



Journal of Toxicology
CLINICAL TOXICOLOGY
Vol. 41, No. 4, pp. 339–347, 2003

ARTICLE

Vitamin C, Glutathione, or Lipoic Acid Did Not Decrease Brain or Kidney Mercury in Rats Exposed to Mercury Vapor[†]

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ABSTRACT

Some medical practitioners prescribe GSH and vitamin C alone or in combination with DMPS or DMSA for patients with mercury exposure that is primarily due to the mercury vapor emitted by dental amalgams. *Hypothesis.* This study tested the hypothesis that GSH, vitamin C, or lipoic acid alone or in combination with DMPS or DMSA would decrease brain mercury. *Methods.* Young rats were exposed to elemental mercury by individual nose cone, at the rate of 4.0 mg mercury per m³ air for 2 h per day for 7 consecutive days. After a 7-day equilibrium period, DMPS, DMSA, GSH, vitamin C, lipoic acid alone, or in combination was administered for 7 days and the brain and kidneys of the animals removed and analyzed for mercury by cold vapor atomic absorption. *Results:* None of these regimens reduced the mercury content of the brain. Although DMPS or DMSA was effective in reducing kidney mercury concentrations, GSH, vitamin C, lipoic acid alone, or in combination were not. *Conclusion.* One must conclude that the palliative effect, if any, of GSH, vitamin C, or lipoic acid for treatment of mercury toxicity due to mercury vapor exposure does not involve mercury mobilization from the brain and kidney.

Key Words: Mercury vapor; Vitamin C; Glutathione; Lipoic acid; Mercury; Brain mercury.

[†]This paper is dedicated to Henry B. Wallace, who has generously and critically supported the research on heavy metals of HLSQ and HVA for many years. In addition, he has been a very thoughtful and understanding friend.

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INTRODUCTION

DMPS (2,3-dimercaptopropanesulfonate, DIM-AVAL[®]), alone or in combination with glutathione (GSH) and/or vitamin C (ascorbic acid, Na ascorbate, NaAsc), has been prescribed by some physicians for decreasing mercury toxicity (1). The patients usually have been dentists exposed to mercury during their practice or patients with a wide spectrum of complaints thought to be due to mercury exposure via amalgams, foods, vaccines, and/or other sources. The use of intravenous vitamin C is the direct result of its long history of use by physicians who believed it effectively and safely reduced the toxic effect of mercury from overdose of mercurial diuretics while treating high blood pressure (2).

DMPS is an orally active chelating agent that was first introduced in the former Soviet Union during the late 1950s (3,4). Since then, it has been approved for the treatment of mercury intoxication in Germany. Investigations and reviews of its pharmacological properties and efficacy in animals and humans for the treatment of heavy metal exposure have been extensive (5–15). DMPS has never been submitted for FDA approval via a New Drug Application. It has been used, however, in the United States without an Investigational New Drug (IND) or a Compassionate Use application to the FDA. It has been supplied by compounding pharmacists.

Another chelating agent, meso 2,3-dimercaptosuccinic acid (DMSA, succimer, Chemet[®]) introduced in the Western world by Friedheim and Graziano (16) and in China by Ding and Liang (17), also has been successfully used to increase the urinary excretion of mercury (18–21). It has been approved by the FDA for the treatment of children with blood lead levels ≥ 45 $\mu\text{g}/\text{dl}$.

There have been conflicting reports as to whether DMPS or DMSA will remove mercury from the brain. Some of these reports indicated small decreases (10). Others stated there was no change (14).

The major forms of mercury that are of toxicological interest are elemental mercury (Hg^0); inorganic mercury, such as mercuric (Hg^{+2}) and mercurous (Hg^{+1}) mercury; and organic mercury, primarily methylmercury (MeHg) and ethylmercury (EtHg). Mercury vapor (Hg^0) and organic mercury are potent central nervous system neurotoxins. Reviews of the toxicology of these different forms of mercury have appeared recently (22,23).

