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ORIGINAL PAPER

EVALUATION OF ZINC AND COPPER TOXICITY CAUSED BY INGESTION OF TURKISH COINS: AN *IN VITRO* STUDY

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Abstract

Coins are foreign objects that are commonly ingested by children and pets due to their shiny appearance and bright colors. The current study investigated whether Turkish coins can lead to zinc (Zn) and copper (Cu) toxicity as a result of exposure to simulated gastric juice (i.e. hydrochloric acid solution simulating the gastric environment). Five groups of coins were exposed to simulated gastric juice (0.15 N, pH:1-2) for a period of 4 (Group 1), 12 (Group 2), 24 (Group 3), 48 (Group 4), 72 (Group 5) and 120 h (Group 5) at body temp. (37°C). Zinc and copper levels were determined in the gastric acid solution by using an inductively coupled plasma optical emission spectrophotometer (ICP-OES). The coins were also evaluated for corrosive damage and weight loss. Group 5 had statistically higher Cu and Zn levels versus the other groups. However, at body temp. (37°C), copper and zinc levels increased steadily in parallel to the duration for which the coin remained in the stomach after ingestion. After 120-hour exposure at 37°C, all coins had various types of damage compared to the baseline, such as color alteration, erosion, and visible surface cavities. The mechanisms relating to local and systemic copper and zinc toxicity caused by coin ingestion is yet to be clarified for both Turkish and international coins. Therefore, it can be foreseen that intervention is required in the first 24 h after ingesting 5 kuruş coins and, unless removed spontaneously in 48 h, such intervention is needed for the other coins.

Keywords: Turkish coins, children, zinc, copper, toxicity.

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INTRODUCTION

Ingestion of foreign bodies is one of the most common problems resulting in pediatric and veterinary emergencies. Coins are the objects most frequent swallowed by children and pets (Cheng, Tam 1995, Uyemura 2005), and they cause medical emergencies due to metal toxicity (Hassan et al. 2000, Kumar, Jazieh 2001). It has been demonstrated that coins reaching the stomach and intestines of children generally pass smoothly through the remainder of the gastrointestinal tract. Many ingested coins, however, can become lodged in the esophagus and duodenum (Cheng, Tam 1995, Bothwell et al. 2003, Bothwell et al. 2004, Conners 2005). There is general agreement that foreign bodies lodged in the esophagus should be removed without delay. Esophageal coins in children pass to the stomach spontaneously in some cases, thereby eliminating the need for invasive procedures to remove the coins (Cheng, Tam 1995, Hoff et al. 1998, Soprano et al. 1999, Hambidge 2000). In the current literature, swallowed coins are generally considered as harmless as long as they stay in stomach no longer than 4 weeks (Blaho et al. 1999, Seo 1999). Due to the fact that coins contain various elements, the possibility and the risk of gastrointestinal system damage and toxicity caused by elements dissolved from coins should not be underestimated. Dissolution of several metals from different European and US coins in gastric acid simulating solutions has been studied (O'hara et al. 1999, Puig et al. 2004, Rebhandl et al. 2007). To the best of our knowledge, Turkish coins have not been investigated so far.

The new Turkish coins minted in 2009 (still in use) contain more zinc and copper than nickel alloys, and come in different weight, diameter and thickness (Mint and Printing General Manager 2014). It is likely that these variables may have the effect of increasing the likelihood of chemical reactions. Dissolution of these elements may reach toxic levels in the gastric tract with time. Thus, this *in vitro* study was conducted to evaluate the levels of zinc and copper released from Turkish coins at 4, 12, 24, 48, 72 and 120 h when exposed to simulated gastric acid at 37°C.

MATERIAL AND METHODS

Five groups of Turkish coins (5, 10, 25, 50 kuruş and 1 lira; n=7 each) minted in 2009 were selected for the study, and their original weights were 3.15, 4.00, 6.80 and 8.20 g, respectively (Mint and Printing … 2014). All coins were rinsed in distilled water, dried and weighed (Radwag Balances and Scales), then their photographs were taken before and after the experimental procedure.

