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DIPHOTERINE® FOR EMERGENT DECONTAMINATION OF SKIN/EYE CHEMICAL SPLASHES: 24 CASES

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Chemical skin/eye splashes can cause burns. Standard references recommend decontamination with water. Diphoterine, a polyvalent, hypertonic, amphoteric, chelating solution is an alternative. Occupational medical records of 24 workers in a German metallurgy firm from 1994 to 1998 were reviewed. There were 11 acid eye splashes, 8 acid skin splashes, 4 base eye splashes, and 1 base skin splash. Following Diphoterine decontamination, no burns developed and there were no requirements for burn treatment or sequelae. Three workers had 1 lost workday each. Diphoterine decontamination successfully prevented skin/eye burns in this group of metallurgy workers.

Keywords: Chemical splashes; Decontamination; Decontamination eye/skin; Diphoterine®

INTRODUCTION

Chemical skin/eye splashes resulting in burns in the industrial setting are significant problems, resulting in pain, requirements for medical or surgical burn treatment, sometimes long-term sequelae, and lost work time. Chemical agents do not "burn" in the classic sense of tissue destruction by heat. Rather they act by coagulating protein through oxidation, reduction, salt formation, corrosion, protoplasmic poisoning, metabolic competition or inhibition, desiccation, or vesicant activity and resultant ischemia (1). More than 25,000 chemicals including corrosives, oxidizing agents, and reducing agents have been identified as having the potential to cause burns (2). In the United States, the Occupational Safety and Health Administration (OSHA) regulations mandate emergency eye wash stations and quick-drench water showers in all facilities where potentially dangerous chemical agents are used (2).

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Standard references almost universally recommend decontamination of skin/eye chemical splashes with copious amounts of water, adding a mild soap if the chemical is fat soluble (3–5). Water is supposed to have the following mechanisms of action: 1) chemical agent dilution; 2) rinsing the chemical agent off the surface of the cornea or skin; 3) decreasing the chemical reaction rate; 4) decreasing tissue metabolism and therefore the inflammatory reaction; 5) minimizing the hygroscopic effects of chemicals that produce them; and 6) restoring normal skin pH in acid and alkali burns (6). However, despite the ready availability of water decontamination, large numbers of persons have skin/eye chemical splash exposure each year and many develop burns (7–9) some of which are fatal (10–12) despite early water decontamination.

Water washing is passive decontamination. Another approach used in European workplaces for a number of years is active skin/eye decontamination with Diphoterine. Diphoterine is a water-soluble powder, and the rinsing and diluting effects of an equal volume of water (in the commercial preparations) are most likely retained. It is a polyvalent (actively binds multiple substances), amphoteric, hypertonic, chelating molecule with active binding sites for acids, bases, oxidizing agents, reducing agents, vesicants, lacrimators, irritants, solvents, and so on. Reported here are the results of Diphoterine skin/eye chemical splash emergent decontamination in a group of 24 German metallurgy workers.

MATERIALS AND METHODS

The records of all consecutive cases of skin/eye chemical splash exposure occurring in a German metallurgy facility (Mannesmann Hoesch Prazisrohr, Remscheid, Germany) during the years 1994–1998 were collected and reviewed by the occupational doctor from forms containing the following information: type of splash (acid, base, specific chemical(s) involved when known, concentration), body area exposed, type of initial and secondary decontamination, sequelae, and whether there was lost work time. Initial Diphoterine decontamination was done by the workers themselves or coworkers immediately at the incident site, and then all workers were required to be evaluated in the company infirmary where a second Diphoterine decontamination was done.

Diphoterine is a water-soluble powder manufactured by Laboratoire Prevor, Valmondois, France, and provided for use dissolved in water and sterilized by autoclaving. As supplied for use, it is an odorless and colorless liquid with a pH of 7.4, a boiling point of 100°C, a freezing point of -1°C, and a specific gravity of 1.034 g/cm^3 (from the manufacturer's material safety data sheet (MSDS) available at www.prevor.com). The chemical formula and generic chemical name are considered to be proprietary and confidential by the manufacturer. The general properties of Diphoterine are listed previously in the Introduction section.

