PENTETATE ZINC TRISODIUM

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PENTETATE ZINC TRISODIUM

0.0 OVERVIEW

LIFE SUPPORT

CLINICAL EFFECTS

LABORATORY/MONITORING

TREATMENT OVERVIEW

RANGE OF TOXICITY

0.1 LIFE SUPPORT
   A) This overview assumes that basic life support measures have been instituted.

0.2 CLINICAL EFFECTS
   0.2.1 SUMMARY OF EXPOSURE
      A) WITH THERAPEUTIC USE
         1) Headache, lightheadedness, pruritus, nausea, vomiting, diarrhea, pelvic pain, and trace element
            deficiency have been reported following therapeutic use of pentetate zinc trisodium (Zn-DTPA).
      B) WITH POISONING/EXPOSURE
         1) There is no current information regarding acute overdose in humans.

   0.2.20 REPRODUCTIVE
      A) Animal studies have demonstrated no evidence of impaired fertility or fetal harm with multiple doses of
         Zn-DTPA. A slight decrease in average birth weight was the only reported effect.
      B) It is recommended that chelation treatment for pregnancy women begin and continue with Zn-DTPA, if
         available, except in cases of high internal contamination with radioactive material. The risk of radiation-induced
         toxicity to the mother and fetus must be weighed against the risk of toxicity with Zn-DTPA therapy. Since
         Ca-DTPA is more effective than Zn-DTPA in the first 24 hours after high internal contamination, a single dose
         of Ca-DTPA with zinc-containing vitamin and mineral supplements may be an appropriate initial treatment. In
         these cases, the risk of radiation-induced toxicity to the mother and fetus must be weighed against the risk of
         toxicity with Ca-DTPA therapy.
      C) The US Food and Drug Administration's Pregnancy Category B.

0.3 LABORATORY/MONITORING
   A) Monitor fluid and electrolyte status in patients with significant vomiting and/or diarrhea.
   B) Monitor serum electrolytes and essential metals and obtain complete blood counts.

0.4 TREATMENT OVERVIEW
   0.4.3 INHALATION EXPOSURE
      A) There is no current information regarding acute overdose in humans. In cases of pentetate zinc trisodium
         overdose, treatment should be symptomatic and supportive.
      B) Cough and/or wheezing have been reported in two patients who received nebulized Ca-DTPA; one patient
         had a history of asthma. However, these effects have not been reported with Zn-DTPA.
      C) INHALATION: Move patient to fresh air. Monitor for respiratory distress. If cough or difficulty breathing
         develops, evaluate for respiratory tract irritation, bronchitis, or pneumonitis. Administer oxygen and assist
         ventilation as required. Treat bronchospasm with inhaled beta2 agonist and oral or parenteral corticosteroids.

   0.4.6 PARENTERAL EXPOSURE
      A) There is no current information regarding acute overdose in humans. In cases of pentetate zinc trisodium

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redistributed or otherwise used for commercial purposes.
overdose, treatment should be symptomatic and supportive.

0.5 RANGE OF TOXICITY
A) A minimum toxic dose has not been established. There is no current information regarding acute overdose in humans.

1.0 SUBSTANCES INCLUDED/SYNONYMS

THERAPEUTIC/TOXIC CLASS

SPECIFIC SUBSTANCES

AVAILABLE FORMS/SOURCES

1.1 THERAPEUTIC/TOXIC CLASS
A) Pentetate zinc trisodium (Zn-DTPA), a chelating agent, increases the rates of radiocontaminant elimination by forming stable chelates with metal ions.

1.2 SPECIFIC SUBSTANCES
1) Zn-DTPA
2) Trisodium zinc diethylenetriaminepentaacetate
3) Molecular Formula: Na3-Zn-C14-H18-N3-O10

1.6 AVAILABLE FORMS/SOURCES
A) FORMS
1) Zn-DTPA is available as a sterile solution in 5 mL single-use clear glass ampoules (1000 mg of Zn-DTPA per ampoule) at a concentration of 200 mg/mL for intravenous use. Each mL has 200 mg of Zn-DTPA (obtained from 150.51 mg pentetic acid, 31.14 mg zinc oxide and NaOH) in water for injection, USP. If internal contamination is only by inhalation within the preceding 24 hours, patients can receive Zn-DTPA by nebulized inhalation (Prod Info Pentetate Zinc Trisodium Injection, 2004).

