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Evaluation of Children with Acute Pancreatitis

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Introduction: Although acute pancreatitis (AP) is uncommon in children, causes significant morbidity and mortality. This study aims to evaluate the clinical and laboratory findings, treatment approaches, complications of children with acute pancreatitis.

Material and methods: Thirty children who were diagnosed as acute pancreatitis during January 2008-April 2013 were evaluated.

Results: The most common etiology of acute pancreatitis was the drugs (30%), particularly L-asparaginase (44.5%). The biliary tract diseases (26.7%), infection (16.7%), hyperlipidemia (10%), cystic fibrosis (3.3%), and post-endoscopic retrograde cholangiopancreatography pancreatitis (3.3%) were other causes, and among 10%, no reason was detected. Abdominal pain (83,3%), nausea (70%), loss of appetite (63.3%), vomiting (56.7%), and fever (20%) were the most common symptoms. In 86.6% of cases amylase, in 73.9% lipase, and in 66.7% pancreatic amylase were elevated three times the upper limit of normal. The alanine transaminase, total and direct bilirubin levels in not drug-induced pancreatitis were higher than drug-induced pancreatitis ($p<0.05$). Ultrasonography, abdominal tomography, magnetic resonance cholangiopancreatography revealed pancreatitis related changes 63.3%, 85%, 70% of patients, respectively. Oral feeding was started on 4 ± 5.6 days, with polymeric diet (30%), and medium chain triglyceride rich enteral diet (70%). The length of hospitalization was 16.5 ± 15.1 days (4-66 days). The patients fed with polymeric diet had a shorter hospitalization duration ($p<0.05$). The delayed initiation of oral feeding caused longer LOH ($p<0.001$). Pseudocyst (6,7%), sepsis (6.7%), and necrosis (3.3%) were the complications developed in patients.

Conclusion: Consequently, this study underlines the children with acute abdominal pain, especially who use drugs like asparaginase and valproic acid, or that are known to have gallstone/biliary sludge, need to be examined for acute pancreatitis through pancreatic enzymes and ultrasonography. Moreover, the study also highlights that early feeding in acute pancreatitis is related with shorter hospitalization duration.

Keywords: Acute pancreatitis, children, etiology, treatment

Akut Pankreatitli Çocukların Değerlendirilmesi

Giriş: Akut pankreatit (AP) çocuklarda nadir görülmekle birlikte önemli morbidite ve mortaliteye neden olmaktadır. Bu çalışmada AP'li çocuklarda klinik ve laboratuvar bulgularının incelenmesi ve komplikasyonlarının yanı sıra tedavi yaklaşımlarının değerlendirilmesi amaçlanmıştır.

Materyal ve metod: Hastanemizde Ocak 2008-Nisan 2013 yılları arasında AP tanısı ile izlenen 30 olgu incelendi.

Sonuç: Akut pankreatit etyolojisinde en sık neden ilaçlar (%30), özellikle de L-asparaginaz (%44.5) idi. Biliyer hastalıklar (%26.7), enfeksiyon (%16.7), hiperlipidemi (%10), kistik fibrozis (%3.3), endoskopik retrograde kolanjiopankreatografi sonrası pankreatit (%3.3) diğer nedenlerdi ve %10'unda bir neden saptanamadı. Hastaların %83.3'ünde karın ağrısı, %70'inde bulantı, %63.3'ünde iştahsızlık, %56.7'sinde kusma ve %20'sinde ateş saptandı. Olguların

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%86.6'sında amilazın, %73.9'unda lipazın, %66.7'sinde pankreatik amilazın normalin üst sınırının en az 3 katı kadar artışı vardı. İlaça bağlı olmayan pankreatitte alanin transaminaz, total ve direkt bilirubin düzeyleri ilaca bağlı pankreatite göre daha yüksekti ($p<0,05$). Hastaların %63.3'ünde ultrasonografi, %85'inde bilgisayarlı tomografi ve %70'inde magnetik rezonans kolanjiopankreatografi ile pankreatit ile uyumlu değişiklik saptandı. Ağızdan beslenmeye başlama zamanı $4 \pm 5,6$ gün idi ve %30'u polimerik diyet, %70'i orta zincirli trigliseridden zengin enteral ürün ile beslendi. Hastanede yatış süresi $16,5 \pm 15,1$ gün (4-66 gün) idi. Polimerik diyet ile beslenenlerin hastanede yatış süresi daha kısaydı ($p<0,05$). Oral başlama süresi uzadıkça hastanede yatış süresi artmıştı ($p<0,001$). Hastalarda psödokist (%6,7), sepsis (%6,7) ve nekroz (%3,3) gelişti.

