

Antidotal Effect of Succimer and CaNa₂ EDTA on Workers Exposed to Lead, Cadmium and Arsenic

Georgieva VG*, Boyadzhieva V, Kuneva T and Pavlova S

University Multiprofile Hospital for Active Treatment "St. Iv. Rilski" Sofia, Bulgaria

*Corresponding author: Georgieva VG, University Multiprofile Hospital for Active Treatment "St. Iv. Rilski" Sofia, Bulgaria, Tel: +359888988665; E-mail: viktoria_georgieva2@abv.bg

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Abstract

A comparative evaluation was made between the antidotal effect of Succimer and CaNa₂ EDTA on workers, exposed simultaneously to lead, arsenic and cadmium. The studied patients were divided into two groups: 1st group -15 individuals, treated with peroral administration of Succimer (DMSA) in a dosage of 2.1 grams per day (3 × 0.7 grams) during the first 5 days and in a dosage of 1.4 grams (2 × 0.7 grams) per day from the 6th to the 20th day; and 2nd group -20 individuals who underwent 3-day intravenous therapy, 1 gram of CaNa₂ EDTA per day. Blood concentrations of lead, cadmium, arsenic, copper and zinc were measured before and after therapy, observing their urinary excretion as well. The data obtained show that both drugs have a pronounced antidotal effect on lead. The chelating effect of Succimer on arsenic is much better than that of CaNa₂ EDTA. The therapy with Succimer does not lead to higher excretion of copper and zinc in urine, in comparison to CaNa₂ EDTA. Appropriate for workers with low-level exposure to lead is a 7-day course of treatment with Succimer in a dosage of 2.1 grams per day.

Keywords: Succimer; CaNa₂ EDTA; Arsenic and Cadmium

Introduction

The classic antidote used in lead poisoning is CaNa₂EDTA [1-7]. In patients with contraindications for its administration (thrombophlebitis, diabetes, ischemic heart disease, etc.) it is especially important to use other drugs with decorporating efficacy [8-15]. In the literature, one finds a series of studies on the effect of various antidotes, such as trisodium salt of diethylenetriaminepentaacetic acid [16-19], 2,3-dimercaptosuccinic acid (DMSA, Succimer, Chemet) [6,8,9,11,19], d-Penicillamin [1,10]. We found no data about its application as an antidote in workers, exposed simultaneously to metals. Therefore, we aimed at comparing, in a clinical environment, the curative effect of Succimer and CaNa₂ EDTA on workers, exposed to lead, cadmium and arsenic, with no visible clinical signs of intoxication.

Materials and Methods

The study covers 35 workers from a metallurgical plant, exposed to the combined effects of lead, arsenic and cadmium. The selected workers are hospitalized in the Clinic of Occupational Diseases, having no evidence of alcohol or drug abuse and no major organ damage. The studied individuals are divided into two groups:

- 1st group- 15 individuals (average age of 39 ± 8 and specialized length of service 14 ± 7.8 years) were treated with Succimer. The drug was taken orally in a dosage of 2.1 grams per day (3 × 0.7 grams) during the first 5 days and in a dosage of 1.4 grams (2 × 0.7 grams) per day from the 6th to the 20th day.
- 2nd group- 20 individuals (average age of 43.5 ± 5 and average specialized length of service 18.5 ± 6 years) passed a 3-day intravenous therapy with CaNa₂ EDTA in a dosage of 1 gram per day.

For all workers, blood and urine concentrations of lead, cadmium, arsenic, copper and zinc were studied, before and after therapy.

The heavy metals were determined using flame atomic absorption spectroscopy Analyst 400 Perkin Elmer.

The processing of the results was made by variation analysis-paired sample t-test. All statistical analyses were performed using Origin 9.0. The quantitative variables are presented as mean ± SD, and the categorical variables are presented as number (%). P-values less than 0.05 are considered statistically significant.

Results and Discussion

The average content of lead in the blood (plumbemia) of the exposed individuals before treatment is in the same range in both groups: for the 1st group - 1.03 ± 0.08 and for the 2nd group - 1.17 ± 0.1 μmol/l, thus allowing a comparative analysis to evaluate the efficacy of the two antidotes (Figure 1). On the fifth day after the start of administration of the drugs the level of lead reliably decreases (p<0.05) and is 0.71 ± 0.4 and 0.73 ± 0.09 μmol/l, respectively, i.e. in the said peroral dosage Succimer shows equal efficacy to the intravenously applied CaNa₂ EDTA. On the 20th day of the treatment with Succimer the lead content in blood reliably decreases (p<0.05) compared to the 5th day, reaching 0.38 ± 0.06 μmol/l.

The results from the daily administration of Succimer and CaNa₂ EDTA show a significant increase in lead excretion for both groups of workers. In all studied days of the treatment the plumburia is many times higher than the basal (Figure 2). It is worth noting that with both antidotes the maximum release of lead is to be observed in the first day and then the excretion gradually decreases. It should be emphasized that after the third intravenous application of CaNa₂ EDTA the lead content is still much higher than the baseline (p<0.001).

