of admission. Exclusion criteria were: (1) patients with AP and SAP on admission: multisystem organ failure, SIRS, local pancreatic complications (such as necrosis, hemorrhage, pseudocyst formation), or respiratory complications; and (2) patients with pancreatitis related to trauma, gallstone pancreatitis, or postsurgery if they were admitted to the surgical service or ICU.

Demographic data were collected, as well as data on the type and rate of IVF administered during the first 24 hours of admission, and whether the child was nil per os (NPO) or received EN during the first 48 hours. The nutritional status of a patient was determined through chart review and based on documentation of by the presence of documented, consumed nutrition per os (PO) or tube feeds and not just the presence of a diet order. Nasogastric or nasojejunal tubes were not placed during the first 48 hours, but preexisting enteral tubes were used to provide nutrition. Data on the LOS, vital signs, lab values, SIRS, multiorgan failure leading to ICU transfers, respiratory complications, surgery to the pancreas, and death were collected.

Statistical Analyses

Analysis was conducted to see if EN or IVF administration in itself as a single treatment had any effect on the measured outcomes. The outcomes measured included LOS, rate of SAP (defined by the development of local pancreatic complications, organ dysfunction, or SIRS that required ICU care, development of respiratory complications, or death), respiratory complications (defined by oxygen requirement or development of pulmonary edema or pleural effusions on chest radiographs), and hospital readmission rate (within 72 hours of discharge). A factorial design was applied to group the patients according to combinations of treatment arms. The treatment groups were the following: NPO for the first 48 hours + IVF low (lo) within 24 hours, NPO for 48 hours + IVF high (hi) within 24 hours, EN within 48 hours (PO) + IVF lo within 24 hours, and PO within 48 hours + IVF hi within 24 hours.

Because of skewedness of LOS observations, LOS was analyzed on logarithmic scale. Some patients had multiple encounters. To account for intrapatient correlation in the analysis of LOS, a linear model with repeated measurements was applied. The interaction between EN status and IVF rate also was tested. For categorical response variables (eg, SAP, ICU transfer), we applied a generalized linear mixed effect model to account for intrapatient correlation, where the binary response is associated with predictors through a logit link.

Pairwise comparison analysis was also performed to determine whether there were significant differences between the treatment groups. Multiplicity adjustment of P values was made with Tukey method for LOS. Bonferroni adjustment was applied to binary response multiple comparisons.

To determine whether IVF rate affected the rate of respiratory complications, Fisher exact test was performed.

Results

A total of 201 children were included in the study; 49.7% received EN within 24 hours of admission (data not shown) and 75% received EN within 48 hours, and 62% received 1.5-2 times the maintenance IVF during the first 24 hours of admission.

Based on the timing of nutrition and fluid administration rates, patients were divided into 4 groups: NPO + IVF lo, NPO + IVF hi, PO + IVF lo, and PO + IVF hi.

Table I shows the demographics and baseline clinical variables of the patients in the different groups. The groups were not significantly different in patients' demographics; age, sex, weight, and body mass index on admission. Patients had comparable lab values on admission and other clinical variables measured. Statistical significance was seen in the mean white blood count on admission between the groups, with the highest being 13.6 k/μL and the lowest 9.89 k/μL. The breakdown of etiologies was different between groups; however, our management order set was built to be used for mild AP regardless of the etiology.