Each group of coins was immersed in a 100 ml beaker containing 50 ml of 0.15 N HCl (pH 1-2; representing postprandial concentration of gastric acid) (FOSMIRE 1990) and samples were slowly and continuously incubated in a water bath (Nuve) at body temperature (37°C), under a foam hood for 4, 12, 24, 48, 72 and 120 hours. During the study, sample solutions in each beaker were kept air-tight using plastic wrap coverings. The coins were removed from the acid, dried, weighed, and the solutions were renewed after sample collection at each time point. The weight loss of all coins was determined at the end of the study, and surface deformations were photographed (Figure 1 and 2).

The analyses of the copper and zinc levels in HCl dissolved from the coins were carried out using an inductively coupled plasma-optical emission spectrophotometer (ICP-OES Thermo iCAP 6000 series) at the Trace Element Analysis Laboratory of the Biophysics Department of Cerrahpasa Medical Faculty in Istanbul, Turkey. The ICP-OES was operated with suitable wavelengths for Cu and Zn (327.396 nm, 206.200 nm, respectively).

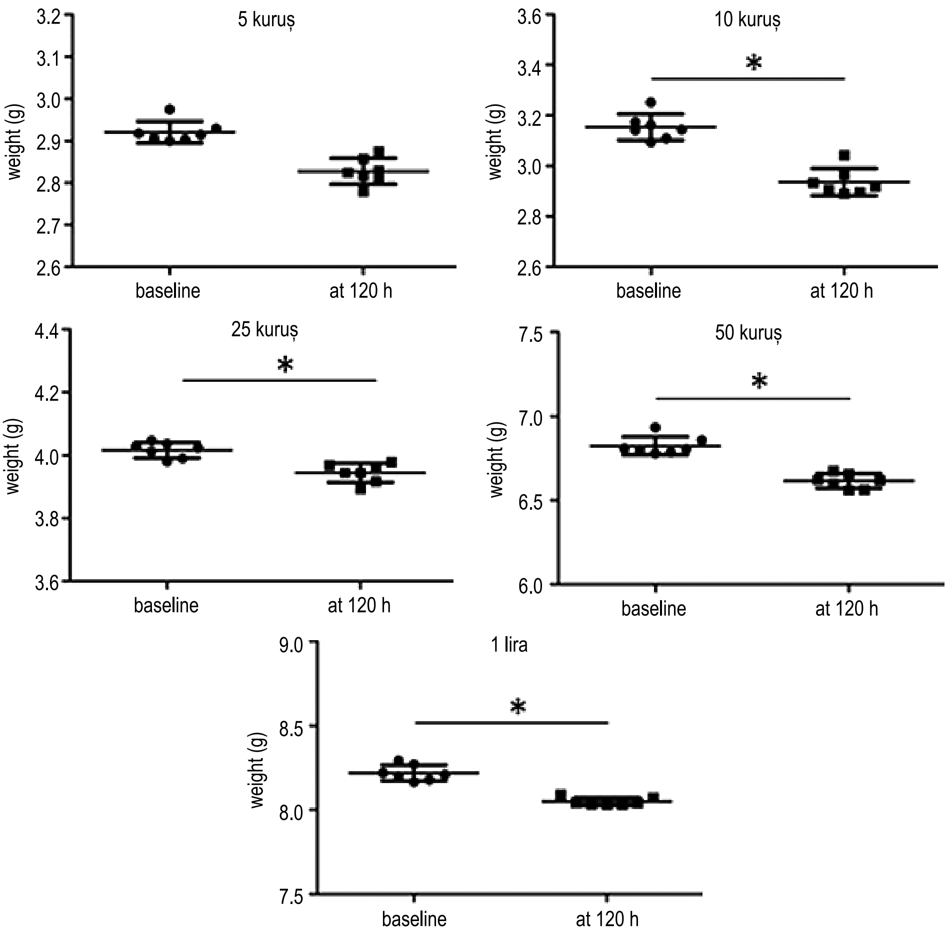

Fig. 1. Weight loss of Turkish coins before and after 120 h exposure in simulated gastric juice

