



The effects of the use of Diphoterine[®] solution on chemical burns in the Tarapur industrial complex, India



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ABSTRACT

Aim: Tarapur is the biggest industrial complex in India. Chemical burns are relatively frequent due to the use of corrosive agents within these industries. Diphoterine[®], a polyvalent hypertonic amphoteric first-aid solution has been adopted by some of the companies but not others. We decided to compare the cases of chemical injury which had been treated with Diphoterine[®] solution with those who had not.

Methods: A prospective study of all chemical skin injuries attending the Ashirwad Clinic Boisar between 16/9/15 and 21/11/16 (14 months). The mechanism of injury, delay in treatment, first aid treatment performed, pain improvement, site of injury, size of burn, time off work and time to healing were recorded. The costs of all treatments were also recorded.

Results: There were 65 chemical skin burns during the time of the study. 56 were treated with water as the only first aid method. Nine cases also had Diphoterine[®] applied. The average delay in applying Diphoterine[®] was 27 min. The water only group took an average of 13.65 days to heal, compared to 4 days in the Diphoterine[®] group ($p < 0.01$). The water only group required an average of 17 days off work compared to 5 in the Diphoterine[®] group ($p = 0.14$). The water only group treatment costs were 13,223 INR (205 USD) compared with 7150 INR (111 USD) in the Diphoterine[®] group ($p = 0.50$). The Diphoterine[®] group also experienced a significant improvement in pain ($p < 0.001$).

Conclusions: The use of Diphoterine[®] solution in treating chemical burns results in less pain, less time off work and less overall treatment costs.

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1. Introduction

Tarapur in India is the biggest industrial complex in India. The concentration of heavy industries in this area, together with an attitude to Health and Safety which is typical of the developing world, means that chemical burns are relatively frequent. The Ashirwad Clinic, Boisar is located at the edge of the industrial complex and is the main initial referral unit for all such injuries in the area. The clinic has developed a wealth of experience in treating chemical injuries over the last 28 years.

After any industrial chemical injury standard practice until recently has been to place the patient in a shower for 15 min [1].

Diphoterine[®] solution, a polyvalent hypertonic amphoteric first-aid solution which neutralizes acids and alkalis is widely used in Europe and Canada [2,3]. It is a washing solution for ocular and chemical splashes. Diphoterine[®] solution contains an amphoteric molecule that can modulate the pH of irritant/corrosive agents

without heat release. It is also a hypertonic solution (about 800 mosmoles/kg) which limits diffusion of the chemical agent and create a gradient from the inside of the tissues to the outside. It has been available in India since 2007, but has only started being adopted by certain companies within the Tarapur industrial complex for the past two or three years. Diphoterine[®] has very low toxicity with oral and dermal rat LD₅₀s greater than 2000 mg/kg [4], and is available as a spray for skin splashes.

Sadly most companies within the complex do not have access to Diphoterine[®] solution. We decided to compare the results of patients who had been treated with Diphoterine[®] solution with those who had not.

2. Methods

A prospective study of all chemical skin injuries attending the Ashirwad Clinic, Boisar between 16/9/15 and 21/11/16 (14 months) was designed and ethical approval to perform the study was obtained from the Hospital Ethics Committee. The mechanism of injury, delay in treatment, first aid treatment performed, site of injury, size of burn, time off work and time to healing were

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recorded. The costs of all treatments were also recorded, based on the following costs:

- Diphoterine® Dispenser 100 ml (Micro Dap; 50 s of washing): 3167 INR (Indian Rupee)/50 USD (American dollar)
- Diphoterine® Dispenser 200 ml (Mini Dap; 1 min 30 s of washing): 4667 INR/73 USD
- Diphoterine® Dispenser 500 ml (LPM; 3 min of washing): 6667 INR/104 USD
- Half day hospital stay: 2000 INR/31 USD
- Full day hospital stay: 3500 INR/54 USD
- Dressing costs under 2% TBSA: 250 INR/4 USD per dressing change
- Dressings cost over 2% TBSA: 500 INR/8 USD per dressing change

The duration of the water lavage at the scene of the accident (before the arrival at the clinic) could not be recorded.

The patients were asked to rank their pain before irrigation with either water or Diphoterine® solution from 1 to 10, and then to rank their pain after irrigation using a Visual Analogue Score.

Healing was assessed clinically as being complete.

Statistical analysis was performed using the Mann-Whitney U test based on non-normal data distribution [5] using R software (version 3.4.3 Foundation for Statistical Computing Vienna, Austria).

3. Results

There were 65 chemical skin burns during the time of the study. All patients were male. 56 were treated with water as the only first aid method. Nine cases also had Diphoterine® solution applied in addition to water.

There was no difference in age between the two groups (Table 1) ($p = 0.62$). All burns were thought to be partial thickness initially.