Sonuç olarak bu çalışmada L-asparaginaz, valproik asit gibi ilaç kullanan veya safra taşı/çamuru olduğu bilinen ve akut karın ağrısı olan çocukların pankreas enzimleri ve ultrasonografi ile AP için değerlendirilmesi gerektiği ve AP'de erken beslenmenin hastanede kalış süresini kısalttığı vurgulanmaktadır.

Anahtar kelimeler: Akut pankreatit, çocuklar, etyoloji, tedavi

Introduction

Acute pancreatitis (AP) is an inflammatory condition of the pancreas. Acute pancreatitis defined as the presence of pancreatic digestive enzymes in the serum and/or urine and the presence of radiological changes in the pancreas with clinically sudden abdominal pain (1-2). Acute pancreatitis has increased in recent years because of increasing drug usage, diagnostic tests and systemic diseases in children (3-5).

The most common causes of AP are biliary causes, systemic diseases, drugs, trauma in children as well as alcohol and gallstones are common in adults (2-6).

Acute pancreatitis is usually mild in children. However, some patients may develop serious illness and death (7). Acute pancreatitis may present with various clinical manifestations. Abdominal pain, which is the most common symptom, is present in 80-95% of the cases. However, the absence of abdominal pain does not exclude the diagnosis of AP. The second most common symptom is nausea and vomiting at a rate of 40-80%. Irritability is a finding indicated by parents in young children who do not describe abdominal pain (2,8).

The aim of this study was to investigate the demographic and clinical features, laboratory and imaging findings, treatment modalities, complications, mortality and morbidity rates of patients with AP.

Materials and Methods

In our study, we evaluated the medical records of 30 children who diagnosed as AP with history, clinical and laboratory findings at Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital from January 2008 to April 2013 retrospectively. All patients had at least two features of the Atlanta criteria (9) (typical abdominal pain, serum amylase and/or lipase >3 times the upper limit of normal, characteristic findings of AP on imaging studies). If a patient had recurrent episodes of pancreatitis during study, only the first episode was included. Patients with chronic pancreatitis were excluded from the study. The study was approved by the local Clinical Research Ethics Committee (06.08.2012, numbered 126).

The demographic and clinical features, treatment modalities, complications, length of hospitalization (LOH), mortality and morbidity rates were recorded. In addition, complete blood count, biochemical parameters, blood lipid profile, amylase, lipase, pancreatic amylase values, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), coagulation parameters, specific investigations for etiology and imaging findings (ultrasonography (USG), computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP) of the

abdomen) were evaluated. The length of hospitalization and initiation time of oral feeding was compared between patients fed with polymeric diet/medium chain triglyceride (MCT) and Total parenteral nutrition (TPN).

The patients who could not detect any etiological cause by laboratory tests and imaging methods were called idiopathic. Gallstones, biliary sludge, annular pancreas, choledochal cyst, biliary system diseases was reported as biliary groups. Drug-related pancreatitis was defined as regression of pancreatitis after drug use and drug discontinuation.

The mean age, gender distribution, LOH, amylase, pancreatic amylase, lipase, Alanine aminotransaminase (ALT), Aspartate aminotransferase (AST), Gamma-Glutamyl Transferase (GGT), total bilirubin (t.bil) and direct bilirubin (d.bil) levels were compared between biliary and non-biliary groups and drug not-drug induced pancreatitis groups.

Statistical analysis

Statistical analysis of the data was performed with Statistical Package for Social Sciences (SPSS) for Windows-version 11.5. Descriptive statistics were presented as mean± standard deviation or mean (minimum-maximum) for continuous variables, and categorical variables as number of cases. The Student's t-test was used to assess the differences in means. The Mann-Whitney U test was used to assess the differences in medians. Categorical variables were evaluated by Fisher's exact test. Spearman's correlation test was used to determine whether there was a statistically significant correlation between discrete numerical variables. $P < 0.05$ was considered statistically significant.

Results

Thirty children who were diagnosed as AP were included. Of the patients, 18 (60%) were male, 12 (40%) female and there was no statistically difference in terms of gender ($p > 0.05$). The mean age of the patients was 12.4 ± 4.3 (3-18) years. The most common symptom was abdominal pain in 25 (83.3%) patients. Other symptoms were given in figure 1. While in 52% of the patients had epigastric abdominal pain, most frequently it radiated to back (32%). The most common etiology of AP was the drugs (30%), particularly L-asparaginase (44.5%). The list of etiology of AP was given in Table 1.