RESULTS

During the study period, 24 workers (all males) aged 21–62 years sustained skin or eye chemical splashes with either weak or strong acids or bases. The type of exposure, body area involved, initial and secondary decontamination with Diphoterine, and outcomes are shown in Tables 1–4. Industrial processes involved were degreasing, transferring liquid or solid chemicals, stripping, suctioning, cleaning, placing metal pipes in a chemical bath, and direct contact with spilled chemicals. Of the 24 cases, acid splashes involved the eyes in 11 and the skin in 8. Base splashes involved the eyes in 4 cases and the skin in 1 case.

Despite exposures that would have been predicted to result in chemical burns requiring medical and/or surgical treatment, following a nearly immediate (within the first 30–120 seconds after exposure) initial on-site Diphoterine decontamination and a second Diphoterine decontamination in the company infirmary, no further treatment was required, there were no sequelae, and only 3 workers each had 1 lost workday due to hospital observation rather than injury. These 3 workers had eye exposures to acids (20% H_2SO_4; a mixture of 5% H_3PO_4/35% HNO_3; and a mixture of 5% H_2SO_4/7% HNO_3).

Acid eye splashes (n = 11) involved chemicals such as phosphoric acid/nitric acid mixtures and sulfuric acid in either solid forms or liquids in concentrations from 5% to 35%. Following initial decontamination with Diphoterine at the worksite and a second Diphoterine decontamination at the company infirmary (not necessarily needed but dictated by company policy), outcomes were as follows: no treatment other than initial Diphoterine decontamination was required, there were no sequelae, and 3 workers each had 1 day of lost work time (Table 1).

For base eye splashes (n = 4), workers were exposed to 30% sodium hydroxide, a "basic solution" at a 30% concentration, or calcium oxide (concentrations not recorded). There was no need for treatment other than initial Diphoterine decontamination, there were no sequelae, and none of these workers had lost work time (Table 2).

For acid skin splashes (n = 8), chemicals involved were nitric acid, sulfuric acid, and phosphoric acid in concentrations from 15% to 75%. Following initial worksite Diphoterine decontamination and secondary Diphoterine lavage in the company infirmary, no additional treatment was necessary, there were no sequelae, and no worker had lost work time (Table 3).

One worker sustained a skin splash of 45% sodium hydroxide. Following initial Diphoterine worksite and secondary company infirmary Diphoterine decontamination, no additional treatment was required, no sequelae occurred, and there was no lost work time (Table 4).

No irritant or other adverse effects attributable to Diphoterine decontamination were noted in these 24 caustic substance exposed workers.

DISCUSSION

Following removal of contaminated clothing, which may decrease chemical skin contamination by up to 80% (3), standard references recommend water or normal saline for immediate decontamination of skin/eye chemical splashes, also adding soap if the substance is fat soluble (3–5,13). Soap should not be used in the eyes. Older literature suggests that immediate eye flushing for about 30 minutes from the nearest shower or faucet should be done following sodium or ammonium hydroxide exposure (14).

Table 1 Acid eye splashes

Chemical product	Concentration	Involved eye	Initial decontamination	Secondary decontamination	Additional treatment	Lost work time (days)	Sequelae
Mixture H_3PO_4/ HNO_3	H_3PO_4 5%/ HNO_3 30–35%	Left	Diphoterine	Diphoterine	None	0	None
H_2SO_4	20%	Right	Diphoterine	Diphoterine	None	0	None
NH_2SO_3H	Powder	Right	Diphoterine	Diphoterine	None	0	None
H_2SO_4	20%	Not reported	Diphoterine	Diphoterine	None	0	None
NH_2SO_3H	Powder	Not reported	Diphoterine	Diphoterine	None	0	None
H_2SO_4	20%	Right	Diphoterine	Diphoterine	None	1	None
Mixture H_3PO_4/ HNO_3	H_3PO_4 5%/HNO_3 35%	Left	Diphoterine	Diphoterine	None	1	None
H_2SO_4	20%	Left	Diphoterine	Diphoterine	None	0	None
Mixture H_2SO_4/HNO_3	H_2SO_4 5%/HNO_3 35%	Left	Diphoterine	Diphoterine	None	1	None
H_2SO_4	20%	Right	Diphoterine	Diphoterine	None	0	None
H_2SO_4	20%	Left	Diphoterine	Diphoterine	None	0	None