Fig. 2. Progressive corrosion of Turkish coins after120 h in simulated gastric juice

The plasma operating settings for the ICP-OES system in this study were 5 l min^{-1} plasma gas flow rate, 0.5 argon carrier flow rate, 1.5 1 min^{-1} sample flow rate, and elution flow rate. The speed of the peristaltic pump was 100 rpm. Transport lines were made using a 1.25-mm-i.d. polytetrafluoroethylene tubing. Each measurement was performed four times and averages were used for the analysis. Results were expressed in microgram per milliliter (µg ml^{-1}) of samples. Single element solutions (Redoks Laboratory Analytical Systems, Istanbul/Turkey) were used to prepare calibration and standard solutions. Test standards for the ICP-OES analysis were prepared from proper stock solutions containing 1000 µg ml^{-1} for each tested element obtained from Chem - Lab NV (Belgium). All reagents were of analytical reagent grade, and deionized water was used as a blank solution. The blank was analyzed to check for any contribution from the reagents and laboratory environment. Stock solutions of Cu and Zn were prepared by taking appropriate amounts of standards in deionized water. Standard solutions were prepared just before use. The calibration graph was obtained from the ICP-OES device using blank and standard solutions, and the element level analyses of the prepared coins were carried out. Deionized water was used for the blanks throughout (Ates Alkan et al. 2019).

Values were reported as the means ± standard deviation (SD). The data were statistically analyzed using the SPSS 17.0 statistical software package. For parametrically distributed data, comparisons were made for intergroup data by using the ANOVA test. For non-parametrically distributed data, the Kruskal-Wallis test was used wherever appropriate. p value < 0.05 was considered as statistically significant.

RESULTS AND DISCUSSION

The results of the present study pertain to the potential toxicity of Turkish coins exposed to simulated gastric juice in order to show patterns of copper and zinc levels. There are fewer data concerning these processes in children and pets. To the best of our knowledge, this is the first study copper and zinc levels of Turkish coins investigated in simulated gastric acid at body temperature. The present *in vitro* study demonstrates that copper and zinc levels in renewed HCl solution (pH = 1 - 2). Also, at body temperature (37°C), copper and zinc levels increase steadily depending on the type and size of a coin, and the time the coin stays in the stomach after ingestion.

Coins are the foreign objects that is commonly ingested by children and pets. Due to their shiny appearance and bright colors, they are attractive to children between the ages of 10-12 months, who have a tendency to put objects into their mouth for discovery. Pediatric coin ingestion is too common in young children, with an incidence of up to 5%, and a mean age of occurrence just below 3 years old (O'Hara et al. 1999, Bothwell et al. 2003,). Coins of 5 and 10 kuruş are made of 65% copper, 6% nickel, 29% zinc; coins of 25 kuruş are made of 60% copper, 14% nickel, 26% zinc; 50 kuruş coins are made of 75% copper, 15% nickel, 10% zinc; and coins of 1 lira are made of %81 Cu -%4 Ni -%15 Zn (Mint and Printing ... 2014). Zinc is highly reactive with gastric acid, and can potentially cause local corrosion and systemic toxicity (Bothwell et al. 2003).

Five groups of Turkish coins (5, 10, 25, 50 kuruş and 1 lira; n=7 each) were incubated in 0.15 N HCl (37°C) and samples were collected at 4, 12, 24, 48, 72 and 120 hours. During the experiment, the appearance of coins changed immediately because of the chemical reactions occurring when simulated gastric acid induced bubble formation. On their surface, color alteration, erosion, and surface cavities were visible but holes were not seen (Figure 1). The activity of hydrogen ions (pH) of the samples was determined at 37°C using a standard pH electrode (Hanna Instruments pH211 Microprocessor) that was calibrated with three calibration solutions (pH; 4.01, 7.01, 9.18, respectively) before each determination. During the experiment in all groups, pH values remained between the normal gastric pH limits and varied within 1.0 and 1.5 (Figure 3). There was statistically significant weight loss between 10, 25, 50 kuruş and 1 lira after 120 h after exposure ($p < 0.05$), whereas no significant difference in weight loss was detected in 5 kuruş after 120 h exposure relative to their original weight ($p > 0.05$) – Figure 2.