In 86.6% of cases amylase, in 73.9% of cases lipase, and in 66.7% of cases pancreatic amylase were elevated three times the upper limit of normal level. Amylase, pancreatic amylase, lipase values and mean increases at the time of diagnosis are given in Table 2. Laboratory findings of biliary-non biliary groups and drug not-drug induced pancreatitis groups are given in Table 3. Alanine transaminase, total and direct bilirubin levels in not drug-induced pancreatitis were higher than drug-induced pancreatitis ($p < 0.05$). Also amylase, ALT, AST, GGT, total and direct bilirubin levels in biliary-groups were higher than non-biliary groups ($p < 0.05$). Ultrasonographic evaluation was performed in all patients, but the pancreas of seven patients (23.4%) could not be evaluated by gas and pancreas imaging was normal in four patients (13.4%). In four of seven patients who could not be evaluated for pancreas, CT showed increased pancreatic size and decreased pancreatic echogenicity or heterogeneous appearance. Ultrasonography, CT, MRCP revealed pancreatitis related changes 63.3%, 85%, 70% of patients, respectively. Imaging findings are summarized in Table 4. Abdominal USG, tomography and MRCP evaluation of the patients revealed multiple findings.

All patients were initially discontinued oral feeding and intravenous fluid was given. Oral feeding was started on 4 ± 5.6 days, with polymeric diet (n:9, 30%), or MCT diet (n:21, 70%). The length of hospitalization of all patients was 16.5 ± 15.1 days (4-66 days). The length of hospitalization was 8 ± 10.2 days (4-34 days) in the patients fed with polymeric diet, LOH was 23 ± 16 days (4-66 days) in the patients who fed with MCT diet. The difference between the groups was statistically significant ($p < 0.05$). Total parenteral nutrition was administered in six (20%) of patients on 4 ± 2.5 days and continued for 14.5 ± 15.9 days. The length of

hospitalization was 37 ± 18.8 days (18-66 days) for TPN receiving patients and 13 ± 9.6 days (4-40 days) for not receiving TPN. The difference between the groups was statistically significant ($p < 0.05$). The delayed initiation day of oral feeding caused long LOH ($p < 0.001$).

Pseudocyst (6.7%), sepsis (6.7%), and necrosis (3.3%) were developed in patients. There was no death due to AP. However, two patients (6.7%) died related to the underlying systemic disease. Recurrence was detected in four (13.4%) patients. None of the patients had chronic pancreatitis and pancreatic insufficiency.

Discussion

Acute pancreatitis is a painful inflammatory disease that causes important health problems (10). It has been observed that AP has increased in children in the last 10-15 years (11).

In addition to typical abdominal pain, increasing pancreatic enzymes play significant role in the diagnosis of AP. The value of amylase is high for diagnosis of AP, especially in the first 24 hours when symptoms occur. Lipase is more reliable in the diagnosis of AP and continues to be high for a longer time than amylase. In our study, 86.6% of patients had increased amylase levels, 73.9% of patients had increased lipase and 66.7% of had increased pancreatic amylase. In 56.5% of the patients had both increased amylase and lipase levels and all of the enzymes increased in 50% of patients. According to the literature, increased lipase is more specific for diagnosis of AP (12). In our study we detected increased lipase levels less than amylase levels. It may be related the fact that lipase was not assied in our hospital laboratory and was sent to an external center. In addition, although amylase could be analysed in all patients, lipase could be analysed in 23 (76.7%) of patients.

In childhood pancreatitis, lipase, AST, ALT, total bilirubin levels were higher in the biliary group than in the non-biliary group (13). Similarly, in our study, mean amylase, ALT, AST, GGT, total and direct bilirubin levels were significantly higher in the biliary group than non-biliary group ($p < 0.05$). We determined high levels of amylase, ALT, AST, GGT, total and direct bilirubin should be considered for primarily consider biliary causes with imaging

Methods.

Nutrition is an important element in the treatment of AP. It was believed that pancreatic secretion was reduced by stopping oral feeding of patients with AP before 20 years. However, large controlled studies found that pancreatic complications were decreased with early feeding (14). Oral feeding is recommended to be started in the first 24-48 hours in patients with mild pancreatitis (2). In our study, initiation time of oral feeding was 4 ± 5.6 days. The delayed initiation time of oral feeding caused longer LOH. This may be due to atrophy of the gastrointestinal tract and increased complications with bacterial translocation without enteral feeding.