The major source of mercury exposure for the general population has been elemental mercury (Hg^0) of dental amalgams (22,24,25). Hg^0 exposure also occurs via industrial accidents particularly in chloro-alkali plants (21,26). For people who eat a significant amount

of seafood and have few amalgams, methylmercury from their diet is the major source of mercury exposure (22).

In the last 15 to 20 years there has been considerable interest by the alternative medicine practitioners in lowering the mercury body burden of many patients. In particular, there has been the never-validated belief that by doing this there would be subsequent improvement of the patient's motor and mental activity. For these reasons, DMPS, DMSA, alpha lipoic acid, and other compounds such as GSH and vitamin C have been prescribed. Since N-acetyl-cysteine can be a precursor of GSH, it has been claimed to be active as a mercury antidote (27). Insulin was another agent evaluated because it has been reported to increase the uptake of drugs across the blood-brain barrier (28).

In this paper, we report our experiments evaluating the effects of the above agents on brain mercury concentrations. Specifically, we present data that GSH, vitamin C, or lipoic acid alone or in combination with DMPS or DMSA did not decrease brain mercury in rats exposed to elemental mercury. The kidney concentrations of mercury were decreased by DMPS or DMSA administration, but GSH, vitamin C, and lipoic acid had no such activity and did not enhance the activity of DMPS or DMSA. Kidney mercury was studied to show, as a positive control, that DMPS or DMSA could mobilize mercury and in the case of the other agents that their lack of mobilizing activity was not connected with the blood-brain barrier.

METHODS

Chemicals and Animals

Elemental (metallic) mercury (CAS# 7439-97-6), 99.99⁺% pure, was obtained from Aldrich Chemical Co., Milwaukee, WI. Na ascorbate, GSH, and N-acetylcysteine were purchased from Sigma, St Louis, MO. DMPS was purchased from Heyl, Berlin. DMSA was a gift from Johnson and Johnson, Skillwood, NJ. All dosing solutions were prepared fresh in sterile, isotonic saline and frozen until used. Solutions were not refrozen.

Male Sprague-Dawley rats (6 to 7 weeks old on arrival; Charles River Breeding Laboratories, Raleigh, NC) were acclimated for 10 days after arrival. During acclimation, animals were uniquely identified by tattoo, weighed and randomized in treatment groups using a computer-generated randomization scheme. They received NIH-07 feed and deionized tap water ad libitum.

This study was conducted under federal guidelines for the use and care of laboratory animals and was



approved by the NIEHS, U.S. EPA, and University of Arizona Animal Care and Use Committees. Animals were housed in a humidity- and temperature-controlled, HEPA-filtered, mass air displacement room in facilities accredited by the American Association for Accreditation of Laboratory Animal Care. Animal rooms had a light–dark cycle of 12 h (light from 0700 to 1900 h). Sentinel animals housed in the animal facility as part of an ongoing surveillance program for parasitic, bacterial, and viral infections were pathogen-free throughout the study.

Exposure Protocol

Mercury Vapor Exposure System

Generation and monitoring: Elemental mercury vapor was generated by passing conditioned air (HEPA filtered, charcoal-scrubbed, temperature and humidity controlled) through a flask containing 10–20 g of Hg⁰. The flask containing Hg⁰ was immersed in a temperature-controlled water bath maintained at approximately 2°C above ambient. The resulting Hg⁰ vapor was diluted and delivered to the exposure system at a controlled rate using mass flow controllers.

Control animals were exposed to conditioned air in a stainless steel, 52-port nose-only exposure system (Lab Products, Rockville, MD). A second nose-only exposure system was used for Hg⁰ vapor exposures to 4 mg/m³. The airflow through both systems was maintained at approximately 12 L/minute. Each experiment consisted of a group of animals exposed to one Hg⁰ vapor concentration or a concurrent air-exposed control group. Exposure concentrations were measured from the nose-only system once every 15–30 minutes, and air samples from the room, scrubber, and the exposure system enclosure were analyzed once every hour. Air samples were analyzed using a Jerome Model 431-X Mercury analyzer (Arizona Instruments Phoenix, AZ) that is specific for elemental mercury vapor.