B) USES
1) Pentetate zinc trisodium (Zn-DTPA) is used to treat individuals with known or suspected internal contamination with transuranium ions, specifically plutonium, americium, and/or curium, to increase rates of elimination (Prod Info Pentetate Zinc Trisodium Injection, 2004).

3.0 CLINICAL EFFECTS

SUMMARY OF EXPOSURE

NEUROLOGIC

GASTROINTESTINAL

DERMATOLOGIC

MUSCULOSKELETAL

METABOLISM

REPRODUCTIVE

3.1 SUMMARY OF EXPOSURE

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A) WITH THERAPEUTIC USE
   1) Headache, lightheadedness, pruritus, nausea, vomiting, diarrhea, pelvic pain, and trace element deficiency have been reported following therapeutic use of pentetate zinc trisodium (Zn-DTPA).

B) WITH POISONING/EXPOSURE
   1) There is no current information regarding acute overdose in humans.

3.7 NEUROLOGIC
   3.7.2 CLINICAL EFFECTS
     A) CENTRAL NERVOUS SYSTEM FINDING
        1) WITH THERAPEUTIC USE
           a) Headache and lightheadedness have been reported with Zn-DTPA treatment (Prod Info Pentetate Zinc Trisodium Injection, 2004).

3.8 GASTROINTESTINAL
   3.8.2 CLINICAL EFFECTS
     A) GASTROINTESTINAL TRACT FINDING
        1) WITH THERAPEUTIC USE
           a) Nausea, vomiting, and diarrhea have been reported with Zn-DTPA treatment (Anon, 2002).

3.14 DERMATOLOGIC
   3.14.2 CLINICAL EFFECTS
     A) ITCHING OF SKIN
        1) WITH THERAPEUTIC USE
           a) Pruritus has been reported with Zn-DTPA treatment (Anon, 2002).

3.15 MUSCULOSKELETAL
   3.15.2 CLINICAL EFFECTS
     A) PAIN
        1) WITH THERAPEUTIC USE
           a) Pelvic pain have been reported with Zn-DTPA treatment (Prod Info Pentetate Zinc Trisodium Injection, 2004).

3.17 METABOLISM
   3.17.2 CLINICAL EFFECTS
     A) METABOLIC FINDING
        1) WITH THERAPEUTIC USE
           a) Zn-DTPA therapy has been associated with endogenous trace element deficiency including magnesium and manganese depletion (Prod Info Pentetate Zinc Trisodium Injection, 2004).

3.20 REPRODUCTIVE
   3.20.1 SUMMARY
     A) Animal studies have demonstrated no evidence of impaired fertility or fetal harm with multiple doses of Zn-DTPA. A slight decrease in average birth weight was the only reported effect.
     B) It is recommended that chelation treatment for pregnancy women begin and continue with Zn-DTPA, if available, except in cases of high internal contamination with radioactive material. The risk of radiation-induced toxicity to the mother and fetus must be weighed against the risk of toxicity with Zn-DTPA therapy. Since Ca-DTPA is more effective than Zn-DTPA in the first 24 hours after high internal contamination, a single dose of Ca-DTPA with zinc-containing vitamin and mineral supplements may be an appropriate initial treatment. In these cases, the risk of radiation-induced toxicity to the mother and fetus must be weighed against the risk of toxicity with Ca-DTPA therapy.
     C) The US Food and Drug Administration's Pregnancy Category B.

3.20.2 TERATOGENICITY

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ANIMAL STUDIES

1) Mouse studies have demonstrated no evidence of impaired fertility or fetal harm with multiple doses of pentetate zinc trisodium (Zn-DTPA). Mice received Zn-DTPA at doses 31 times the recommended daily human dose. A slight decrease in average birth weight was the only reported effect (Prod Info Pentetate Zinc Trisodium Injection, 2004).

3.20.3 EFFECTS IN PREGNANCY

A) PREGNANCY CATEGORY


2) It is recommended that chelation treatment for pregnancy women begin and continue with Zn-DTPA, if available, except in cases of high internal contamination with radioactive material. The risk of radiation-induced toxicity to the mother and fetus must be weighed against the risk of toxicity with Zn-DTPA therapy. Since Ca-DTPA is more effective than Zn-DTPA in the first 24 hours after high internal contamination, a single dose of Ca-DTPA with zinc-containing vitamin and mineral supplements may be an appropriate initial treatment. In these cases, the risk of radiation-induced toxicity to the mother and fetus must be weighed against the risk of toxicity with Ca-DTPA therapy (Prod Info Pentetate Calcium Trisodium Injection, 2004; Prod Info Pentetate Zinc Trisodium Injection, 2004).