The commonest chemical involved were strong corrosives, such as sulfuric acid (42%) (Figs. 1 and 2) followed by sodium hydroxide (22%). Half of the sulfuric acid burns involved acid at 98% concentration.

Size of burn: The average size of the burns was 5% in the water only group and 3% in the Diphoterine® group (Table 1).

Both groups had water applied as first aid. The water only group had an average delay in applying water of about 12 min. The patients who subsequently went on to have Diphoterine® solution applied had an average delay of 10 min before they had water first aid applied. The average delay from time of injury to the application of Diphoterine® solution in this group was about 27 min (Table 1).

The parts of the body typically affected were hands, wrists, arms, forearms followed by thigh and feet (Table 2). Multiple exposures were also often recorded affecting face, shoulder, back, chest, neck and ankle. There was no significant difference between the groups ($p = 0.31$). The eyes were also affected in 4 cases, 3 in the water group and 1 in the Diphoterine® group.

Table 1
Demographics.

	Water only (n = 56)	Water plus Diphoterine® (n = 9)
Mean age of patient (range)	33 (27–40)	34.44 (28–42)
Average %TBSA burned (range)	5% (1–3.25%)	3% (1–10%)
Delay from exposure to irrigation in minutes (range)	12.11 (5–120)	Water – 10 (10–15) Diphoterine® – 27.47 (25–30)

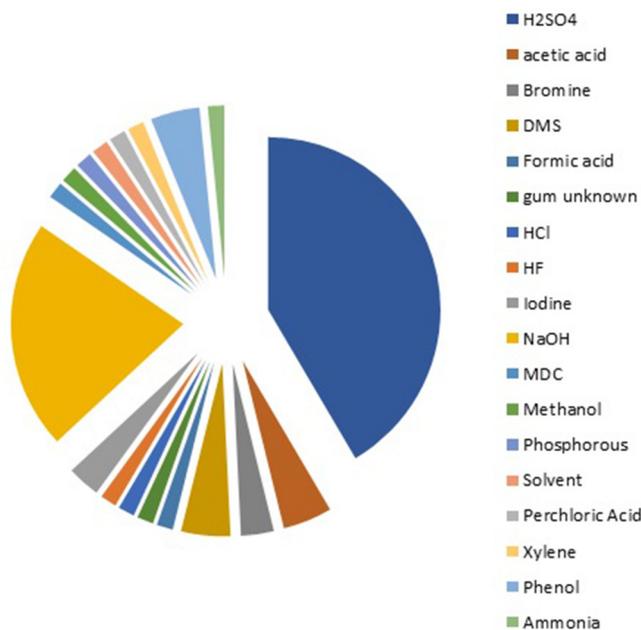


Fig. 1. Chemicals causing the injuries.



Fig. 2. Typical sulfuric acid burn.

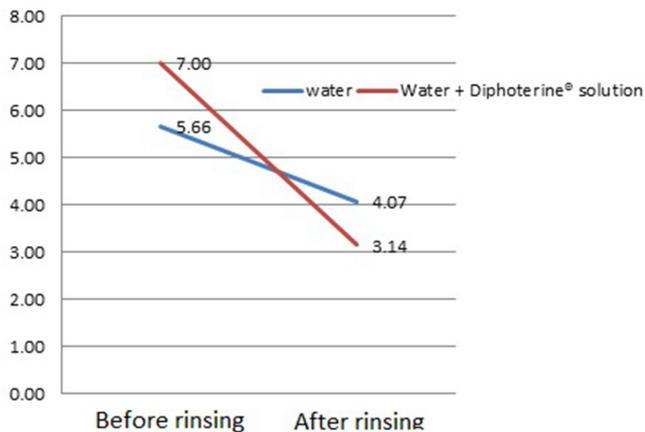
Table 2
Affected area by chemical splash.

Repartition (body parts)	Water	Water + Diphoterine® solution
Hands, wrists, arms, forearms	24	4
Thigh	7	1
Abdominal wall	2	
Feet	6	1
Face	3	1
chest	2	1
Multiple exposures (face, shoulder, back, chest, neck, ankle)	11	1
Unknown	1	
Total	56	9

Table 3
Sequelae.

	Water only (n = 56)	Water plus Diphoterine® (n = 9)
Days work loss (range)	16.75 (3–20.2)	4.67 (2–7)
Time to heal (range)	13.65 (3–20)	3.24 (2–5)
Treatment costs INR (range)	13,223 (2250–20500)	7150 (4167–8167)

Assessment of pain before VS after rinsing

**Fig. 3.** Reduction in pain scores.

Time off work: The water only group required an average of 16.75 days off work compared to 4.67 in the Diphoterine® group (Table 3) ($p = 0.14$).

