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Original Article

Retrospective Analysis of the Pediatric Intoxication Cases

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ABSTRACT

Objective: Various pharmaceuticals may be involved in pediatric intoxications, and treatment can be challenging for physicians. However knowledge of the clinical manifestations and prognosis of intoxication will be of assistance to physicians in conducting an appropriate clinical evaluation. The purpose of this study was to analyze the patient characteristics, outcomes and clinical features of pediatric intoxication.

Methods: One hundred eighty five children aged between 1 and 17 years with pharmaceutical intoxication (135 mild, 18 moderate, and 32 severe cases) were included in the study. Demographic characteristics, clinical features, and outcomes were compared between the subgroups of clinical severity and in terms of reasons for exposure.

Results: Suicidal behaviour was responsible for 61.1% and accidental exposure for 38.9% of intoxications. The drug group most frequently responsible for intoxication was analgesic-antipyretic medications. Clinical severity, length of hospitalization, and multiple drug intoxication rates were higher in the suicide group than in the accidental group ($p=0.037$, $p=0.016$, and $p<0.001$ respectively). Mortality occurred in one patient.

Conclusion: Analgesics and neurological system agents were responsible for the majority of intoxications. Intoxication for purposes of suicide resulted in longer hospital length of stay, and greater clinical severity than accidental poisoning. Understanding the differences between intentional and accidental intoxication may be assistance to physicians in performing appropriate assessments.

Keywords: Pediatric poisoning, pharmaceutical, accidental, suicidal

INTRODUCTION

Acute intoxications head the list of global preventable health problems in the pediatric age group. Pharmaceutical intoxications are one of the principal causes of presentations to pediatric emergency departments.[1]

Although toxic substances frequently result in a moderate illness course, they may occasionally cause morbidity and/or mortality, depending on the dose and the substance involved. Pediatric intoxications differ from those seen in other age groups because children are more susceptible to poisoning and suffer greater damage from it.[1] The causes of intoxication, the type of agent, and the age groups and genders involved may vary between different countries, between different parts of the same country, and even among communities in the same region.[2] Understanding the causes of intoxication and taking appropriate measures against the potential risks may therefore help to prevent such poisonings.

Despite the fact that numerous studies on intoxications have been published previously, the number of studies dealing only with pharmacological intoxications is limited. Each region should determine and update its own epidemiological data in order to design suitable prevention and treatment approaches, train health personnel, and increase public awareness.

This study was performed to determine the patient characteristics, outcomes, and clinical features of pediatric pharmaceutical intoxications in the emergency department.

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MATERIALS AND METHODS

Study Population

This retrospective study was conducted at the pediatric emergency department of a tertiary referral hospital in Turkey between December 2020 and 2021. One hundred eighty five children aged between 1 and 17 years with histories of pharmaceutical intoxications were included.

Definitions

Pharmaceutical intoxication was defined as the ingestion, either accidentally or for purposes of suicidal behaviour of chemical substances at doses eliciting toxic responses.

Clinical presentations were classified based on the Poisoning Severity Score:[3]

0: Asymptomatic: with no distressing symptoms, and with no specific findings following physical examinations in the pediatric emergency department

1: Mild, transient, spontaneously resolving symptoms

2: Prolonged symptoms and findings

3: Life-threatening symptom and findings

Patients were divided into three subgroups based on the severity of the clinical findings as mild (scores 0 or 1) moderate (score 2) and severe (score 3).

A flow chart for patient selection and the subgroups of clinical severity are shown in Figure 1.

Heart rate and systolic and diastolic blood pressures were defined according to normal values for age groups.[4]

All patients were consulted with the National Poison Advice Center. Gastric lavage and/or activated charcoal were applied as indicated depending on the type of substance involved.

The reasons for intoxication in children were classified as accidental or suicidal behaviour.

Exclusion Criteria

Patients with missing information and data in the medical records, with exposure to pharmaceuticals which could not be identified, with non-pharmaceutical intoxications, with food or plant poisoning, or patients intoxicated by insecticides or pesticides, insect bites and stings, cleaning materials, carbon monoxide, or hydrocarbons were excluded from the study.