Rats were exposed to mercury vapor, via individual nose cone, for 2 h per day for 7 consecutive days. A 7-day exposure was chosen because a single acute exposure was not wanted and because elemental mercury is converted to mercuric mercury in the brain very rapidly. Control rats, air inhalation only, were placed in holding tubes in a nose-only exposure system and exposed to conditioned air at the same flow rate as rats receiving Hg vapor. They were kept on a different cage rack from the Hg exposed rats but otherwise treated in the same manner.

Treatment Regimen

Inhalation exposures. After each daily 2 h exposure to mercury or air, animals were returned to individual holding cages and given food and water ad libitum.

Holding period. After the 7-day mercury vapor exposures, a 7-day holding period was required for equilibration of tissue Hg concentrations. This was done by taking the rats immediately after the last inhalation exposure, and transferring them from the inhalation exposure system to individual polycarbonate holding cages, where they were given food and water ad libitum for 7 days. Air-exposed control animals were housed on a separate cage rack from Hg-exposed animals.

Post-exposure treatments. After the 7-day holding period, groups of 5 air-exposed or Hg-exposed rats were treated with DMPS, DMSA, NaAsc, GSH, or lipoic acid alone or in combination once a day for 7 consecutive days. The doses and treatment regimens are given in the legends of the figures. Injection volumes were 400 to 500 μ l. Treatment with both DMPS and DMSA was accomplished by injecting the drugs into opposite sides of the abdominal cavity (ip) with about 30 minutes between injections. DMPS and DMSA also were given by gavage (po) to evaluate the efficacy of this route of administration relative to ip injection. Control animals received sterile isotonic saline (400 μ l) by ip injection.

When insulin was used, animals were injected ip each time with 1.5 units of human insulin twice daily for 7 days. Lipoic acid was dissolved in saline and a dose of 10 mg/kg body weight was administered by gavage each time twice a day for 7 days. This dose was chosen because it has been used to treat autistic children.

Necropsies

The morning after the last postexposure treatment, rats were euthanized by CO₂ inhalation and thoracotomy. The surgery was performed using acid-washed dissecting tools. During tissue collection dissecting tools were rinsed in dilute acid and deionized water after each tissue to prevent cross contamination. Tissues were collected from control animals before Hg-exposed animal. Kidneys were removed and trimmed free of adrenal glands and perirenal fat prior to weighing. The brains were carefully removed from the cranium. Tissues were placed in individual acid-washed vials, frozen at –20°C and shipped overnight in dry ice by air courier to The University of Arizona in Tucson. They were stored at –70°C, until thawed and analyzed. The procedure for the cold vapor atomic absorption analysis used in this

laboratory and its validation has been published previously (7).

Statistical Analysis

The unpaired t test was used to compare the means of the Hg-exposed treated groups as well as the Hg unexposed groups. The statistical analysis was determined by using GraphPad InStat computer package (Mc 1997).

RESULTS

Hg Vapor Exposure

Mean mercury levels ($\mu\text{g/g}$ tissue) in brain and kidneys of air-exposed control rats ranged from 0.001 to 0.017 and 0.010 to 0.025, respectively (Figs. 1–8). Seven days after saline treatment, Hg vapor-exposed rats had brains with a mean $\mu\text{g Hg/g}$ tissue range of 0.509 to 0.897. Kidneys of such rats had Hg concentrations more than 60–70 fold higher than those of brain (34.8 to 52 $\mu\text{g Hg/g}$).