Healing time: Healing time was assessed clinically based on epithelialization. The observers were not blinded. The water only group took an average of 13.65 days to heal. The Diphoterine® group took an average of 3.24 days to heal ($p = 0.01$) (Table 3).

Treatment costs: No surgery was required for any patient. All patients were treated by the same nursing team using the same simple dressings. India has no social security system and the patients (or their companies) are billed directly for all costs involved. The water only group treatment costs were 13,223 INR (205 USD) compared with 7150 (111 USD) in the Diphoterine® group (we have included the cost of the Diphoterine® solution used) ($p = 0.50$).

Pain: Pain was assessed using a Visual Analogue score once the patients had reached the hospital. Patients were asked to rate their pain before and after irrigation. We accept that this will rely on the patient to remember what their pain had been like, and that there will be a degree of unreliability in this measurement. The Diphoterine® group experienced a significant improvement in pain, reducing from 7.0 before application to 3.1 after application. The water only group had a reduction in pain scores from 5.7 to 4.1 after irrigation (Fig. 3) ($p < 0.001$).

4. Discussion

During the 14 months of this study, 65 patients attended with chemical burns to the skin (we intend to describe the ocular results in a separate paper). This equates to more than one per week.

The commonest cause of injury was sulfuric acid, which in high concentrations can cause significant thermal and chemical injuries [1]. The second commonest cause of injury was sodium hydroxide; a strong base which is well known for producing burns which continue to evolve if efficient decontamination is not performed [1].

There was one Hydrofluoric acid burn in this series. It is worth mentioning that the best treatment for this agent would be either calcium gluconate gel after initial decontamination with Hexafluorine® solution.

Diphoterine® solution is an external rinsing solution of the skin and the eye. This is the first clinical study that compares skin chemical decontamination in India between Diphoterine® solution and water. We have chosen to evaluate work loss and cost of hospitalization as industries here need to have workers back to work as soon as possible and because there is no social insurance in India.

These results are similar to a German industrial study that included forty-two exposures with concentrated sodium hydroxide [6]. In the German study, the splashes were rinsed at the workplace. The number of days lost from work they report were 0.18 ± 0.4 days for irrigation with Diphoterine® solution, 2.91 ± 4.3 days for irrigation with acetic acid and 8 ± 8.12 days for irrigation using water alone.

In Australia a study of the experiences of 3 alumina refineries described 180 cases of cutaneous exposures due to alkalis (usually sodium hydroxide) [7]. A comparison was made between workers that washed the splash first with either Diphoterine® solution or with water. This is the largest human study in industry. One hundred and thirty-eight cases were decontaminated first with Diphoterine® solution and forty-two cases were rinsed first with water. No sign of chemical burn was observed in 52.9% of the cases with Diphoterine® rinsing compared to 21.4% in the water group. Blisters and more severe burns were observed in 7.9% of the cases washed with Diphoterine® solution compared to 23.8% in the water only group.

Our results also confirm what was measured in an *in vivo* study with a concentrated burn due to hydrochloric acid. In this study, β -endorphin and substance-P levels were measured. β -endorphin was significantly increased when washing performed with Diphoterine® solution compared to no washing or using other washing solutions [8]. Substance-P levels were significantly decreased if irrigation with Diphoterine® was performed. Interleukin IL₆ levels are also significantly decreased by irrigating with Diphoterine® [9].

It is clear that the earlier the irrigation the better. Our study showed that on average patients were waiting 27 min before Diphoterine was applied, which is not ideal. Having said that, it appears that Diphoterine® solution may have clinical value up to 24 h after injury [10].

Studies into the clinical efficacy of Diphoterine® solution have been previously reviewed and criticized [11–13]. A perfect study into the efficacy of Diphoterine® solution would involve identical chemicals for all patients, identical burn sizes and identical delays prior to irrigation. Like previous studies, our study reflects the fact that in real life chemical injuries are heterogenous and not everyone has immediate access to either water or Diphoterine® solution. Our study is also flawed by not having an objective measure of burn depth, such as by Laser Doppler Imaging. Nevertheless, by gathering prospective data we have been able to show a significant benefit in the use of Diphoterine® solution.

The ideal form of evidence to prove once and for all whether Diphoterine® does actually what it claims to do would be to perform a randomized controlled trial. That is never going to happen. The only way therefore to gain such knowledge is for the medical community to amass as much lower-grade evidence as possible and publish it. That is what we hope to achieve here.

5. Conclusions

The introduction of Diphoterine® solution in the irrigation method for treating chemical burns appears to result in less pain, faster healing, less time off work and less overall treatment costs.

The cost of such treatment is more than made up for in savings in treatment.

Author contributions

Study conception and design: Jeffery, Kulkarni.

Acquisition of data: Kulkarni.

Analysis and interpretation of data: Jeffery.

Drafting of manuscript: Jeffery, Kulkarni.

Critical revision: Jeffery, Kulkarni.

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