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Emergency treatment of eye burns: which rinsing solution should we choose?

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Abstract *Background:* In the treatment of eye burns few data on the comparative application of rinsing solutions exist. We present experiments in vitro and ex vivo on the pH changes that can be achieved in alkali eye burns with currently distributed and propagated rinsing fluids like water, saline solution, Cederroth Eye Wash Solution (including borate buffer), Diphoterine, Ringers lactate solution and phosphate buffer. *Methods:* Titration curves in beakers are compared with ex vivo experiments on isolated rabbit eyes. We exposed eyes to burns from filter paper soaked in 2 mol NaOH, continuously measuring the anterior chamber pH by means of a micro pH electrode placed near the endothelium. In each experiment—repeated five times—the corneal burn of 20 s in 2 mol NaOH was followed by a period of 15 min of rinsing under a defined flow of 66 ml/min. *Results:* We found highly significant differences in intracameral pH related to different types of rinsing solutions. The return of the intracameral pH to normal was not achieved by any of the rinsing fluids, but the best results were noted for of Cederroth Eye Wash Solution (Cederroth Industrial Products, Upplands Väasby, Sweden) and the Diphoterine- and Previn solutions (Prevor, Cologne, Germany). Water played an intermediate role whereas saline and phosphate buffer were not efficient at lowering intracameral pH after alkali burns. *Conclusion:* In alkali burns we recommend efficient buffering solutions. The tested isotonic phosphate buffer (PBS) was not effective at buffering the intraocular pH. Water was found to be much less efficient than Previn, Diphoterine or Cederroth Eye Wash solution in balancing intraocular pH.

Keywords Rinsing · Emergency · Alkali · Burn · Buffer · First aid · Amphoters

Introduction

Severe chemical eye burns cause up to 26.5% of all traumatic ocular injuries [9, 17, 24]. More than 23% of all patients suffer from permanent bilateral visual impairment.

The group at greatest risk are young men [10, 19]. Most of these accidents occur at work and in domestic situations. A smaller number of burns result from personal assault [10]. Alkali burns occur more frequently than eye burns caused by acid substances. Alkali-induced eye burns require long-term treatment [29]. Despite the maximal medical efforts, in some cases it is impossible to achieve rehabilitation [11]. This study tries to qualify and quantify the effects and importance of immediate emergency rinsing of the eye. It shows the measurable effects of the application of therapeutic emergency rinsing solutions on a burnt eye for a sufficient period. We aim to show the scientific background of factors of efficiency in the emergency treatment of eye burns.

In cases of chemical and thermal eye burns there is consensus about the immediate therapeutic first aid rinsing of the burnt eye [1, 12, 21, 22]. The typical pathophysiological course is characterized by a sudden change in tissue pH, which is suspected to have a great influence on the extent of the damage [13, 20, 29]. The immediate change in pH is not the real biological effect, but a primary estimation of the biochemical changes that occur between the caustic substance and the eye tissue. As the pH rises from the anterior stroma towards the inner eye we record pH changes in the anterior chamber within 1–2 min of alkali burns [6, 18]. At this point immediate and emergency rinsing of the burnt eye is important. Irrigation prevents additional injury of the eye by elimination and dilution of the corrosive and by its pH neutralization.

The therapeutic solutions used in emergency rinsing differ according to type of chemical reaction and buffer capacity. Further differences can be found concerning osmolarity and, accordingly, in the recommendations for their use. According to the recommendations of the ANSI Standard (The American National Standards Institute) from 2004 (Z358.1-2004) [35] rinsing starting with a maximum delay of 10 s after eye burns should be carried out for a period of no less than 15 min with a sufficient quantity of 500–1,000 ml of the isotonic physiological saline solution NaCl 0.9% or with the available solution, which in most cases is tap water [12, 14, 20, 24, 27]. These recommendations are also made by the labour protection organisations in addition to lowering the pain factor and protecting the healthy second eye from injury [33–35]. There are different recommendations on the use of rinsing fluids, varying from 3 min for rinsing with Diphoterine or Previn [3, 31] to 15 min for water, according to the ANSI standard. However, we know that the recommendation of 15 min is a long time and that clinical experience indicates the use of much shorter rinsing time in reality. Still, the official guideline of 15 min seems to be an important fact.