Study Design

The patients' age and gender, the drug/drugs causing intoxication, the reason for poison exposure (accidental or suicidal behaviour), presenting complaints on admission, vital signs, gastric lavage and activated charcoal administration during hospitalization, length of hospital stay, place of hospitalization, and outcome of intoxication (discharge/mortality) were recorded retrospectively from patients medical files. Reasons for exposure were reported by family members, the patients themselves, or witnesses.

Patients were classified based on clinical severity following evaluation of the initial history and physical examination findings.

Approval for the study was granted by the Aydın Adnan Menderes University Local Ethics Committee (decision no: 04-2022/17, date: 27.01.2022).

Statistical Analysis

Statistical analyses were performed on Statistical Package for the Social Sciences for Windows (SPSS Inc., Chicago, IL, USA) version 22 software. Variables were expressed as median, minimum and maximum count (n) and percentage (%). The normality of the distribution of numerical variables was assessed using descriptive statistics, histogram charts, and the Kolmogorov-Smirnov test. Student's t-test and one-way analysis of variance were applied for normally distributed parameters, and the Mann-Whitney U test and Kruskal-Wallis tests for non-normally distributed parameters. The chi-square test was used for categorical variables. P values <0.05 were regarded as statistically significant.

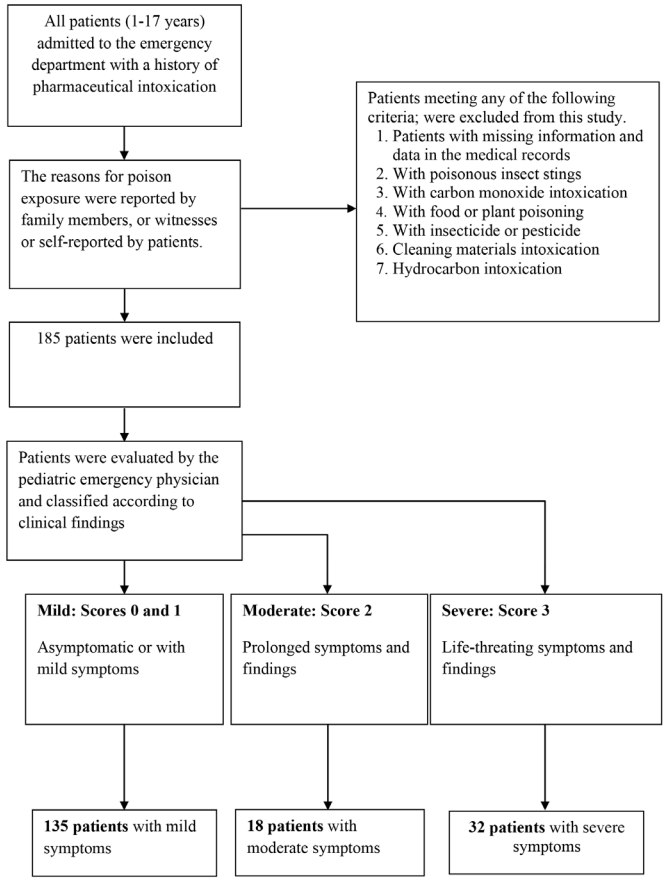

Figure 1. A flow chart for patient selection and the clinical severity subgroups

RESULTS

Patient Characteristics

One hundred eighty five children with pharmaceutical intoxication (135 mild, 18 moderate, and 32 severe case) were included in the study (Figure 1).

The patients' demographic characteristics and clinical presentations are shown in Table 1 and Figure 2.

Intoxication was the result of suicidal behaviour in 61.1% of patients and it was accidental in 38.9%.

The mean age of the patients with suicidal behaviour was 15.0 (11.0-17.0) years and 89.4% were girls, while the mean age in the accidental intoxication group was 3.0 (1.0-7.0) years and 68.1% were boys.

One hundred nine patients (58.9%) were intoxicated by a single drug, 37 (20%) by two, and 39 (21.1%) by multiple drugs. Gastric lavage was performed on 13 (%7) patients, activated charcoal was administrated to 21 (11.4%), while 105 (56.8%) received both gastric lavage and activated charcoal. Seventy-three percent of patients were asymptomatic at the time of presentation, while nausea and vomiting (8.1%) were the most common presenting symptoms.