3.20.4 EFFECTS DURING BREAST-FEEDING

A) BREAST MILK

a) It is unknown if pentetate zinc trisodium (Zn-DTPA) is excreted in breast milk. However, radiocontaminants are known to be excreted in breast milk. Whether receiving chelation therapy or not, women with suspected or known internal contamination should not breast feed. Precautions should be taken when discarding breast milk (Prod Info Pentetate Zinc Trisodium Injection, 2004).

4.0 LABORATORY/MONITORING

4.1 MONITORING PARAMETERS/LEVELS

4.1.1 SUMMARY

A) Monitor fluid and electrolyte status in patients with significant vomiting and/or diarrhea.
B) Monitor serum electrolytes and essential metals and obtain complete blood counts.

4.1.2 SERUM/BLOOD

A) Monitor CBC with differential, BUN, serum chemistry and electrolytes (including calcium, magnesium and manganese) and urinalysis regularly during therapy.

4.1.4 OTHER

A) OTHER

1) Measure the radioactivity in blood, urine, and fecal samples weekly to monitor the radioactive contaminant elimination rate. A baseline estimate of the total body burden of transuranium element should be obtained by whole-body counting and bioassay when possible.

6.0 TREATMENT

LIFE SUPPORT

MONITORING

ORAL EXPOSURE

PARENTERAL EXPOSURE

INHALATION EXPOSURE

6.1 LIFE SUPPORT

A) Support respiratory and cardiovascular function.
6.4 MONITORING
   A) Monitor fluid and electrolyte status in patients with significant vomiting and/or diarrhea.
   B) Monitor serum electrolytes and essential metals and obtain complete blood counts.

6.5 ORAL EXPOSURE
6.5.1 PREVENTION OF ABSORPTION/PREHOSPITAL
   A) SUMMARY
      1) Pentetate zinc trisodium is only available for intravenous or inhalation use. In the unlikely event of
         ingestion, administer activated charcoal.

6.6 PARENTERAL EXPOSURE
6.6.2 TREATMENT
   A) SUPPORT
      1) There is no current information regarding acute overdose in humans. In cases of pentetate
         trisodium overdose, treatment should be symptomatic and supportive.
   B) MONITORING OF PATIENT
      1) Monitor fluid and electrolyte status in patients with significant vomiting and/or diarrhea.
      2) Monitor serum electrolytes and essential metals and obtain complete blood counts.
   C) ENHANCED ELIMINATION PROCEDURE
      1) LACK OF INFORMATION
         a) There is no information regarding the effectiveness of hemodialysis or hemoperfusion for the
            removal of pentetate zinc trisodium from plasma.

6.7 INHALATION EXPOSURE
6.7.1 DECONTAMINATION
   A) Cough and/or wheezing have been reported in two patients who received nebulized Ca-DTPA; one patient
      had a history of asthma. However, these effects have not been reported with Zn-DTPA (Prod Info Pentetate
      Zinc Trisodium Injection, 2004).
   B) DECONTAMINATION: Move patient from the toxic environment to fresh air. Monitor for respiratory
      distress. If cough or difficulty in breathing develops, evaluate for hypoxia, respiratory tract irritation, bronchitis,
      or pneumonitis.
   C) OBSERVATION: Carefully observe patients with inhalation exposure for the development of any systemic
      signs or symptoms and administer symptomatic treatment as necessary.
   D) INITIAL TREATMENT: Administer 100% humidified supplemental oxygen, perform endotracheal intubation
      and provide assisted ventilation as required. Administer inhaled beta adrenergic agonists if bronchospasm
      develops. Exposed skin and eyes should be flushed with copious amounts of water.

6.7.2 TREATMENT
   A) SUPPORT
      1) There is no current information regarding acute overdose in humans. In cases of pentetate
         trisodium overdose, treatment should be symptomatic and supportive.
   B) MONITORING OF PATIENT
      1) Monitor fluid and electrolyte status in patients with significant vomiting and/or diarrhea.
      2) Monitor serum electrolytes and essential metals and obtain complete blood counts.