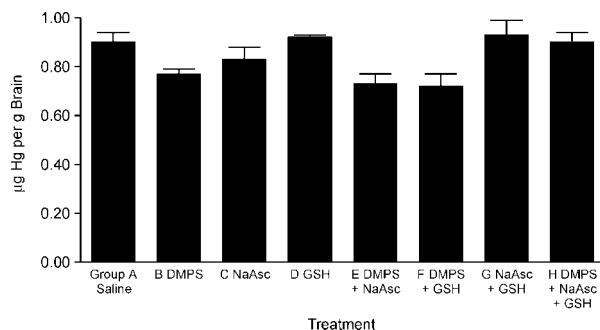


Figure 1. DMPS, Na ascorbate, or GSH, alone or in combination, did not decrease mercury concentration in the brain. Hg^0 dose was 4.0 mg/m^3 for 2 h per day for 7 days by nose-cone inhalation. All treatments began 7 days after Hg^0 exposures were completed and were each day for 7 days. DMPS, 1 mmol/kg, was given subcutaneously; Na ascorbate, 71 mg/kg, intraperitoneally; GSH, 225 mg/kg, intraperitoneally. Each group initially contained 5 rats. One rat of B and D died. Control rats (5 per group), receiving air instead of mercury and treated with saline, 1.0 mmol DMPS/kg, 71 mg NaAsc/kg, 225 mg GSH/kg or a combination of all of these treatments had $0.001 \pm 0.001\text{SE}$, $0.001 \pm 0.001\text{SE}$, 0.005 ± 0.002 , 0.019 ± 0.002 , or $0.005 \pm 0.002 \mu\text{g Hg per g}$ tissue, respectively. $p < 0.05$: A vs. B; A vs. E; A vs. F; B vs. H; B vs. D; E vs. G.

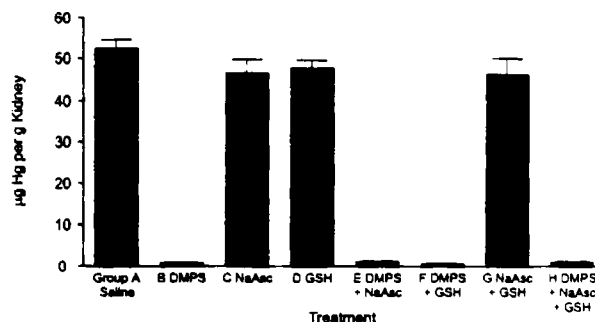


Figure 2. Na ascorbate and GSH did not decrease mercury concentration in the kidney of rats exposed to mercury vapor. Exposure and treatments were identical to those cited in the legend of Fig 1. Air control + saline was $0.017 \pm 0.005 \mu\text{gHg/gm}$. $p < 0.05$: A vs. B; A vs. E; A vs. F; A vs. H; B vs. C; B vs. D; B vs. G; C vs. E; C vs. F; C vs. H; D vs. E; D vs. F; E vs. G; F vs. G; G vs. H. The mean of group B was $0.82 \pm 0.03 \text{ Hg}/\mu\text{g}$ kidney. A duplicate of it exposed at the same time and treated in the identical manner had a mean of $0.868 \pm 0.039 \text{ Hg}/\mu\text{g}$.

Postexposure Treatments

DMPS and DMSA: Postexposure treatment with DMPS (1 mmol/kg) treatment caused a slight but statistically significant ($p = 0.047$) decrease in brain Hg concentration relative to saline-treated controls (Fig. 1). However in subsequent groups of animals

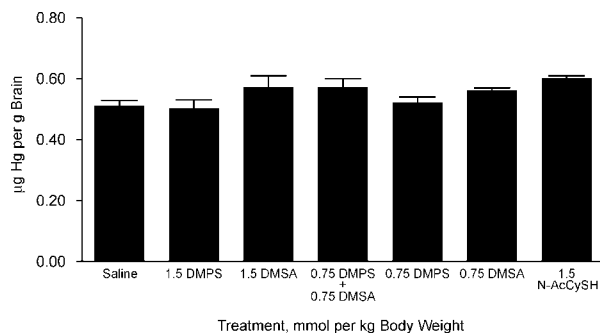


Figure 3. Brain mercury was not decreased by DMPS, DMSA, alone or in combination, or by N-acetylcysteine. Exposure and treatment schedules (but not specific agents used for treatments) were identical to those cited in the legend of Fig. 1. The numbers in the abscissa are the amounts administered expressed as mmol/kg body weight. DMPS was given intraperitoneally; DMSA intramuscularly; N-acetylcysteine intraperitoneally. Each group initially contained 5 rats. One rat died in each of the second, third, fifth and seventh groups. Control rats, receiving air instead of mercury, and treated with saline had $0.001 \pm 0.001 \mu\text{g Hg per gram}$ brain.