The patients' demographic characteristics by severity subgroups are shown in Table 2.

The majority of patients (73%) had mild intoxication. There were no significant gender differences between the patient subgroups (p=0.981). The median age of the mild intoxication group was significantly lower than the moderate group (p=0.029). All patients in the severe intoxication group and 33.3% of the moderate severity group were admitted to the pediatric intensive care unit (p<0.001). Length of hospital stay was significantly longer in the severe intoxication group (p<0.001). Respiratory support in the form of mechanical ventilation was required in one patient.

A comparison of patients' demographic characteristics between the two causes (accidental or for purpose of suicide) is presented in Table 3 and Figure 2.

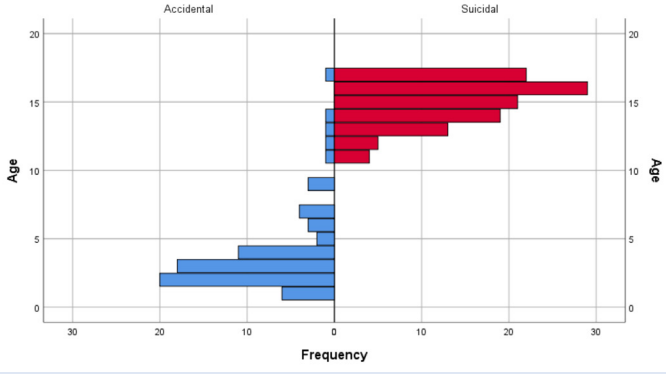

Figure 2. Patients' age distribution between the two causes (accidental or for purposes of suicide)

Table 1. Patient characteristics and clinical presentations

Parameter	Patient group (n=185)	Percentage (%)
Gender		
Male	61	33.0
Female	124	67.0
Reason for poison		
Accidental	72	38.9
Suicidal behaviour	113	61.1
Number of agents		
One	109	58.9
Two	37	20.0
More than two	39	21.1
Procedure administered		
Observation	46	24.9
Gastric lavage	13	7.0
Activated charcoal	21	11.4
Gastric lavage+activated charcoal	105	56.8
Place of hospitalization		
Emergency care	49	26.5
Pediatric ward	98	53.0
Intensive care	38	20.5
Clinical features		
Asymptomatic	135	73.0
Nausea-vomiting	15	8.1
Somnolence	6	3.2
Hypotension	6	3.2
Tachycardia	4	2.2
Double vision	4	2.2
Seizure	3	1.6
Toxic hepatitis	2	1.1
Abdominal pain	1	0.5
Pancreatitis	1	0.5
Hypokalemia	1	0.5
Bradycardia	1	0.5
Headache	1	0.5
Hypertension	1	0.5
Dysmetria	1	0.5
Dystonia	1	0.5
Hypokalemia	1	0.5
Exitus	1	0.5

Table 2. Demographic characteristics by severity subgroups

Parameter	Mild		Moderate		Severe		p-value
	n	%	n	%	n	%	
Gender							
Male	4	2.6	6	3.3	1	4.4	0.981
Female	1	7.4	2	6.7	1	65.6	
Age (years)*	13.0 (1.0-17.0)		15.0 (3.0-17.0)		14.0 (1.0-17.0)		**0.029**[a]
Place of hospitalization							
Emergency care	9	6.3	0	0	0	0	**<0.001**[b]
Pediatric ward	6	3.7	2	6.7	0	0	
Intensive care	0	0	6	3.3	2	100	
Number of agents							
One	5	3.0	8	4.4	6	50.0	0.058
Two	8	0.7	2	1.1	7	21.9	
More than two	2	6.3	8	4.4	9	28.1	
Length of hospitalization (days)*	2.0 (1.0-5.0)		3.0 (1.0-6.0)		4.0 (1.0-14.0)		**<0.001**[c]

*Median (minimum-maximum). Chi-square test was used for comparison of categorical data, Kruskal Wallis test was used for comparison of numerical data (Dunn's test was used for pairwise analysis).

[a]Mild vs moderate, p<0.05.

[b]Mild vs moderate, mild vs severe, moderate vs severe, p<0.05.