7.0 RANGE OF TOXICITY

SUMMARY

THERAPEUTIC DOSE

7.1 SUMMARY
   A) A minimum toxic dose has not been established. There is no current information regarding acute overdose in
7.2 THERAPEUTIC DOSE

7.2.1 ADULT

A) INTRAVENOUS

1) INITIAL DOSE - During the first 24 hours after internal contamination, it is recommended to administer pentetate calcium trisodium (Ca-DTPA) as the initial dose, followed by Zn-DTPA for maintenance therapy. A single intravenous dose of 1 gram of Ca-DTPA is recommended (Prod Info Pentetate Trisodium Injection, 2004; Prod Info Pentetate Zinc Trisodium Injection, 2004).

2) Zn-DTPA intravenous route (1 gram in 5 mL solution either by a slow intravenous push over 3 to 4 minutes or by intravenous infusion diluted in 100 to 250 milliliters of 5% dextrose in water, lactated Ringer's, or normal saline) is recommended. The intravenous route should be used if the route of internal contamination is not known or if multiple routes of internal contamination are likely (Prod Info Zinc Trisodium Injection, 2004).

3) Patients should drink plenty of fluids and void frequently to promote dilution of the chelated radioc contaminant in the urine and reduce radiation exposure directly to the bladder (Prod Info Zinc Trisodium Injection, 2004).

4) Other therapies may be needed (eg: Prussian blue, potassium iodide) if internal contamination with agents other than plutonium, americium, or curium is suspected, or if the radioc contaminant is unknown (Prod Info Pentetate Zinc Trisodium Injection, 2004).

5) MAINTENANCE DOSE - The day after the initial dose, if additional chelation therapy is needed, pentetate zinc trisodium (Zn-DTPA) is preferred, if available, due to safety concerns with prolonged Ca-DTPA administration. An intravenous dose of 1 gram of Zn-DTPA once daily is recommended for maintenance treatment. Ca-DTPA should not be given simultaneously with Zn-DTPA (Prod Info Calcium Trisodium Injection, 2004; Prod Info Pentetate Zinc Trisodium Injection, 2004).

B) INHALATION

1) If internal contamination is only by inhalation, patients can receive Zn-DTPA by nebulized inhalation. Dilute Zn-DTPA for nebulization at a 1:1 ratio with sterile water or saline. After nebulization, patients should not swallow any expectorant (Prod Info Pentetate Zinc Trisodium Injection, 2004).

7.2.2 PEDIATRIC

A) INTRAVENOUS

1) ADOLESCENTS -

a) INITIAL DOSE - An initial single intravenous dose of 1 gram of pentetate calcium trisodium (Ca-DTPA) is recommended (Prod Info Pentetate Calcium Trisodium Injection, 2004; Prod Info Pentetate Zinc Trisodium Injection, 2004).

b) MAINTENANCE DOSE - The day after the initial dose, if additional chelation therapy is needed, switch to pentetate zinc trisodium (Zn-DTPA), if available, due to safety concerns with prolonged Ca-DTPA administration. If Zn-DTPA is not available, treatment with Ca-DTPA may continue, but concomitant zinc supplementation should be given as needed. An intravenous dose of 1 gram of Zn-DTPA once daily is recommended for maintenance treatment. Ca-DTPA should not be given simultaneously with Zn-DTPA (Prod Info Pentetate Calcium Trisodium Injection, 2004; Prod Info Pentetate Zinc Trisodium Injection, 2004).

2) CHILDREN LESS THAN 12 YEARS OF AGE -

a) INITIAL DOSE - An initial single intravenous dose of 14 milligrams per kilogram, not to exceed 1 gram, of pentetate calcium trisodium (Ca-DTPA) is recommended for children less than 12 years of age (Prod Info Pentetate Calcium Trisodium Injection, 2004; Prod Info Pentetate Zinc Trisodium Injection, 2004).

b) MAINTENANCE DOSE - The day after the initial dose, if additional chelation therapy is needed, switch to pentetate zinc trisodium (Zn-DTPA), if available, due to safety concerns with prolonged Ca-DTPA administration. If Zn-DTPA is not available, treatment with Ca-DTPA may continue, but concomitant zinc supplementation should be given as needed. In pediatric patients (less than 12 years of age), an intravenous dose of 14 milligrams per kilogram (not to exceed 1 gram per day) of Zn-DTPA once daily is recommended for maintenance treatment (Prod Info Pentetate Calcium Trisodium Injection, 2004; Prod Info Pentetate Zinc Trisodium Injection, 2004).