Table 2 Base eye splashes

Chemical product	Concentration	Involved eye	Initial decontamination	Secondary decontamination	Additional treatment	Lost work time (days)	Sequelae
NaOH	30%	Right	Diphoterine	Diphoterine	None	0	None
"Basic solution"	30%	Right	Diphoterine	Diphoterine	None	0	None
Quicklime (Calcium oxide)	Unknown	Right	Diphoterine	Diphoterine	None	0	None
Quicklime (Calcium oxide)	Unknown	Left	Diphoterine	Diphoterine	None	0	None

Table 3 Acid skin splashes

Chemical product	Concentration (%)	Body area involved	Initial decontamination	Secondary decontamination	Additional treatment	Lost work time (days)	Sequelae
HNO_3	53	Head	Diphoterine	Diphoterine	None	0	None
H_2SO_4	20	Right cheek	Diphoterine	Diphoterine	None	0	None
H_2SO_4	20	Throax	Diphoterine	Diphoterine	None	0	None
H_3PO_4	16	Left forearm	Diphoterine	Diphoterine	None	0	None
H_2SO_4	20	Face	Diphoterine	Diphoterine	None	0	None
H_3PO_4	15	Right hand	Diphoterine	Diphoterine	None	0	None
H_3PO_4	75	Throax, genitals, right thigh	Diphoterine	Diphoterine	None	0	None
H_2SO_4	20	Right hand	Diphoterine	Diphoterine	None	0	None

Table 4 Base skin splashes

Chemical product	Concentration	Involved body area	Initial decontamination	Secondary decontamination	Additional treatment	Lost work time (days)	Sequelae
NaOH	45%	Knee	Diphoterine	Diphoterine	None	0	None

The ANSI Z358.1-1998 standard for emergency water decontamination equipment for the skin and eyes specifies that emergency showers and eyewash stations should be clearly marked and that it should take a chemical-exposed worker no more than 10 seconds to reach them (15). For eye decontamination, "The ideal flushing solution is a sterile, isotonic, preserved, physiologically balanced solution" and "At a minimum, flushing fluid should be clean and non-toxic," which would include potable water (16).

Chemical burn injuries comprise only a small percentage of total burn injuries, but their human and economic impact is significant. Although immediate water decontamination has generally been shown to decrease the severity of chemical skin/eye burns, it does not always prevent such burns from developing, especially following exposure to strong corrosives (4,11,12,17–20). Recent *in vitro* experiments on corneal cell cultures performed by Schrage et al. (21) have shown that water decontamination could have a deleterious effect on cells, with hypo-osmolar effects increasing the cell volume with resultant lysis from increased intracellular osmotic pressure. New active decontamination modalities that are polyvalent (act against a wide variety of chemical agents/groups), amphoteric (act against opposed chemical groups such as acids/bases, oxidizers/reducing agents, etc.), nontoxic, nonsensitizing (22), and water-soluble (so that beneficial diluting and rinsing effects of an equal volume of water are retained) should be critically evaluated. Diphoterine is such a decontamination solution.

In *in vivo* eye/skin experiments, Diphoterine was significantly more efficacious than no decontamination or normal saline rinsing (23–25): with Diphoterine decontamination, there is a rapid return to physiological pH and decreased inflammation and pain, as demonstrated by biochemical marker assays with a decrease in substance P and an increase of β-endorphin. In ocular splashes, stromal edema was shown by Kubota and Fagerholm (26) to impede corneal tissue repair. Decontamination with Diphoterine induces corneal healing improvement as it stops the activity of the involved chemical product. A case report of an ocular splash with delayed Diphoterine rinsing is also suggestive of such action (27).

In European industrial settings, Diphoterine has been used as an eye/skin chemical splash decontaminant solution for several years. Before initiating the use of this active decontamination solution, workers are trained in its use so that no time from exposure to beginning of decontamination will be lost. Supply of the decontaminant in portable containers may decrease the time between exposure and decontamination.