[c]Mild vs moderate, mild vs severe, p<0.05

Table 3. A comparison of demographic characteristics between the accidental and suicidal behaviour groups

Parameter	Suicidal behaviour		Accidental		p-value
	n	%	n	%	
Gender					
Male	12	10.6	49	68.1	**<0.001**
Female	101	89.4	23	31.9	
Age (years)	15.0 (11.0-17.0)		3.0 (1.0-7.0)		**<0.001**
Place of hospitalization					
Emergency care	28	24.8	21	29.2	**0.014**
Pediatric ward	54	47.8	44	61.1	
Intensive care	31	27.4	7	9.7	
Number of agents					
One	51	45.1	58	80.6	**<0.001**
Two	26	23.0	11	15.3	
More than two	36	31.9	3	4.2	
Length of hospitalization (days)	3.0 (1.0-14.0)		2.0 (1.0-9.0)		**0.016**
Severity					
Mild	75	66.4	60	83.3	**0.037**
Moderate	13	11.5	5	6.9	
Severe	25	22.1	7	9.7	

*Median (minimum-maximum)

Chi-square test was used for comparison of categorical data, Mann Whitney U test was used for comparison of numerical data

Table 4. Pharmaceuticals causing poisoning in children			
Pharmaceuticals	**Patient group (n = 185)**	**Suicidal (n=113)**	**Accidental (n=72)**
Analgesic-antipyretic			
Paracetamol	49 (26.5)	30 (26.5)	19 (26.4)
Proven derivative	27 (14.6)	18 (15.9)	9 (12.5)
Phenylacetic acid derivative	11 (5.9)	2 (1.7)	9 (12.5)
Metamizole	3 (1.6)	3 (2.6)	0 (0.0)
Acetyl salicylic acid	2 (0.5)	1 (0.8)	1 (1.3)
Neurological system agents			
SSRI	21 (11.3)	18 (15.9)	3 (4.1)
CNS stimulant	21 (11.3)	17 (15)	4 (5.5)
Antipsychotic	18 (9.7)	11 (9.7)	7 (9.7)
SNRI	12 (6.5)	8 (7)	4 (5.5)
Antiepileptic	6 (3.2)	5 (4.4)	1 (1.3)
Tricyclic antidepressant	5 (2.7)	4 (3.5)	1 (1.3)
Anxiolytic	2 (1.1)	1 (0.8)	1 (1.3)
Anti-Parkinson	2 (1.1)	1 (0.8)	1 (1.3)
Cardiovascular system drugs			
Beta-blocker	7 (3.8)	6 (5.3)	2 (2.7)
Calcium channel blocker	5 (2.7)	3 (2.6)	1 (1.3)
Other drugs			
Antihistaminic	19 (10.2)	17 (15)	2 (2.7)
Antibyotic	17 (9.2)	16 (14.1)	1 (1.3)
Antispasmodic	15 (8.1)	12 (10.6)	3 (4.1)
Hormone and vitamin	8 (4.3)	6 (5.3)	2 (2.7)
Proton pump inhibitor	8 (4.3)	7 (6.1)	1 (1.3)
Antidiabetic	6 (3.2)	5 (4.4)	1 (1.3)
Iron	6 (3.2)	5 (4.4)	1 (1.3)
Colchicine	5 (2.7)	4 (3.5)	1 (1.3)
Antiemetic	3 (1.6)	2 (1.7)	1 (1.3)

The male gender was predominantly associated with accidental poisoning, while the female gender was more associated with suicidal behaviour ($p<0.001$). The median ages of the two groups also differed significantly ($p<0.001$). Children treated for suicidal poisoning were significantly older than those treated due to accidental poisoning [15.0 (11.0-17.0) vs. 3.0 (1.0-7.0) years, respectively].

Clinical severity and the rate of intoxication resulting from multiple drug ingestion were significantly higher in the suicide group than in the accidental group ($p=0.037$, and $p<0.001$, respectively). Length of hospital stay was longer among the children in the suicidal group [3.0 (1.0-14.0) days] compared to those in the accidental intoxication group [2.0 (1.0-9.0) days].

Psychiatric consultation was requested for all the patients intoxicated as a result of suicidal behaviour.

The drugs responsible for intoxication are shown in Table 4.