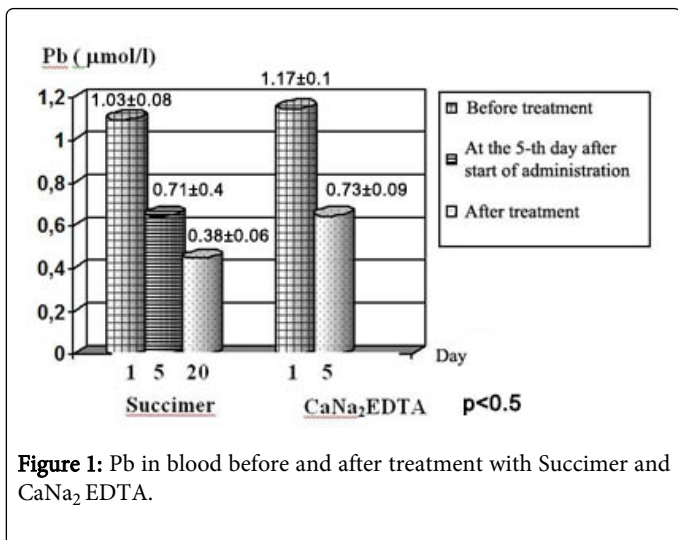


Figure 1: Pb in blood before and after treatment with Succimer and CaNa₂ EDTA.

In the Succimer treatment after the 5th day is observed a balanced release of lead. After 10 days of drug administration the concentrations of lead in urine reach the reference values, thus indicating the efficacy of the drug at longer administration, very well tolerated and with no danger for the patients. Similar are the results obtained by Restek S et al. in treatment with DMSA - acceleration of urinary lead excretion, mostly during the first five days, followed by a decline in the average plumbemia up to 15% of the levels before the treatment - and they assume that DMSA may effectively reduce chelate lead in occupationally exposed workers.

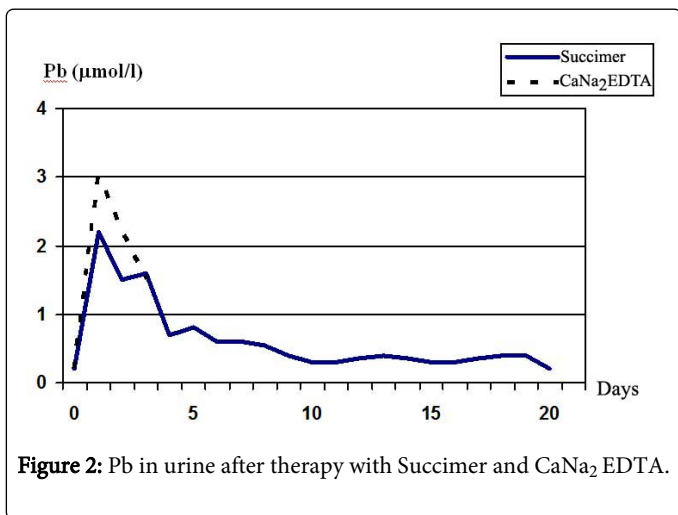


Figure 2: Pb in urine after therapy with Succimer and CaNa₂ EDTA.

In the application of both antidotes the average released arsenic content is not above the reference values (1.47 µmol/l), although it is higher than the basal. With one exception, the application of CaNa₂ EDTA does not lead to higher excretion above 1.47 µmol/l. Peroral administration of Succimer, however, leads to its increased release compared to the baseline in the first 5 days of the treatment ($p < 0.05$) (Figure 3). The individual analysis shows that in 6 out of 15 studied patients the released amount is 2 to 3 times higher than the reference values. It is noteworthy to point out the reliably ($p < 0.05$) higher excretion of arsenic at therapy with Succimer in comparison to CaNa₂ EDTA, which is an evidence of the better chelating effect of Succimer with respect to arsenic.

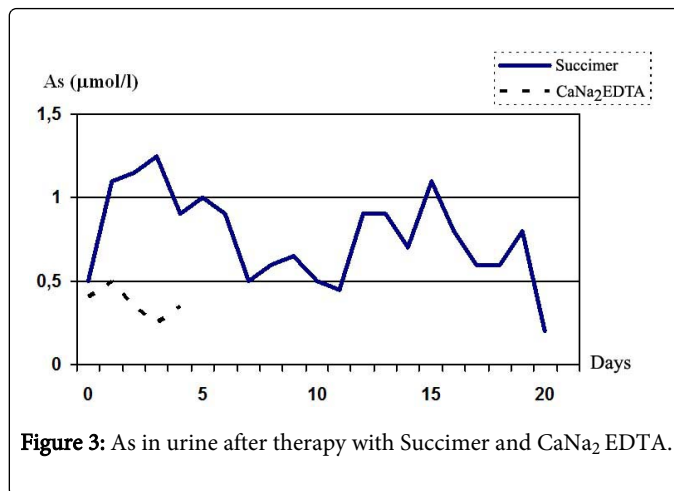


Figure 3: As in urine after therapy with Succimer and CaNa₂ EDTA.