There are no systematic clinical or experimental studies on tap water efficiency at eye rinsing. The recommendation to use water is related to the availability of water in most places and to its low osmolarity. Osmolarity is the concentration of the ionised active particles in a certain quantity of solution (mosmol/l) or in a mass of cornea (mosmol/kg). The osmolarity of a rinsing solution is an important factor in its physical properties and for the direction of water and ion movement. Therefore, we observe the swelling or non-swelling of the cornea depending on the osmolarity of the rinsing solutions [8]. The lower osmolarity of water promotes its rapid penetration into the cornea. This causes an increase in corneal oedema with an increased diffusion way, which is responsible for a delayed rise in anterior chamber pH and a lower peak in the anterior chamber pH due to dilution. Another fact is that using a hyperosmolar solution prohibits the extra flow of water into the stroma of the cornea [8, 9]. The rinsing of a burnt eye, taking high amounts of ions from the burning agent, [8] with tap- or sterilised water causes severe differences in osmolarity leading to cell swelling, dilution and cell death [32]. The intact cornea of the rabbit has an osmolarity of 380–420 mosmol/kg, which changes to 1,280 mosmol/kg after burns [8]. Some studies recommend the use of Ringer lactate as buffer, which as an emergency rinsing solution may be more active than isotonic physiological saline solution NaCl 0.9% or balanced salt solution (BSS) [7]. BSS has the protective property of a weak buffer and prevents the swelling of the cornea under healthy conditions, and at the same time protects the endothelium [16]. Its osmolarity is similar to the osmolarity of aqueous humor and it has a physiological pH; moreover, it includes sodium and citrates [15].

Since the stroma of the burnt cornea has no protection against rinsing solutions, the optimal solution should be adjusted to the altered mineral content of the denuded stroma [33]. The mineral composition of a healthy rabbit cornea is different from that of common rinsing solutions like the physiological saline solution or phosphate buffers. Therefore, they do not have the property required to restore the cornea's mineral balance [33].

In the past, the phosphate buffer PBS was considered an optimal solution, the use of which was recommended by Laux et al. and and Roth [13, 23]. Widespread, this solution is used by many manufacturers. However, an animal experimental study made by Schrage et al. confirmed the complete calcification of the corneal stroma. It occurred in all corneas, which were burnt with 1 N NaOH for 30 s and afterwards continually rinsed three times a day with 500 ml of phosphate buffer for 16 days beginning on day 4 with white corneas in all animals. This calcification is a result of the external reaction of phosphates in the rinsing solution with calcium released from the distorted cells, tears and aqueous humor to form the calcium phosphate compound [25, 30]. The composition of phosphate buffer as an ionic solution is not similar to the ionic composition of cornea [26].

One of the working groups reported good healing results in severe chemical eye burn when treated with Diphoterine, which is an amphoteric molecule neutralising both acids and bases. Moreover, it possesses bond energy for radical parts, oxidation agents and other topological materials [4, 5].

Materials and methods

Measurement of pH in vitro in a beaker

The chemical properties of the therapeutic rinsing solutions described below were examined by means of beaker glass titration, in which the rinsing solutions were each added in steps of 5 ml to 0.5 N NaOH. With each solution three titrations were carried out. Continuous registration of the fluid's pH was performed under stirring at room temperature of 20°C. The solutions examined were: tap water from the University Hospital in Aachen, isotonic physiological saline solution NaCl 0.9% (Braun Melsungen), isotonic phosphate buffer solution PBS, Cederroth Eye Wash Solution (borate buffer), Previn solution and Diphoterine solution. The equipment used was a pH Radiometer PHM 240 Kopenhagen connected by a serial port to a personal computer using the UNI-MESS Light (AK-Computer Wesel) program. The solutions tested are described in Table 1.