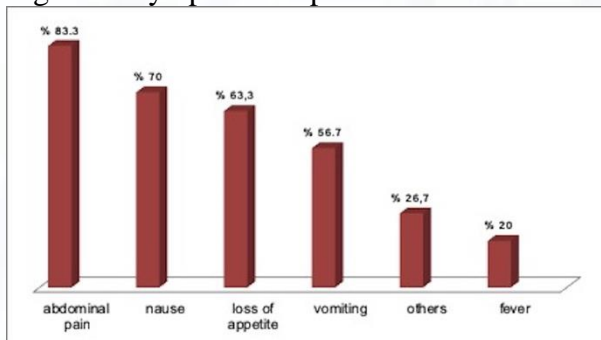
Conclusion

Acute pancreatitis is an important health problem although it is rarely seen in childhood. Acute pancreatitis should be considered in children with abdominal pain especially who use drugs like L-asparaginase and valproic acid, or that are known to have gallstone/biliary sludge, need to be examined for AP through pancreatic enzymes and ultrasonography. Moreover, the study also highlights that early feeding in AP is related with shorter hospitalization duration.

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Figure 1. Symptoms of patients



Other symptoms: jaundice, abdominal distension, weight loss, seizures and drowsiness

Table 1. Etiological classification of acute pancreatitis

Etiology	n	%
Drugs	9	30
L-Asparaginase	4	13,3
Valproic acid	2	6,7
Imipramine hydrochloride	1	3,3
Mesalazine	1	3,3
Carbamazepine	1	3,3
Biliary diseases	8	26,7
Gallstone/biliary sludge	6	20,1
Choledochal cyst	1	3,3
Annular Pancreas	1	3,3
Infection	5	16,7
Mumps	2	6,7
Brucella	1	3,3
Hepatitis A	1	3,3
EBV	1	3,3
Hyperlipidemia	3	10
Idiopathic	3	10
Cystic fibrosis	1	3,3
Secondary to ERCP	1	3,3

Table 2. Amylase, pancreatic amylase (p amylase) and lipase levels of patients at admission

	Mean (\pm SD)	Minimum- Maximum	Mean (times) increase
Amylase(U/L)	586(\pm 667)	250-2658	5
Pamylase (U/L)	206 (\pm 319)	36-1356	4
Lipase(U/L)	305 (\pm 797,9)	23-2922	6.3

Table 3. Comparasion of drug -not drug induced groups and biliary and non- biliary groups

	Biliary groups n:8 Mean (\pm SD) (min-max)	Non- biliary groups n:22	p	Drug-induced groups n:9 Mean (\pm SD) (min-max)	Not drug induce groups n: 21	p
Female	3 (37.5 %)	9 (40.9 %)	0.0723	4 (44.4 %)	8 (38.1 %)	0.214
Male	5 (62.5%)	13 (59.1%)		5 (55.6%)	5 (61.9%)	
Mean age of patients (years)	12.9 \pm 4.3	12.2 \pm 4.4	1.000	10.9 \pm 5.3	13 \pm 3.7	1.000
Amylase (U/L)	1313 \pm 828 (413-2569)	649 \pm 512 (250- 2658)	0.021	405 \pm 259 (270-908)	596 \pm 753 (250- 2658)	0,164

P amylase (U/L)	1356	204.5±197 (36-879)	>0.05	189±129 (36-454)	208±408 (58-1356)	0.315
Lipase (U/L)	1055±1617 (61-2922)	589±657 (23-2868)	>0.05	292±317 (23-980)	450±967 (61-2922)	0.643
ALT (U/L)	199,5±147 (66-468)	15.4±127 (1-521)	<0.001	14±20 (1-67)	75±165 (1-521)	0,019
AST (U/L)	113±174 (28-519)	25.5±348 (10-1662)	<0.001	26±4.7 (15-30)	35 ±364 (10-1662)	0,070
GGT (U/L)	232±395 (108-1317)	18.5±147 (2-548)	<0.001	21±110 (7-349)	93±304 (2-1317)	0.263
T. bil (mg/dl)	8.5±12 (0,4-34.6)	0,5±0.8 (0.1-4.0)	0.004	0.4±0.3 (0.1-1.3)	1.0 ±8.1 (0.2-34.6)	0.007
D. bil (mg/dl)	6±9.2 (0,1-26.4)	0,2±0.6 (0-3.0)	<0.001	0.1±0.1 (0.02-0.4)	0.3±6 (0-26.4)	0.012
The length of hospitalization (day)	13±11.3 (7-40)	17±16.4 (4-66)	>0.05	18±22 (6-66)	16±10.7 (4-40)	>0.05

Table 4. Imaging findings in acute pancreatitis

	Ultrasonography n:30	Computed tomography n:20	MRCP n:10
Enlarged pancreas	18 (60%)	14 (70%)	5 (50%)
Hypoechoic pancreas	13 (43.4)	12 (60%)	3 (30)
Dilated pancreatic duct	3 (10%)	2 (10%)	2 (20%)
Peripancreatic fluid	3 (10%)	4 (20%)	2 (20%)
Pseudocyst	2 (6.7%)	2 (10%)	1 (10%)
Stones or sludge	11 (36.7%)	3 (15%)	4 (40%)