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Brief Communication and Method
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Use of Zeolive (Composition with Zeolites Base) as an Adjunct in the Treatment of Acetaminophen Overdose

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Abstract:

One of the most important of zeolite's applications is the detoxification of toxic substances. This study was planned to evaluate the effect of Zeolive on acetaminophen toxicity. This was a single-blind clinical trial study. The participating population was patients with acetaminophen poisoning in Loghman Hakim Hospital from December 2021 to March 2022. Patients were randomly divided into two groups of 30 patients. The control group was given routine treatments and the intervention group was given 1000 mg of Zeolive per day for 2 weeks in addition to routine treatments. Levels of AST, ALT, ALP and PT were measured before and after the intervention. Data were analyzed by SPSS software.

The mean age was 28.3 ±7.6 in the intervention group and 25.9 ±6.8 years in the control group. The observed decrease in PT and activities of AST, ALT, and ALP after the intervention was not statistically significant with the control group. Statistical analysis of the difference values before and after the intervention for liver enzymes and PT showed no significant difference between the two groups

Zeolive, as an absorbent powder, may not affect the amount of enzymes and blood factors. Further studies and consideration of other factors are recommended.

Keywords: Acetaminophen; clinical trials; liver enzymes; poisoning; Zeolive; zeolites

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1. Brief Introduction

Acetaminophen (APAP, Paracetamol) is one of the most widely used analgesic and antipyretic medicines. Overdose of this medicine can lead to hepatotoxicity and acute liver failure (ALF). In fact, acetaminophen-induced hepatotoxicity is the most common cause of acute liver failure in many countries [1,2]. Serum acetaminophen concentrations should be measured to assess the need for N-acetylcysteine (NAC) in all patients presenting with acetaminophen poisoning. [3].

Zeolites are an active and highly porous biomaterial that in recent years has done a lot of research on its various applications in various sciences [4]. Zeolites are edible, antibacterial, biocompatible and non-toxic with high adsorption properties. The selection of zeolite can be a good choice for drug delivery systems, wound healing, scaffolding in tissue engineering, implant coatings, hemodialysis, gas absorption and removal of toxic ions [4-9]. Zeolites can quite effectively absorb heavy metals such as lead, aluminum, arsenic, cadmium and ammonia, toxic products such as phenols, pesticides and mycotoxins [10]. Also, zeolites can prevent neurotoxicity due to chemotherapy drugs or other various symptoms due to increased oxidative stress [10].

The active ingredient in Zeolive tablets is zeolite. Zeolive tablets act as adsorbent powders. Also, acetaminophen is a drug that increases oxidative stress

and causes toxicity [11,12]. Therefore, this study goal was to evaluate the effect of Zeolive in toxicity due to acetaminophen poisoning.

2. Brief Methodology

This study was a single-blind clinical trial on patients with acetaminophen poisoning in Loghman Hakim Hospital from December 2021 to March 2022.
Sampling method was convenience sampling. Inclusion criteria include: 1) consumption of more than 7.5 grams of acetaminophen, 2) consumption of acetaminophen with an unknown amount and 3) high liver enzymes and toxic level of acetaminophen according to Rumack-Matthew nomogram. Patients with a history of liver disease and sensitivity to zeolite compounds were excluded from the study .
Zeolite-based Zeolive drug was prepared in the form of oral tablets in the Department of Pharmaceutical Chemistry of the Faculty of Pharmacy of Shahid Beheshti University of Medical Sciences.
Sixty patients with acetaminophen poisoning were selected and randomly divided into intervention and control (30 patients for each group). For the patients in the control group, standard treatments were performed and for the intervention group, in addition to the standard treatments, received zeolite 1000 mg by mouth daily for two weeks. In both groups, liver enzymes Aspartate Aminotransferase (AST), alanine transaminase (ALT) and Alkaline phosphatase (ALP) and prothrombin time (PT) were measured at the beginning of treatment and after two weeks.
Data from the study were entered into SPSS software version 26. First, the normal distribution in the statistical population was determined by the Kolmogorov-Smirnov test and in the next step; central and descriptive indices were calculated and expressed.
Depending on the distribution of samples in the statistical population, parametric tests such as paired and independent t-test and non-parametric test Chi-square were used. The significance level was considered P <0.05 for all tests.