Diphoterine decontamination has been used in eye/skin splashes with a wide variety of chemicals such as corrosives and solvents, where it has been found to prevent or decrease the severity of burns, to rapidly decrease pain, and has resulted in fewer requirements for medical or surgical burn care other than initial decontamination and less lost work time (28–30).

In the present case series, even in those workers who had eye or skin exposure to concentrated corrosives such as sodium hydroxide, phosphoric acid, or nitric acid, emergent Diphoterine decontamination prevented burns, no interventions other than decontamination were necessary, and only 3 workers with acid eye splashes each had 1 lost work day due to hospital observation rather than injury.

Similar exposures to strong and concentrated corrosives have been reported to cause severe burns, even when water decontamination was done immediately (31,32).

Nitric acid, for example, has been reported to cause significant burns or death (31,33); the nitric acid concentrations involved were not listed in these references, but the 3 patients involved required multiple plastic surgical procedures for burn treatment, despite early water decontamination in 2 of the 3 (31); decontamination was not described in the third patient (33). In the workers reported here, exposure to nitric acid did not result in burns following Diphoterine decontamination. Without knowing the nitric acid concentrations involved in the patients described in references 31 and 33, comparisons are difficult. Similar results with Diphoterine decontamination were obtained with ocular and cutaneous splashes due to sodium hydroxide, phosphoric acid, or a mixture of strong acids (Tables 1–4).

A training program initiated by the employer's Safety and Health Departments for recognition of the risks of corrosive chemical skin/eye exposures and the immediate use of Diphoterine decontamination may have also contributed to the favorable outcomes noted in these workers.

Among the 24 metallurgy workers with acid or base skin/eye chemical splashes reported here, there was no requirement for additional burn treatment following initial Diphoterine decontamination, there were no sequelae, and only 3 workers had 1 lost workday each due to hospital observation rather than injury. No irritant or other adverse effects attributable to Diphoterine decontamination were noted. All eye/skin splashes due to concentrated strong corrosives such as sodium hydroxide or nitric or phosphoric acids were successfully decontaminated. In this group of workers, Diphoterine was a safe and efficacious solution for initial decontamination of skin/eye caustic chemical splashes.

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REFERENCES

1. Jelenko C. Chemicals that "burn." J Trauma 1974; 14:95–107.
2. Liao C-C, Rossignol AM. Landmarks in burn prevention. Burns 2000; 26:422–434.
3. McMullen MJ, Jones J. Industrial toxicology. In: Haddad LM, Shannon MW, Winchester JF, eds. Clinical Management of Poisoning and Drug Overdose. 3rd ed. Philadelphia: WB Saunders; 1998:919–930.
4. Standing CL, Caniano DA. Burns. In: Harwood-Nuss AL, Linden CH, Luten RC, et al, eds. The Clinical Practice of Emergency Medicine. 2nd ed. Philadelphia: Lippincott-Raven; 1996:1205–1210.
5. NIOSH. NIOSH Pocket Guide to Chemical Hazards. Washington, DC: US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health; 1997:xxxvii–xl.