Observing the urine excretion of zinc of workers, treated with CaNa₂ EDTA, striking is the fact of its massive loss (Figure 4). The concentration of zinc on the first day is 155 ± 24 µmol/l, on the second - 114 ± 7 µmol/l and on the third - 125 ± 26 µmol/l, compared to the basal 8 ± 1.5 µmol/l. Zincuria upon the application of CaNa₂ EDTA is also reported by other authors, (Graziano JH) [2,3,8]. The zinc content in the urine of the individuals, taking Succimer throughout all 20 consecutive days of treatment, is low-less than 10-15 µmol/l, undergoing no significant changes.

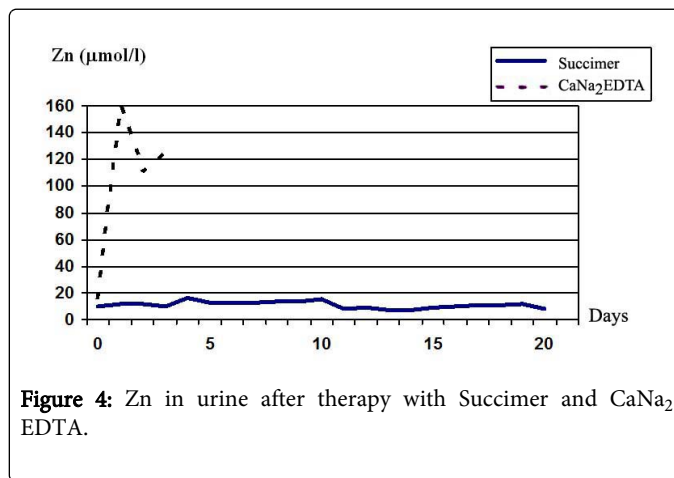


Figure 4: Zn in urine after therapy with Succimer and CaNa₂ EDTA.

The release of copper, upon application of both antidotes, is higher than the baseline; however, it is within the range of the reference values. No statistically significant variations were established with respect to the concentrations of cadmium in both groups of individuals, either. The levels of copper and zinc in blood before and after the therapy are within the range of the reference values, which is evidence that they are extracted from the depots of the organism (Figure 5).

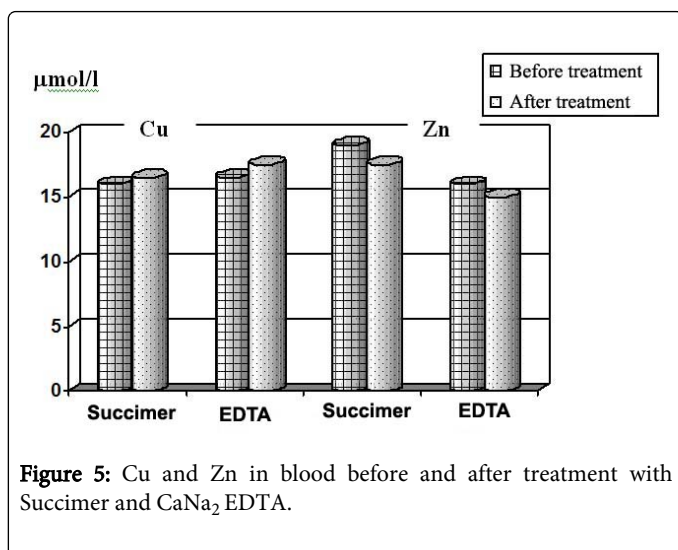


Figure 5: Cu and Zn in blood before and after treatment with Succimer and CaNa₂ EDTA.

Conclusion

A comparative evaluation is made between the antidotal effect of Succimer and CaNa₂ EDTA on workers, exposed simultaneously to lead, arsenic and cadmium. The studied drugs show a marked antidotal effect on lead. The chelating effect of Succimer on arsenic is much better, compared to CaNa₂ EDTA.

The treatment with Succimer results in no change in the excretion of copper and zinc, while CaNa₂ EDTA causes daily 10 to 15-times higher release of zinc with the urine than the reference values.

Succimer (DMSA) is an effective chelator, leading to expressed plumburia, suitable for peroral administration, and may be used with patients who are not hospitalized, due to absence of manifested side effects.

In workers with a low-level lead exposure, a 7-day therapy with Succimer is appropriate, in a dosage of 2.1 grams per day.

Patients with symptoms of lead intoxication and high-level lead absorption are recommended a therapy with CaNa₂ EDTA for rapid and effective decorporating chelation therapy, with parallel administration of substitution therapy with microelements (copper and zinc).

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