B) INHALATION

1) ADOLESCENTS - If internal contamination is only by inhalation, patients can receive Zn-DTPA by nebulized inhalation. Dilute Zn-DTPA for nebulization at a 1:1 ratio with sterile water or saline. After
nebulization, patients should not swallow any expectorant (Prod Info Pentetate Zinc Trisodium Injection, 2004).

2) CHILDREN LESS THAN 12 YEARS OF AGE - The safety and efficacy of the nebulized route of administration have not been established in children (Prod Info Pentetate Zinc Trisodium Injection, 2004).

8.0 KINETICS

8.1 ABSORPTION
A) THERAPEUTIC
1) ORAL
   a) Pentetate zinc trisodium (Zn-DTPA) is poorly absorbed in the gastrointestinal tract. In animal studies, absorption was approximately 5% (Prod Info Pentetate Zinc Trisodium Injection, 2004).

8.2 DISTRIBUTION
8.2.1 DISTRIBUTION SITES
A) TISSUE/FLUID SITES
1) Zn-DTPA is primarily rapidly distributed throughout the extracellular space. There is no significant penetration into erythrocytes or other cells. No accumulation in specific organs has been observed (Prod Info Pentetate Zinc Trisodium Injection, 2004).

8.3 METABOLISM
8.3.1 METABOLISM SITES AND KINETICS
A) WITH THERAPEUTIC USE
1) Metabolism of Zn-DTPA is minimal (Prod Info Pentetate Zinc Trisodium Injection, 2004).

8.4 EXCRETION
8.4.1 KIDNEY
A) In the first few hours after administration, Zn-DTPA is cleared from the plasma through urinary excretion by glomerular filtration. By 24 hours after administration, cumulative urinary excretion was greater than 99% of the injected dose (Prod Info Pentetate Zinc Trisodium Injection, 2004).

8.4.2 FECES
A) Less than 3% (Prod Info Pentetate Zinc Trisodium Injection, 2004).

8.4.4 OTHER
A) OTHER
1) BREAST MILK
   a) It is unknown if pentetate zinc trisodium (Zn-DTPA) is excreted in breast milk. However, radiocontaminants are known to be excreted in breast milk. Whether receiving chelation therapy or not, women with suspected or known internal contamination should not breast feed. Precautions should be taken when discarding breast milk (Prod Info Pentetate Zinc Trisodium Injection, 2004).

9.0 PHARMACOLOGY/TOXICOLOGY

9.1 PHARMACOLOGIC MECHANISM

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A) Pentetate zinc trisodium (Zn-DTPA) is indicated for the treatment of known or suspected internal contamination with transuranium ions that have a molecular weight greater than uranium, specifically plutonium, americium, and/or curium, to increase rates of elimination (Prod Info Pentetate Zinc Trisodium Injection, 2004).

B) Pentetate zinc trisodium (Zn-DTPA) increases the rates of radiocontaminant elimination by forming stable chelates with metal ions. The zinc ion is exchanged for ions with higher binding capacity. The radioactive chelates are then excreted into the urine by glomerular filtration (Prod Info Pentetate Zinc Trisodium Injection, 2004).

C) Zn-DTPA is most effective when radiocontaminants are still circulating or are in interstitial fluids. Since radiocontaminants become sequestered in liver and bone, the efficacy decreases with time following internal contamination. During the first 24 hours after internal contamination, it is recommended to administer pentetate calcium trisodium (Ca-DTPA) as the initial dose, followed by Zn-DTPA for maintenance therapy. Zn-DTPA and Ca-DTPA have equal efficacy after the first 24 hours. If Zn-DTPA is not available, treatment with Ca-DTPA may continue, but concomitant zinc supplementation should be given as needed (Prod Info Pentetate Calcium Trisodium Injection, 2004; Prod Info Pentetate Zinc Trisodium Injection, 2004).

10.0 PHYSICOCHEMICAL

PHYSICAL CHARACTERISTICS

MOLECULAR WEIGHT

10.1 PHYSICAL CHARACTERISTICS
A) Zn-DTPA is a clear, colorless, hyperosmolar (1260 mOsmol/kg) solution (Prod Info Pentetate Zinc Trisodium Injection, 2004).

10.3 MOLECULAR WEIGHT
A) 522.7 Daltons (Prod Info Pentetate Zinc Trisodium Injection, 2004)

12.0 REFERENCES

12.2 GENERAL BIBLIOGRAPHY