Ex vivo pH measurements on rabbit eyes' aqueous humor

After these in vitro experiments we performed experiments in an ex vivo model on rabbit eyes taken immediately after death from the slaughterhouse. This model has been proven to be very similar to real living eye tissue concerning the reactions during a chemical eye burn as we published previously [8]. The rabbit eyes were kept in the orbit and prepared for measurement by small paracentesis of 1.7 mm diameter placing an pHmicroelectrode (MI-414 needle combination pH microelectrodes; Microelectrodes, Bedford, NH, USA) centred in the anterior chamber near to the endothelium. The eyes were kept under tonus by a saline infusion via the optic nerve head. Touching the lens or disruption of the lens excluded the eye from any further experiments. All eyes were burnt in 25 µl of 2 N NaOH for 20 s. The application of the standardized amount was done by filter paper soaked in 2 N NaOH for 20 s (25 µl). The type of filter paper had a medium smooth surface, its weight was 70 g/m^2, its thickness was 0.16 mm, its diameter was 10 mm, and its filtrate speed was medium fast (MN 615 1/4; Machery-Nagel, Düren, Germany). The relevant amount of NaOH was placed by a 10 mm diameter piece of the filter paper giving a reliable quantity of base touching the corneal surface simultaneously. In each group we measured five eyes from different animals. One group

Table 1 The chemical properties of the therapeutic solutions used for rinsing

Rinsing solution	Properties
Tap water	University Clinic of Aachen laboratory
Osmolarity	0.30 mosmol/kg
Previn amphoter Diphoterine German version	
Containing	3.8 g Diphoterine 6/100 ml; NaCl 1.8 g; glycine as stabilizer 0.75 g; Na mandelate 0.05 g (preservative), water demineralized to 100 ml
Measured osmolarity	876.3 mosm/kg
Charge number	P 730101 B
Diphoterine amphoter Diphoterine international version	
Containing	3.8 g Diphoterine 5/100 ml; NaCl 1.8 g; glycine as stabilizer 0.75 g; Na mandelate 0.05 g (preservative); water demineralized to 100 ml
Measured osmolarity	876.3 mosm/kg
Charge number	D 721206 C*
Phosphate buffer: PBS Dulbecco's Powder without Ca & Mg	
Containing	Sodium chloride 8,000 mg/l; potassium chloride 200 mg/l; potassium phosphate monobasic KH2PO4 200 mg/l; sodium phosphate dibasic Na_2HPO_4 anhyd. 1,150 mg/l; grams per litre of powder required to make 1 l liquid media: 9.55 g
Measured osmolarity	279 mosm/kg
Charge number	646 B
Saline solution NaCl 0.9%	
Containing	Natrium chloride 0.9 g/100 ml, water demineralized to 100 ml; electrolyte: Na^+ 154 mmol/l, Cl^- 154 mmol/l
Measured osmolarity	289 mosm/kg
Charge number	26308 D
Cederroth Eye Wash Solution	
Containing	Borate buffer, NaCl 0.9% solution
Measured osmolarity	296 mosm/kg
Charge number	30016