The drug most frequently responsible for intoxication was paracetamol (26.5%) as an analgesic-antipyretic medication. This was followed by the central nervous system (CNS) drug group, selective serotonin reuptake inhibitors (11.3%), CNS stimulants (11.3%), and antipsychotics (9.7%).

The comparison of drugs causing intoxication between children with suicidal behaviour and those with accidental intoxication is shown in Table 4. Paracetamol was the most common causative agent in both groups.

Age distribution of accidental intoxications is shown in Table 5.

A comparison of patients' age distribution and demographic features revealed that accidental poisoning mostly occured in the age group of 3-6 years (47%). Males were more prone to accidental poisoning than females in our study with a male to female ratio of 2:1. Accidental intoxications were mostly caused by a single agent in all age groups (80%).

Table 5. Demographic characteristics of accidental intoxications by age distribution							
Parameter	**0-2 years**		**3-6 years**		**>6 years**		**p-value**
	n	**%**	**n**	**%**	**n**	**%**	
Gender							
Male	18	69.2	22	64.7	9	75.0	0.795
Female	8	30.8	12	35.3	3	25.0	
Place of hospitalization							
Emergency care	6	23.1	14	41.2	3	25.0	0.142
Pediatric ward	18	69.2	20	58.8	7	58.3	
Intensive care	2	7.7	0	0.0	2	16.7	
Number of agents							
One	22	84.6	27	79.4	9	75.0	0.791
Two	3	11.5	5	14.7	3	25.0	
More than two	1	3.9	2	5.9	0	0.0	
Length of hospitalization (days)*	2.0 (1.0-9.0)		2.0 (1.0-4.0)		2.5 (1.0-4.0)		0.324
Severity							
Mild	23	88.5	30	88.2	7	58.3	0.052
Moderate	0	0.0	3	8.8	2	16.7	
Severe	3	11.5	1	2.9	3	25.0	

*Median (minimum-maximum)

Chi-square test was used for comparison of categorical data (exact statistics was used if needed, Kruskal -Wallis test was used for comparison of numerical data (Dunn´s test was used for pairwise analysis)

DISCUSSION

Due to the high rates of morbidity and mortality in pharmaceutical intoxications when interventions are delayed, early diagnosis and treatment are of very great importance.[5]

The reasons for intoxication may vary, depending on factors such as age and sex. Accidental intoxications are more common among boys at the ages of 1-5 years.[6]

Eighty-one per cent of all intoxications below the age of eight years were accidental in a two-year prospective study.[7] Singh et al.[8] described one-third of all poisonings as unintentional. In the present study, in agreement with the previous literature, accidental intoxication was more frequent in boys during the first seven years of life.

The effect of factors of growth and development on accidental intoxication becomes particularly significant during the toddler and preschool periods.[9] As young children grow up and start to become independent, they are drawn to investigate new and fascinating objects and places. Young children may experience accidental intoxications since their ability to protect themselves and self-regulate are less developed than other ages. Drugs must therefore be kept out of the reach of children, who must also be closely supervised by their parents.

Case of suicide is reported to be more frequent in girls, particularly those aged over 10.[10,11]

Adolescent girls are thought to be more susceptible to suicidal behaviour since they are more emotional and experience greater mental conflicts than boys.

The reasons for intoxication may also play an important role in patient outcomes. In the present study, the effective agent was ingested accidentally by 38.9% of the patients, and for suicidal purposes by 61.1%.

Children with suicidal intoxication had significantly longer hospital stays than those with accidental intoxication, and the majority of children admitted to the pediatric intensive care unit were from the suicidal group. It is therefore of particular importance to understand the differences between intentional and accidental intoxication. Identifying the reason for intoxication may therefore be of assistance to physicians in performing appropriate assessments.

Intoxication for purposes of suicide is more common among girls (89.4%), while intoxication due to accidental ingestion of an agent occurs more frequently among boys.

However, in the present study intoxication was more common in girls than in boys, which might be attributable to the predominance of girls among the cases of suicidal poisoning.

The majority of children exposed to toxic agents were shown to expose to only a single substance.[12] Karcıoğlu et al.[13] reported that 53.6% of pharmaceutical intoxications involved a single drug, while Kaygusuz et al.[14] reported that 52.5% of intoxications involved multiple drugs.