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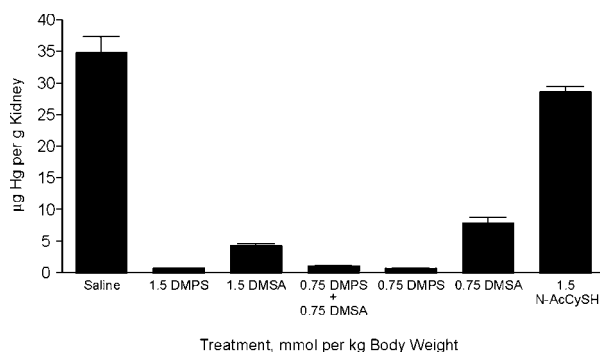


Figure 4. Kidney mercury was decreased by DMPS or DMSA but not by N-acetylcysteine. Exposure and treatments were identical to those cited in the legend of Fig 3. Control rats, receiving air instead of mercury and treated with saline, had 0.022 ± 0.001 µg Hg per gram kidney. $p < 0.05$ for all groups receiving DMPS, DMSA, or both as compared to saline; also for the 0.75 DMPS vs. 0.75 DMSA groups.

treated with 0.75 and 1.5 mmol/kg DMPS there were no significant differences in levels of Hg in the brain (Fig. 3). DMPS (1 mmol/kg) was ineffective in reducing ($p > 0.05$) mean brain Hg concentration when administered by ip injection or by gavage. Similarly, postexposure treatment with DMSA (0.75, 1.0, 1.5 mmol/kg) did not decrease brain Hg levels.

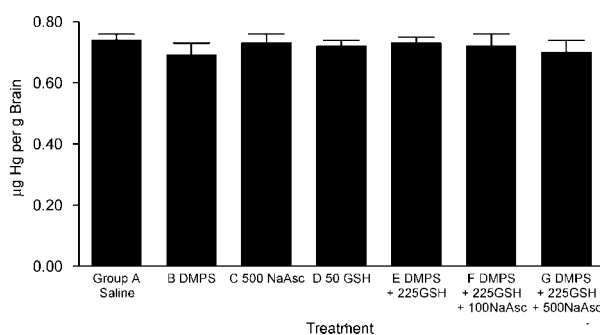


Figure 5. Brain mercury was not decreased by DMPS, Na ascorbate, and/or GSH. Exposure and treatment schedules (but not specific agents used for treatments) were identical to those cited in the legend of Fig. 1. All treatments were administered intraperitoneally. The numbers in the abscissa are the amounts administered expressed as mmol/kg body weight for DMPS and mg/kg for all other compounds. There were five rats per group. When µg Hg/gm brain of each treated group was compared to group A, the difference was not significant, $p > 0.05$. Control rats, receiving air instead of mercury and treated with saline, ip, had 0.017 ± 0.004 µg Hg/gm brain. When µg Hg/gm brain of each mercury-treated group was compared to such control rats, the difference was significant, $p < 0.001$.