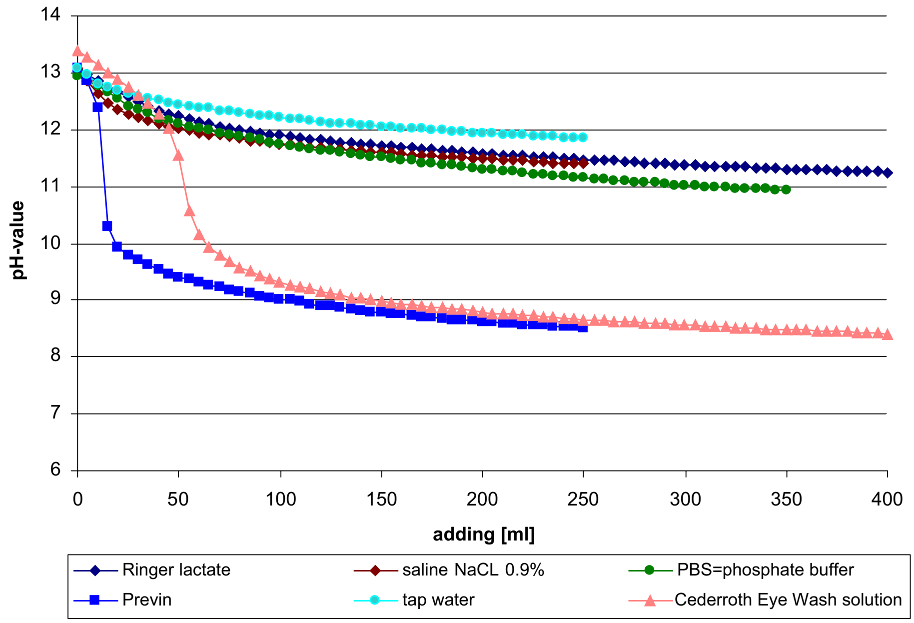

Fig. 1 Titration curves of alkali (caustic) in a beaker glass showing the changing of pH value with the solutions used. Five millilitres of each of the rinsing fluids were added to a 0.5 mol solution of NaOH. The dilution curves mainly appear for saline, tap water, phosphate buffer, and Ringers lactate. Cederroth Eye Wash Solution and Previn proved to be efficient and of high buffering capacity.

was not treated, but measurement of intraocular pH was performed for 1,200 s. Immediately after exposure to the soaked filter paper all other eyes were rinsed for 15 min at a stable flow of 66.66 ml/min. An intravenous infusion system (Braun-Melsungen, Melsungen, Germany) connected to a precision pump with a pumping rate of 66.66 ml/min was connected to the containers delivered by the producers and placed open ended directly over the middle of the cornea. The different eye rinsing solutions were as described above: tap water from the University Hospital in Aachen, isotonic physiological saline solution NaCl 0.9% (Braun Melsungen), isotonic phosphate buffer solution (PBS), Cederroth Eye Wash Solution, Previn solution and Diphoterine solution. For 20 min the intracameral pH value was measured continuously each second.

Results

All rinsing solutions changed the pH in the beaker glasses. Concerning alkali there was no evident difference between tap water, saline solution, phosphate buffer and Ringer's