In the present study, 58.9% of intoxications involved single drug, 20% involved two, and 21.1% involved multiple pharmaceutical agents. The rate of multiple drug intoxication was higher in the suicidal group than in the accidental group. In addition, and consistent with the previous literature, clinical severity and rate of admission to the pediatric intensive care unit were both higher in the suicidal group, and length of hospital stay was longer (p=0.037, p=0.014 and p=0.016, respectively).[15,16]

Many patients exposed to intoxication (48.3-70%) are clinically asymptomatic.[17-19]

Ağın et al.[20] reported that 41% of patients were asymptomatic at the time of presentation, while nausea-vomiting was observed in 18%. Yorulmaz et al.[21] reported that approximately one-third of patients were asymptomatic, the most common presentation symptoms also being nausea-vomiting. Binay et al.[22] also described vomiting as the most common finding.

In the present study, asymptomatic patients accounted for 73.0% of patients, and the most common symptoms were also nausea-vomiting (8.1%). This might suggest that the effect of the toxic substance concerned was low, or that full exposure did not occur.

Pediatric intoxication may involve a broad course spectrum, from mild course to mortality. This may depend on the patient's age, sex, the type and dosage of pharmaceutical agent, the form of exposure, and individual patient characteristics.[23,24]

Clinical severity, length of hospital stay, and rate of admission to pediatric intensive care unit were all higher in the suicide group than in the accidental intoxication group (p=0.037, p=0.016, and p=0.014 respectively). The rate of multiple drug intoxication was also higher than in the accidental group. This finding may indicate the importance of identifying the type of drug ingested, and measuring the drug levels should be seriously considered for early diagnosis

Analgesics and drugs affecting the CNS, such as antidepressants, are the most frequently implicated agents in pediatric poisoning cases.[19,25,26] Moon et al.[27] reported that cardiovascular drugs were more frequently involved in accidental poisonings, while acetaminophen and psychotropic drugs were more frequently involved in suicide attempts. Analgesics are reported to be responsible for 23.7-40% of all drug-related intoxications with paracetamol being involved in 30-45% of such cases.[17,25,28]

Analgesics, followed by neurological system agents, were most frequently associated with pediatric pharmaceutical intoxication in both study groups in the present study.

The incidence of paracetamol-related intoxications among analgesics was higher in both groups. We think that this may be due to analgesics and antipyretics, most of which are packaged in bottles with child safety caps, being available over the counter in Turkey, with no prescription required, making them potentially accessible in the home.

The next most common agents in pediatric intoxications in both groups in this study were drugs affecting the CNS. The most common of these were antidepressants. We attribute this to the increasing use of antipsychotics and antidepressants in recent years creating a tendency for these drugs also to be used for a suicidal purpose.

Intoxication mortality rates range between 0.4% and 7.6%.[1] Unintentional poisoning in children is rarely fatal and is preventable in most of the patients.[29]

Mortality occurred in only one female patient due to calcium channel blocker intoxication as a result of suicide attempt. Our low mortality rate may be attributed to a higher level of parental awareness in terms of the importance of early intervention and treatment in cases of intoxication.

Study Limitations

There are several limitations of this study. In particular, due to its retrospective nature, information concerning the time elapsing before presentation to hospital, whether patients had previously presented to another health institution and, if so, the treatment administered there could not be investigated. Other limitations of this study were limited data and relatively limited number of patients.

CONCLUSION

This study investigated detailed categories of pharmaceutical pediatric intoxications. Analgesics and neurological system agents were found to be involved in the majority of patients. Intoxications due to purpose of suicide resulted in longer hospital stay, and higher clinical severity than accidental intoxication.

Parents should be educated to store these agents appropriately to avoid accidents involving young children. Greater attention is also required to ensure that pharmaceuticals are not made easily available to adolescent children to prevent them from being used in suicide attempts.

Ethics

Ethics Committee Approval: Approval for the study was granted by the Aydın Adnan Menderes University Local Ethics Committee (decision no: 04-2022/17, date: 27.01.2022).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.O., Design: S.Ö., Data Collection or Processing: E.O., Analysis or Interpretation: S.Ö., A.Ç., Literature Search: E.O., Writing: E.O., S.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

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