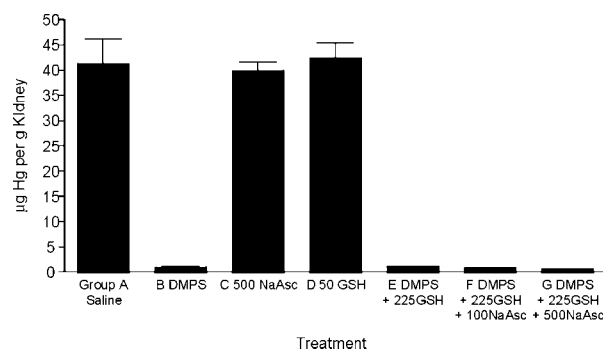


Figure 6. Na ascorbate and/or GSH did not decrease kidney mercury nor enhance the action of DMPS. Exposure and treatments were identical to those cited in the legend of Fig 5. Air control + saline was 0.010 ± 0.003 µg Hg/gm. $p < 0.05$: A vs. B; A vs. E; A vs. F; A vs. G; B vs. C; B vs. D; C vs. E; C vs. F; C vs. G; D vs. E; D vs. F; D vs. G.

For the kidney, the animals treated with DMPS had mean Hg levels that were significantly decreased ($p < 0.001$) (Figs. 2, 4, 6). DMPS was equally effective in reducing kidney Hg when given by ip injection or by oral gavage. DMSA (0.75 mmol/kg) was not as effective as DMPS (0.75 mmol/kg) in reducing kidney Hg concentrations during this period of time, $p < 0.05$ (Fig. 4) but at the higher levels (1.5 mmol/kg) the results were not significantly different. The result of combined DMPS and DMSA treatment was not significantly different than using DMPS alone as far as kidney Hg concentrations (Fig. 4).

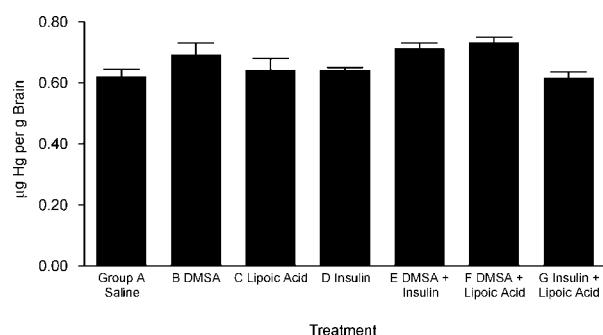


Figure 7. Brain mercury was not decreased by lipoic acid, insulin, DMSA, or combinations of them. Exposure and treatment schedules (but not specific agents used for treatments) were identical to those cited in the legend of Fig. 1 except that DMSA, 1.0 mmol/kg body weight, was administered by gavage; animals were injected ip each time with 1.5 units of human insulin twice daily for 7 days; reduced lipoic acid was dissolved in saline and 10 mg/kg body weight administered by gavage each time twice a day for 7 days.

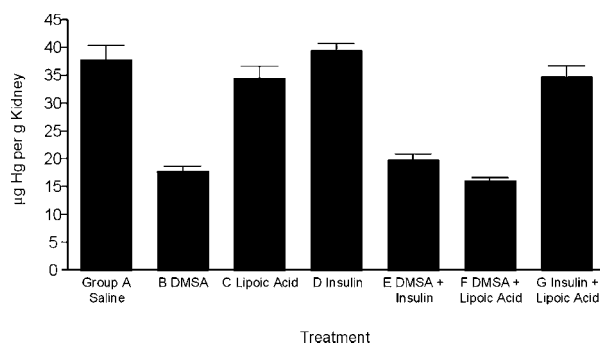


Figure 8. Lipoic acid or insulin did not decrease kidney mercury or enhance DMSA action. Exposure and treatments were identical to those cited in the legend of Fig 7. $p < 0.05$ for A vs. B; A vs. E; B vs. C; B vs. D; B vs. G; C vs. E; D vs. E; E vs. G; F vs. G; and for each group vs. air control. Air control + saline was $0.010\mu\text{g} \pm 0.001\text{Hg/gm}$.

Ascorbic acid and glutathione: Postexposure treatment with NaAsc or GSH alone or in combination had no significant effect ($p > 0.05$) on levels of Hg in the brain relative to saline-treated Hg-exposed controls (Figs. 1 and 5). Similarly, postexposure treatment with N-AcCySH was ineffective in reducing brain Hg concentrations and in fact resulted in a statistically significant increase (Fig. 3).