Trace elements such as copper, zinc, nickel and iron in coins are potentially toxic (Bothwell et al. 2003). After massive ingestion of coin, the toxic effect of zinc absorption includes gastroenteritis, nausea, vomiting, abdominal pain, hematemesis, and ulceration of the stomach. Side effects of extreme zinc ingestion include anemia, pancreatic dysfunction, pancreatitis, hemolysis, alteration of clotting factors, increased amylase activities, copper deficiency, hepatocellular necrosis, acute tubular necrosis, renal failure, and death from multisystem organ failure (Fosmire 1999, Jones 2000, Lee et al. 2005). After absorption, zinc is excreted in the pancreatic secretions and bile, mainly by the pancreas and liver (Hambidge 2000). The primary laboratory parameters of zinc toxicity elevated white blood cell count, amylase, lipase, alka-

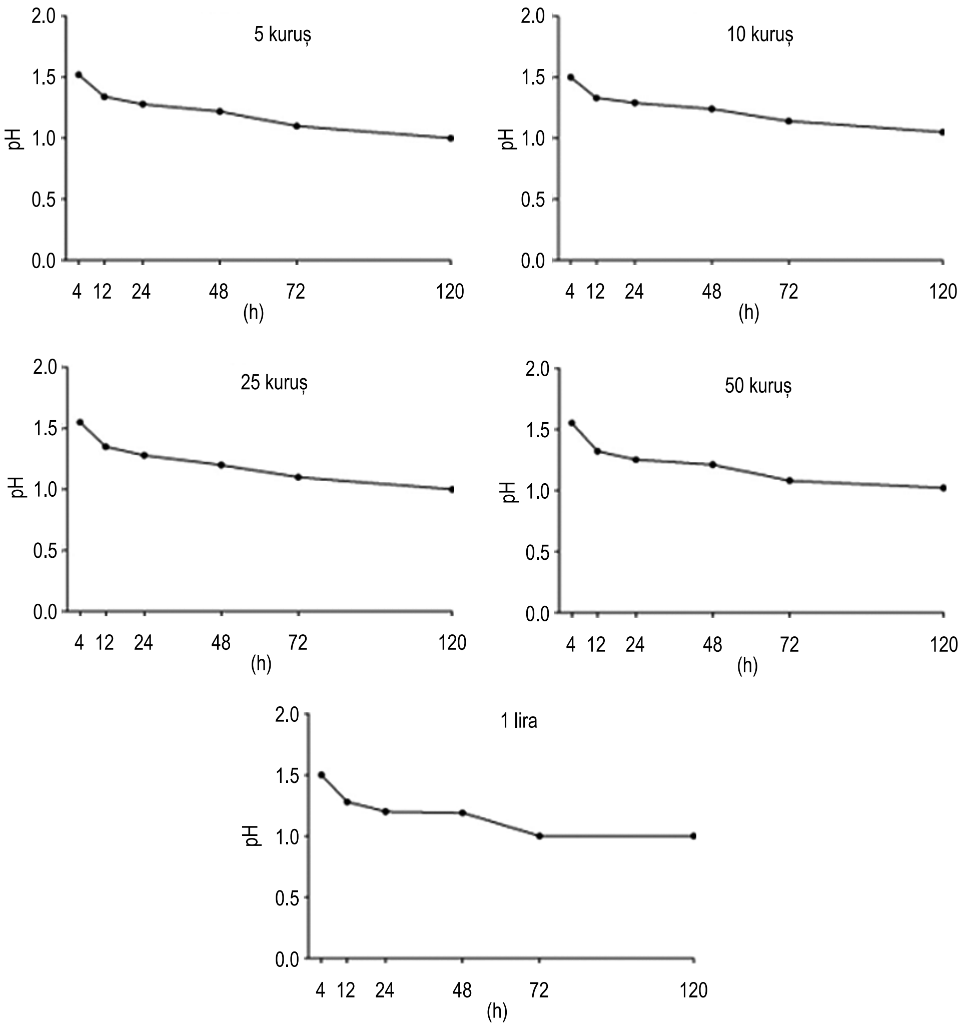

Fig. 3. pH values of simulated gastric juice with immersed Turkish coins during 120 h