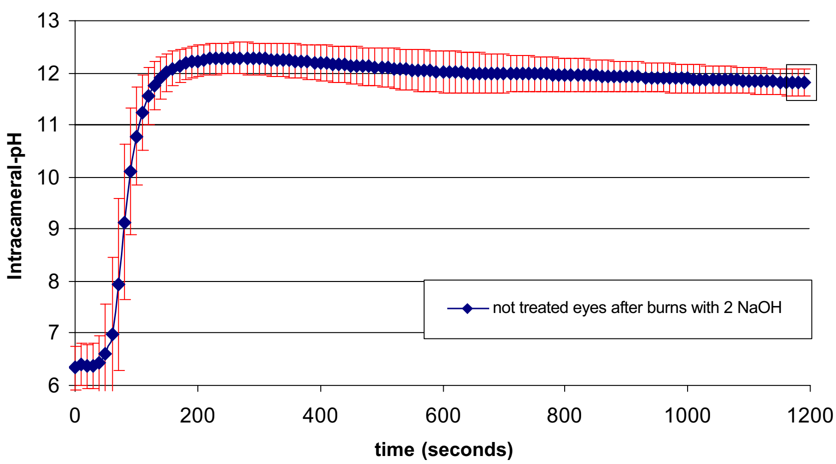

Fig. 2 Mean and standard deviation of the intracameral pH changes of the untreated rabbit eye (n=5) by measuring the pH in the anterior chamber after application of filter paper soaked in 25 µl of 2 mol NaOH solution for 20 s. The pH stays high for a long period of time. After 70 s the pH value rises. We explain this time as being due to the fact that it is the necessary period for the hydroxyl ion to be available in the eye. During this time the cornea is continuously destructed from the external part toward the internal part with the increase in pH value of the anterior chamber. The results are highly significant (p<0.001 in comparative t test).

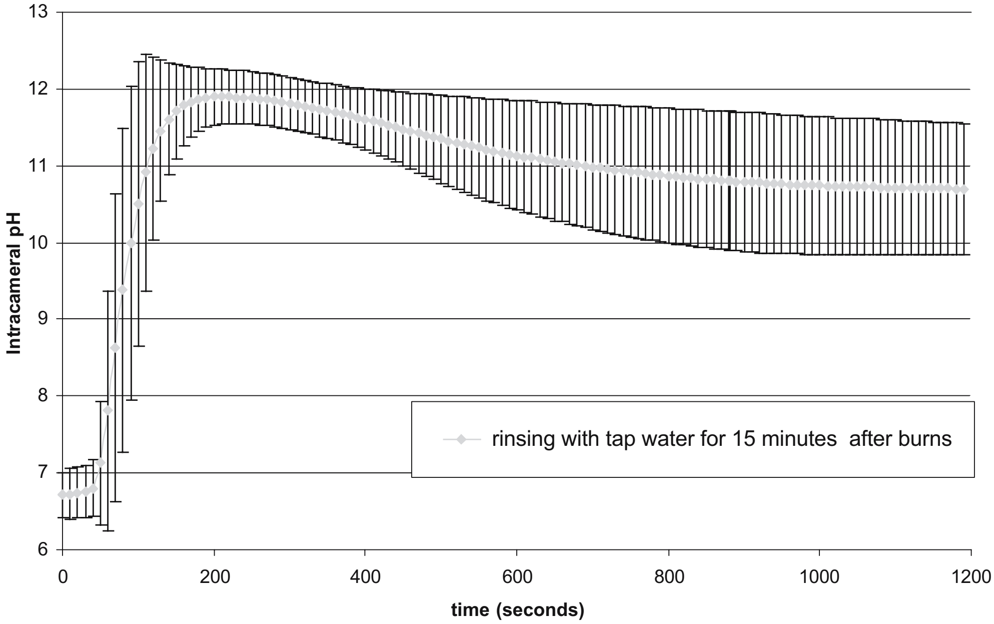

Fig. 3 Mean and standard deviation of the intracameral pH changes in the rabbit eye (*n*=5) by rinsing treatment for 15 min with tap water (ANSI Z-358.1-2004) after alkali burning with 25 µl of 2 mol NaOH for 20 s.

lactate. Buffering characteristics could be found for Previn and Cederroth Eye Wash Solution (Fig. 1). The differences between the two groups described were highly significant at volumes of more than 5 ml solution (p<0.007) for all measurements.

Ex vivo pH measurements on rabbit eyes

In all groups in the ex vivo experiment on rabbit eyes we found a stereotype indicating the penetration of hydroxyl-ions into the anterior chamber (Fig. 2). This was less pronounced in the group rinsed with water (Fig. 3) and more marked for all solutions containing electrolytes. The initial peak was highest for phosphate buffer followed by saline (Figs. 4, 5) and somewhat lower for Diphoterine (Fig. 6), Previn (Fig. 7), and Cederroth Eye Wash Solution (Fig. 8). The lowest initial peak with highest standard deviations was reached by water. Except for phosphate buffer and saline solution there was a considerable lowering of the intraocular pH after more than 200 s. This lowering was weak after tap water rinsing, ending at pH 11, and best after rinsing with Previn, Diphoterine, and Cederroth Eye Wash Solutions. For better comparison we plotted these data into the single solution diagrams of Figs. 2, 3, 4, 5, 6, 7, 8 and all together within one diagram leaving out the standard deviations (see Fig. 10). To exclude differences in the mean starting pH we normalized the starting points to zero and only plotted the differences between the groups (Fig. 9).