For the kidney, postexposure treatment with NaAsc (71 or 500 mg/kg) or GSH (225 or 50 mg/kg) alone or in combination (71 mg/kg NaAsc + 225 mg/kg GSH) had no significant effect ($p > 0.05$) on levels of Hg in the kidney relative to saline-treated Hg-exposed controls (Figs. 2 and 6). As in the brain, N-AcCySH treatment was ineffective in reducing kidney Hg levels (Fig. 4).

DMPS, ascorbic acid, and glutathione: Neither NaAsc nor GSH was able to significantly improve the effects of DMPS on brain Hg (Figs. 1 and 5). Even at doses of 500 mg/kg, NaAsc had no effect on brain Hg levels.

In the kidney, DMPS significantly ($p < 0.001$) reduced Hg levels to about 2% of that detected in saline-treated Hg-exposed controls (Fig. 2). However, combination treatment of DMPS with either NaAsc (71 mg/kg), or GSH (225 mg/kg) did not result in further reduction of kidney Hg levels. Similarly, combined treatment with DMPS, GSH, and up to 500 mg/kg NaAsc (Fig. 6) did not further reduce kidney Hg concentrations as compared to DMPS treatment alone (Group B vs. G, $p > 0.05$).

DMSA, lipoic acid, and insulin: Brain mercury concentrations were not decreased by DMSA, lipoic acid, or insulin alone or in various combinations (Fig. 7). Kidney mercury was decreased by DMSA, but lipoic

acid and insulin treatment did not have such activity (Fig. 8). In addition, neither lipoic acid nor insulin enhanced the mercury mobilizing activity of DMSA for the kidney.

DISCUSSION

The purpose of this study was to test the hypothesis that DMPS, DMSA, GSH, vitamin C, or lipoic acid, alone or in combination, would decrease brain mercury in rats exposed to elemental mercury vapor. Our results clearly indicated that none of these agents did so.

However, it is well established that, except for the brain, tissue Hg is decreased and urinary Hg increased by DMPS or DMSA in experimental animals (5,12,18). It is pertinent to note that as far as the effects of DMPS or DMSA on the kidneys in the present studies are concerned, mercury concentrations were decreased, confirming many studies in humans and experimental animals that have indicated the mercury mobilizing activity of DMPS or DMSA (5–15). Others have shown that intravenous vitamin C did not increase urinary Hg excretion for humans (29).

A number of papers in the literature state that DMSA reduces brain mercury and cite Aaseth et al. (10) as the primary reference. Those experiments, however, dealt only with exposure to methylHg and not to mercury vapor or mercuric Hg. Buchet and Lauwerys (14) demonstrated as early as 1989 that in rats exposed to phenylmercury acetate, mercuric chloride, or mercury vapor, DMPS and DMSA were ineffective in removing mercury from the brain.

Amalgam Mercury

The greatest exposure of the general population to mercury vapor is from dental amalgams (22–25). These so-called silver fillings contain about 50% elemental mercury. The amalgams continuously emit elemental mercury which enters the tissues and is converted to mercuric mercury, especially in the brain (22–25). Whether the mercury vapor emitted from dental amalgams is or is not harmful to human health because of a concentration-dependent toxicity also remains debatable. Unequivocal evidence based on in vivo evidence in humans as to whether dental amalgams are toxic or not still does not exist. Recently, Lorscheider and his associates (30) in a remarkable time-delayed video study demonstrated that snail neurons, in vitro, undergo



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visible neurodegeneration after exposure to amounts of elemental mercury vapor similar to concentrations found in humans. Other heavy metals were devoid of such activity.

Insulin has been claimed to increase the uptake of drugs across the blood-brain barrier (28). If it did this for DMSA, brain Hg might be decreased. It was not.