3. Results and Discussion

Twelve (12) men and 48 women participated in this clinical trial. The mean age was 28.3 ±7.6 in the intervention group and 25.9 ±6.8 years in the control group. Examination of ALT, AST, ALP and PT levels before the intervention showed that there was no significant difference between the two groups (Table 1). There was no significant difference between the two groups in acetaminophen serum concentration.
No significant difference was observed between the two groups in terms of liver enzyme activity and PT after two weeks of treatment (Table 1). Statistical analysis of the difference values before and after the intervention for liver enzymes and PT showed no significant difference between the two groups (table 1).

Table 1. Measured variables in the intervention and control groups.

	Control group	Zeolive group	P-value
Female	26 (86.67%)	22 (73.33%)	0.197
Male	4 (13.33%)	8 (26.67%)	
Age	25.87 ± 6.8	28.3 ± 7.62	0.357
AST before intervention (U/L)	25.47 ± 8.53	29.73 ± 8.14	0.618
AST after intervention (U/L)	19.2 ± 3.76	21.47 ± 3.45	0.318
ALT before intervention (U/L)	21.9 ± 9.57	21.7 ± 10.39	0.525
ALT after intervention (U/L)	16.53 ± 4.66	18.83 ± 7.46	0.136
ALP before intervention (U/L)	167.43 ± 80.31	169.93 ± 55.63	0.762
ALP after intervention (U/L)	124.77 ± 26.54	137.37 ± 29	0.698
PT before intervention	12.65 ± 1.07	13.01 ± 0.75	0.413
PT after intervention	12.41 ± 0.60	12.5 ± 0.57	0.935
APAP levels before intervention (mg/l)	25.9 ± 18.8	37.9 ± 19.7	0.940
Minus AST1-AST2	6.3± 7.9	8.3± 7.4	0.695
Minus ALT1-ALT2	5.4± 7.6	2.9± 8.4	0.910
Minus ALP1-ALP2	42.7± 69.2	32.6± 48.9	0.849
Minus PT1-PT2	0.24± 0.89	0.51± 0.65	0.397

AST: Aspartate Aminotransferase, ALT: alanine transaminase, ALP: Alkaline phosphatase, PT: prothrombin time, APAP: Acetaminophen.

Zeolites are edible substances that do not enter the bloodstream. They mostly act as adsorbents of various substances and their antioxidant effects are unknown due to their absence in the blood [10].

Most studies have been done on aqueous solutions. The results of Li et al.'s study showed that synthetic clinoptilolite could remove Zn2+, Pb2+, Cd2+, and Cu2+ ions from aqueous solutions [13]. A study by Mohamed Khalid et al. showed that purely siliceous BEA zeolite selectively adsorbed phenol from water [14]. Examining the effect of zeolites to remove ammonia and its toxicity, the results showed that zeolite column chromatography well reduces the concentration of ammonia and subsequently its toxicity in marine water [15].

The study on the ability of clinoptilolite to reduce ethanol in vivo by Federico showed that clinoptilolite, a type of zeolite, can reduce ethanol uptake and lower blood alcohol levels in chronic alcohol users [16].

4. Conclusion

Our study showed that no significant difference was observed between Zeolive group and control group. These observations may be because Zeolive is not absorbed into the blood and may not be able to alter enzyme expression.

The limitation of this study was not measuring the level of acetaminophen after the intervention in the groups.

Conflict of interest

The authors declare that they have no competing interests.

Sources of support and fundings declaration

Toxicological Research Center, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences.

Ethics

Informed consent was obtained from the patients or their companions before the study. Also, this study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1400.650). The code of Iranian Registry of Clinical Trials center is IRCT20211213053375N1.

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