line phosphatase and hematuria (BERG, SHI 1996, BOTHWELL 2004, CONNERS 2005).

Conservative treatment or close monitoring are suggested if coins have passed the esophagus (DURAN et al. 2004). Some authors recommend waiting up to several weeks if coins have passed into the stomach, or even recommend no treatment at all if coins are already in the stomach (BERG, SHI 1996, BAHARLOO et al. 1999). Such recommendations are in contrast with reports of toxicity after coin ingestion (BOTHWELL et al. 2003, GHAFOOR et al. 2003). Toxicity in humans and among animals living in zoos have been reported following massive coin ingestion (BENNET et al. 1997, GHAFOOR et al. 2003). The most frequent immediate sign is wheezing, which is often misdiagnosed as asthma. Surprisingly, coin ingestion is diagnosed through the lateral or anteroposterior radiopaque imaging on X-rays (Ghafoor et al. 2003, Puig et al. 2004). Conners (2005) pointed out that the 8-16 h time interval is critical for children. The veterinary literature is also full of reports on zinc toxicity due to multiple ingested pennies in captive animals and household pets (Latimer et al. 1989, Puig et al. 2004). Moreover, Bennet et al. (1997) reported deaths resulting from multiple organ failure.

According to our results, the levels Zn and Cu increased significantly at exposure in simulated gastric juice during 4, 12, 24, 48, 72 and 120 h (Figure 4*a*,*b*,*c*). A significant increase was determined in Cu levels of 5 kuruş coins at 4, 12, 24, 48 and 72 h (Figure 4*a*,*b*); whereas Cu levels at 120 h were significantly lower than the ones of Zn at 120 h (Figure 4*b*,*c*).

O'Hara et al. (1997) observed the case of a 2-year-old child who presented symptoms such as vomiting and abdominal pain four days after having swallowed a single zinc-based coin. This ingested coin was a US penny, which is composed of 97.6% zinc and a 2.4% copper coating. Puig et al. (2004) determined that the levels of zinc were much higher in American coins than in European ones. They also suggested that American coins lead to greater zinc toxicity than European ones. However, we determined higher copper levels than zinc levels in all Turkish coins at 37°C. There is a very interesting finding to be seen in the figures; when the Zn level increases at 4, 24, 48, 72, 120 h, so does the Cu level, except for 5 kuruş coints. This was possibly due to the higher percentage/level of copper in all coins compared to zinc.

All Turkish coins have different diameters, thicknesses and weights. Coins with larger weights may induce the inability of peristaltism throughout the gastrointestinal tract (Seo 1999). 1 lira coins have a large diameter, which leads to stronger chemical reaction. Two of five Turkish coins (50 kuruş and 1 lira coins) are larger than 2 cm in diameter. It is uncertain whether these coins should be removed immediately, since it is not expected that they will be able to pass the pylorus in infants, toddlers and pets. Seo (1999) previously suggested that foreign bodies more than 2 cm in diameter should be removed in infants and children.

Copper has cytotoxic effects *in vitro*, and is more absorbable than the other metals. A certain level of copper excess within the body will result in severe kidney and liver damage (Marquardt, Schafer 2004). In this study, we observed that Turkish coins had higher copper levels compared to zinc levels. A similar study on euros, cents and other international coins was previously performed by Rebhandl et al. (2007). However, no studies have been found in the literature regarding the copper and zinc levels in Turkish coins.