Alpha-lipoic acid is also being used in combination with DMSA or DMPS for treating autistic children (31). It was not effective in decreasing brain or kidney Hg in our studies. Nor was it effective in increasing the activity of DMSA in this regard. The role of alpha-lipoic acid in eukaryotic cells involves protein-bound lipoic acid and free alpha-lipoic acid. The latter has many roles. It can be an enzyme substrate, enzyme inhibitor, a protein modifier involved in redox-dependent and redox-independent reactions, free radical scavenger, metal chelator, and a modulator of GSH metabolism (32).

Alleged Benefits: The question arises as to why do practitioners prescribe GSH, vitamin C, or lipoic acid alone or in combination with DMPS or DMSA for exposures that are primarily due to the mercury vapor emitted by dental amalgams. Our results unequivocally and clearly indicate that GSH and vitamin C do not decrease brain or kidney mercury. Others have shown that intravenous vitamin C given to humans did not increase urinary Hg (29). Yet there are anecdotal accounts that DMPS, GSH, and vitamin C are beneficial for patients with mercury intoxication, allegedly due to mercury vapor being emitted from their dental amalgams. One possibility is that GSH and/or vitamin C have some palliative effect that does not involve mercury mobilization and excretion. For example, both are antioxidants (33,34) and ultramegadolose vitamin C, as IV-C is known to quiet a highly exaggerated inflammatory response (35). The net effect may bring about a more acceptable clinical outcome that is quite independent of mercury excretion. Any such evidence, however, that they are effective for this reason in treating mercury toxicity remains anecdotal and requires experimental evidence in humans. In addition, a possible placebo effect needs to be considered.

Vitamin C treatment of people with high levels of inorganic Hg is not without hazard. In experiments with guinea pigs injected with mercuric chloride, the ingestion of vitamin C along with mega doses of vitamin B₁₂ and/or folate synergistically increased the tissue concentrations of methyl mercury (36). Biomethylation of mercuric ions to methylmercury via methyl B₁₂ has been established in bacteria (37).

N-acetyl-cysteine

There have been reports about the effectiveness of N-acetyl-cysteine for treating mercury intoxication (27). In our studies, it neither decreased mean brain nor kidney Hg concentrations. For the brain, NAC appeared to have increased the mercury concentration as compared to saline-treated control rats that inhaled mercury vapor.

Other Comments

Combination treatment is often discussed and sometimes proposed for treating mercury intoxication. DMPS and DMSA alone or together did not decrease brain mercury at the concentrations used in this study.

Some long-time users of intravenous vitamin C feel strongly that the high osmolar condition created by administering the vitamin in Lactated Ringer's Solution may play a role in removing mercury from the brain or in alleviating general symptoms that are often credited to mercury. This effect could not be assessed by the study we have performed, because the vitamin C in our study was administered by a different route that bypassed any possible effect on osmolarity.

Limitations

Our study, however, has some limitations. They have only involved animals exposed to elemental Hg. Similar experiments as to brain Hg levels in organic mercurial (MeHg- or EtHg-) -exposed animals would be of interest. Also, what happens in the rat may not apply to what happens in the human.

To summarize, DMSA, DMPS, GSH, vitamin C, lipoic acid, alone or in combination, did not reduce the mercury content of the brain. DMSA or DMPS, but not the other agents, did decrease kidney mercury concentrations. One must conclude that the palliative effect, if any, of GSH, vitamin C, or lipoic acid for treatment of mercury vapor toxicity does not involve mercury mobilization from the brain and kidney and may thus represent a placebo effect. Therapeutically useful agents to decrease inorganic mercury levels in the brain are needed.

ACKNOWLEDGMENTS

Supported in part by the Wallace Research Foundation, 30600 N. Pima #56, Scottsdale, AZ 85262.



Inhalation exposures were performed at the NIEHS inhalation facility under contract to ManTech Environmental Technology, Inc., Research Triangle Park, NC. The authors would like to acknowledge the technical support of C. Colegrove, C. Crawford, D. Crawford, N. Gage, T. Godwin, L. Goods, R. Harrison, H. Milligan, H. Price, P. Rydell, and S. Philpot.

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