From the data presented it can be seen that in the setting of severe eye burns the rinsing period of 15 min is effective on the intracameral pH. However, neither of the therapeutic rinsing solutions could return the pH to its normal level, i.e., 7.4. Previn brought it down to 8.6 (Fig. 7) and Diphoterine to 8.4 (Fig. 6), Cederroth Eye Wash Solution led to pH 9.1 (Fig. 8), water to pH 10.7 (Fig. 3) and isotonic physiological saline solution to pH 11.5 (Fig. 4). Twenty

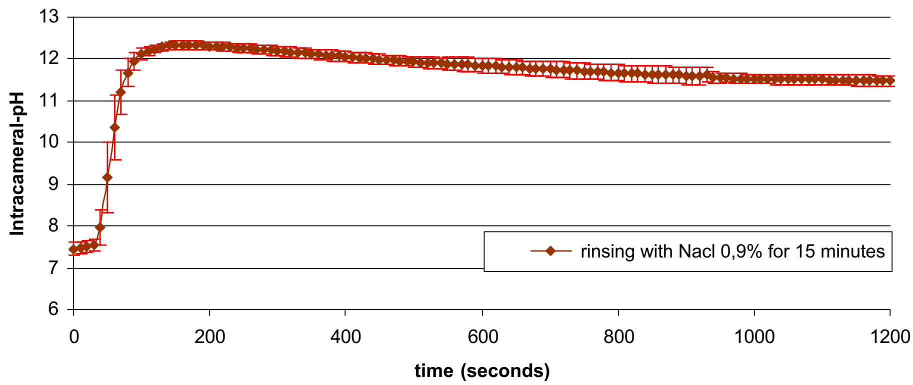

Fig. 4 Mean and standard deviation of the intracameral pH changes by therapeutic rinsing with NaCl 0.9% after chemical burning with caustic soda lye in 25 µl of 2 mol NaOH for 20 s. There is a narrow standard deviation compared with Figs. 2, 3, 5–8.