6. Bromberg BE, Song IC, Walden RH. Hydrotherapy of chemical burns. Plast Reconstr Surg 1965; 35:85-95.
7. Bureau of Labor Statistics, US Department of Labor. http://www.bls.gov/iff/oshwc/, accessed 02/23/04.
8. Morbidity and Mortality Weekly Report. Occupational injury surveillance—United States. MMWR 1981; 30:578–579.
9. McCullough JE, Henderson AK, Kaufman JD. Occupational burns in Washington State, 1989–1993. J Occup Environ Med 1998; 40:1083–1089.
10. Hunt JP, Calvert CT, Peck MD, Meyer AA. Occupation-related burn injuries. J Burn Care Rehabil 2000; 21:327–332.
11. Leonard LG, Scheulen JJ, Munster AW. Chemical burns: Effects of prompt first aid. J Trauma 1982; 22:420–423.
12. Sykes RA, Mani MM, Hiebert JH. Chemical burns: Retrospective review. J Burn Care Rehabil 1986; 7:343–347.
13. Coe JE, Douglas RB. Ocular responses to chemical and physical injury. In: Zenz C, Dickerson OB, Horvath EP, eds. Occupational Medicine, 3rd ed. Philadelphia: WB Saunders; 1994:85–92.
14. Stanley JA. Strong alkali burns of the eye. N Engl J Med 1965; 273:1265–1266.
15. Bollas C, Coffey J. Eyewash & Showers: In case of emergency. Occup Health Saf 1998; 67:50–52, 54, 56.
16. Hurley RB. More than meets the eye. Occup Health Saf 1998; 67:53–57.
17. Gruber RP, Laub DR, Vistnes LM. The effect of hydrotherapy on the clinical course and pH of cutaneous chemical burns. Plast Reconstr Surg 1974; 55:200–204.
18. van Rensberg LCJ. An experimental study of chemical burns. SA Med J 1962; 36:754–759.
19. Cartotto RC, Peters WJ, Neligan PC, Douglas LG, Beeston J. Chemical burns. Can J Surg 1996; 39:205–211.
20. Wolfort FG, DeMeester T, Knorr N, Edgerton MT. Surgical management of cutaneous lye burns. Surg Gynecol Obstet 1970; 131:873–876.
21. Schrage NF, Rihawi R, Frentz M, Reim M. Akuttherapie von Augenverätzungen [Acute therapy for chemical or thermal eye irritations] [German]. Klin Monatsbl Augenheilkd 2004; 221:253–261.
22. Mathieu L, Burgher F, Hall AH: Diphoterine® chemical splash decontamination solution: Skin sensitization study in the guinea pig. J Toxicol Cutan Ocular Toxicol 2006 (in press).
23. Gérard M, Josset P, Louis V, Menerath JM, Blomet J, Merle H. Existe-t-il un délai pour le lavage oculaire externe dans le traitement d'une brûlure oculaire par l'ammoniaque? Comparaison de deux solutions de lavage: Sérum physiologique et Diphotérine [Is there a delay for the external eye rinsing in the treatment of an eye burn due to ammonia? Comparison between 2 rinsing solutions: normal saline and Diphoterine] [French]. J Fr Ophthalmol 2000; 23:1–10.
24. Cavallini M, Casati A. A prospective randomized, blind comparison between saline, calcium gluconate and Diphoterine for washing skin acid injuries in rats: Effects on substance P and β-endorphin release. Eur J Anaesthesiol 2004; 1:389–392.
25. Cavallini M, de Brocard F, Corsi MM, Fassati LR, Baruffaldi, Preis FW. Serum proinflammatory cytokines and chemical acid burns in rats. Ann Burns Fire Disasters 2004; 17:84–87.
26. Kubota M, Fagerholm P. Corneal alkali burn in the rabbit. Water balance, healing and transparency. Acta Ophthalmol 1991; 69:635–640.
27. Gérard M, Merle H, Chiambaretta F, Rigal D, Schrage N. An amphoteric rinse used in the emergency treatment of a serious ocular burn. Burns 2002; 28:670–673.

28. Hall AH, Blomet J, Mathieu L. Diphoterine for emergent eye/skin chemical splash decontamination: A review. Vet Hum Toxicol 2002; 44:228–231.
29. Falcy M, Blomet J. Evaluation de l'efficacité des premiers soins lors de projections de produits chimiques [Evaluation of the efficacy of first aid measures during chemical product splashes] [French]. Documents pour le Médecine du Travail 1993; 53:137–146.
30. Falcy M, Blomet J. Premiers soins en cas de projections oculaires [First aid in cases of eye splashes] [French]. Documents pour le Médecine du Travail 1993; 53:33–41.
31. McAdams AJ, Krop S. Injury and death from red fuming nitric acid. JAMA 1955; 158:1022–1024.
32. Orimo H, Yamamoto O, Kobayashi M, Yasuda H. [Occupational induced nitric acid and sulfuric acid burns: An analysis of 2 patients from the aspect of occupational health] [Japanese]. The Japanese Journal of Occupational and Environmental Health 2001; 23:69–75.
33. Kumar P. L-shaped flap for moustache reconstruction in a patient with an acid burn of the face. Burns 1996; 22:413–416.