Despite the high number of *in vivo* and *in vitro* studies performed internationally on the uptake of dissolved metals, and their side effects on the human metabolism, there are few data about the mechanisms involved (Hassan et al. 2000, Byrne et al. 2002). Moreover, children and pets are at the risk of toxic effects produced by copper and zinc. However, as much as we we able

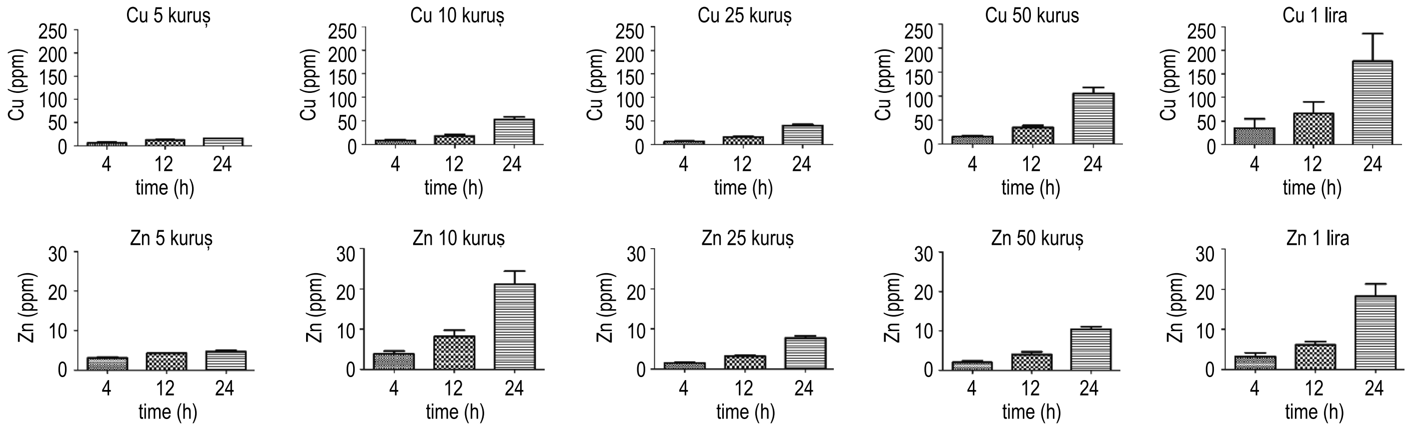

Fig. 4*a*. Copper and zinc levels from Turkish coins at 4, 12 and 24 h

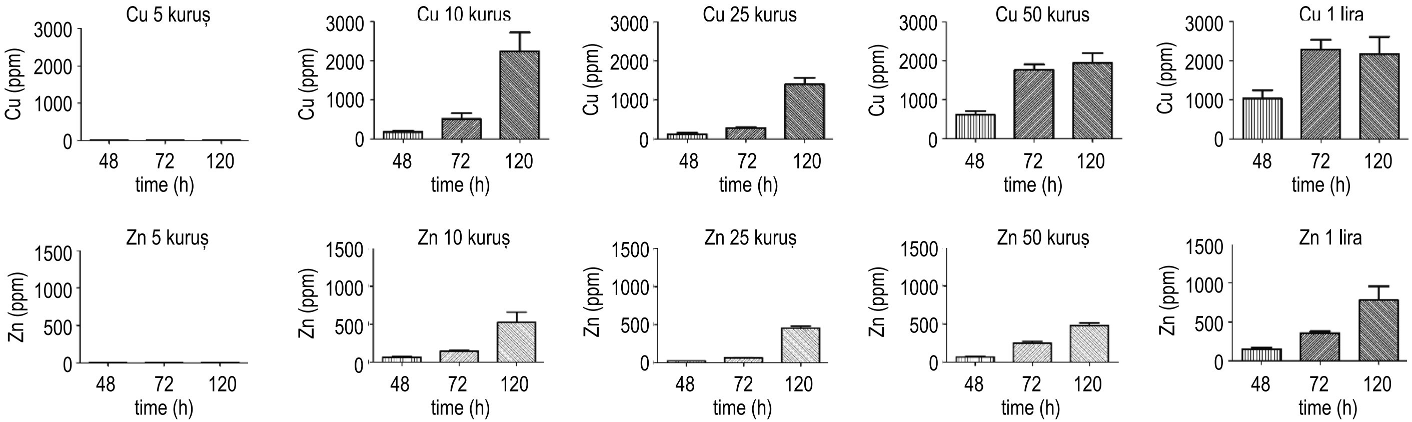

Fig. 4*b***.** Copper and zinc levels from Turkish coins at 48, 72 and 120 h

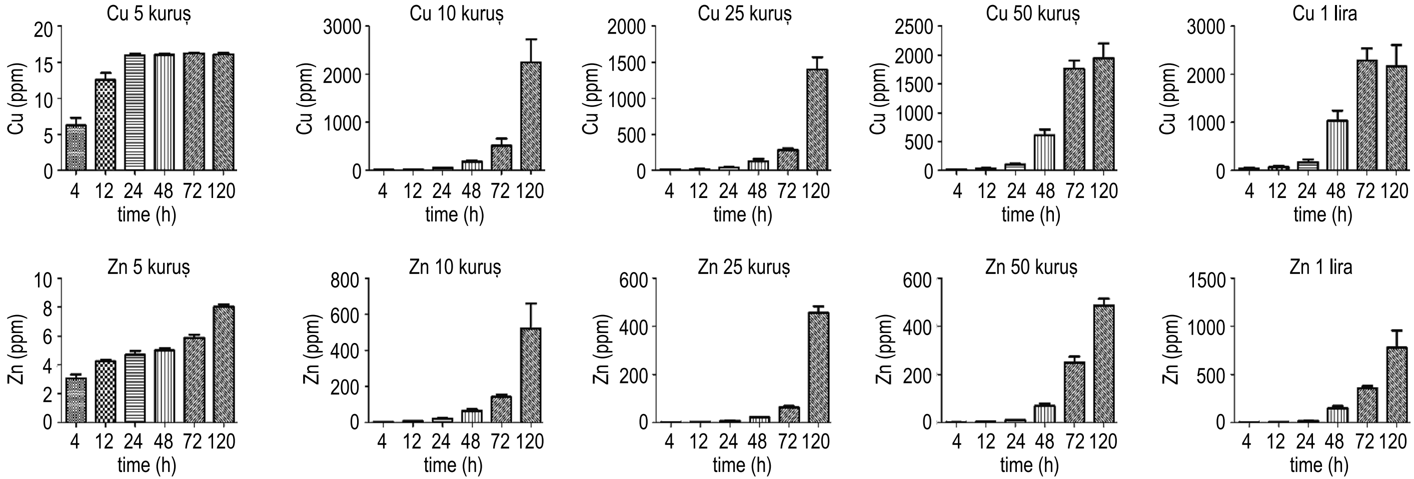

Fig. 4*c*. Copper and zinc levels from Turkish coins at 4, 12, 24, 48, 72 and 120 h

to review the literature in Turkey, we failed to encounter any studies on Turkish coins.

CONCLUSIONS

1. The ingestion of foreign bodies such as coins involves the following steps: absorption, distribution and elimination. Our results show that the amount of zinc relased from 5 kuruş coins increases over time; meanwhile the maximum copper concentration was reached after 12 hours.

2. Concerning the other coins (10, 25, 50 kuruş and 1 lira), the concentrations of copper and zinc did not change much in the first 48 h but increased to 200 µg ml^{-1} in the following hours.

3. The mechanisms relating to local and systemic copper and zinc toxicity caused by coin ingestion have yet to be clarified for both Turkish and international coins. Research on the ingestion of other coins implicates that intervention is needed in the first 24 h after ingesting a 5 Turkish kuruş coin, and after 48 h following the ingestion of the other coins unless they have been removed spontaneously.

Conflict of interest

The authors declare that they have no conflict of interest.

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