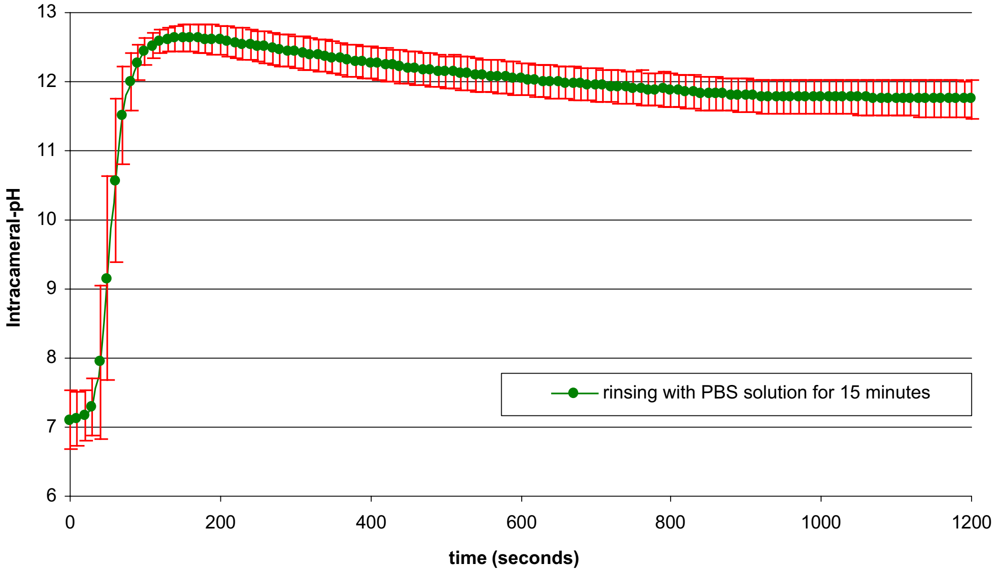

Fig. 5 Mean and standard deviation of intracameral pH changes by the therapeutical rinsing with PBS phosphate buffer after chemical burning with 25 µl of 2 mol NaOH for 20 s.

minutes after the burning irrigation with phosphate buffer and saline solution could not change the intracameral pH considerably. Similar results have been found in pig corneas [8, 32].

Figure 10 extracts the results of measurements of ex vivo intracameral pH.

The statistical study has been performed using the comparative *t* test for each group. The results of rinsing for a period of 15 min in the paired *t* test is not significantly different for non-rinsing versus phosphate buffer treatment, tap water and isotonic physiological saline solution. For Diphoterine, Previn and Cederroth Eye Wash Solution the efficiency of rinsing in alkali burns within 15 min was statistically proven (p<0.001 for all observations except for tap water versus saline solution [p=0.75]).

Discussion

The immediate first aid rinsing for a period exceeding 10 min is recommended by Laux [13]. Moreover, emergency rinsing using a buffer solution decreases the pH of the conjunctiva and in the eye in general [7]. The cornea is conditioned by the rinsing fluids, which could be demonstrated for phosphate buffer [29]. From our previous data we know that this is similar for all other substances being tested here [27], even for the amphoteric solutions like Previn or Diphoterine, which are able to neutralize bases and acids at the same time. An earlier study [12] with burning for 30 s in 1 N NaOH and immediate irrigation for 5 min showed similar results for the anterior chamber pH.

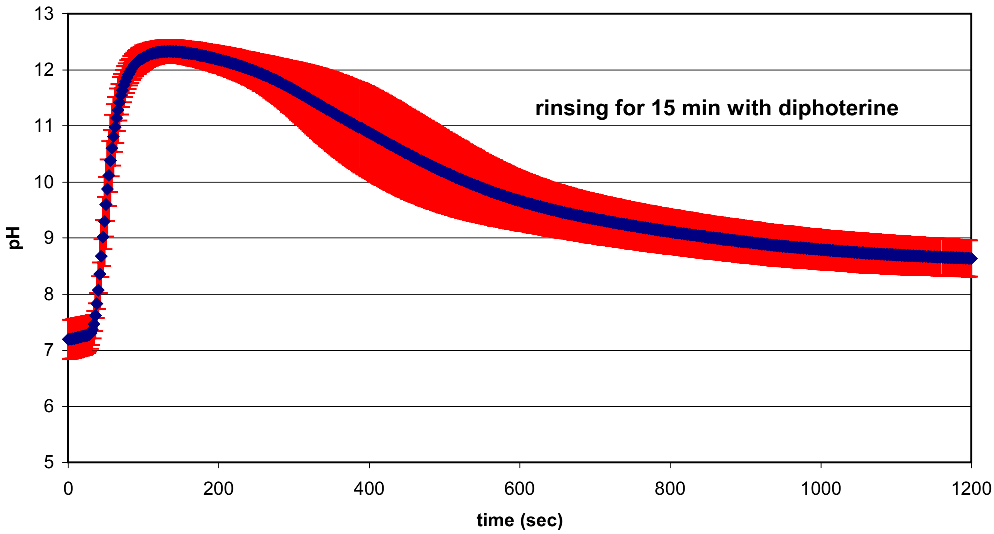

Fig. 6 Mean and standard deviation intracameral pH changes by the therapeutical rinsing with Diphoterine after chemical burning with caustic soda lye (25 µl of 2 mol NaOH for 20 s).

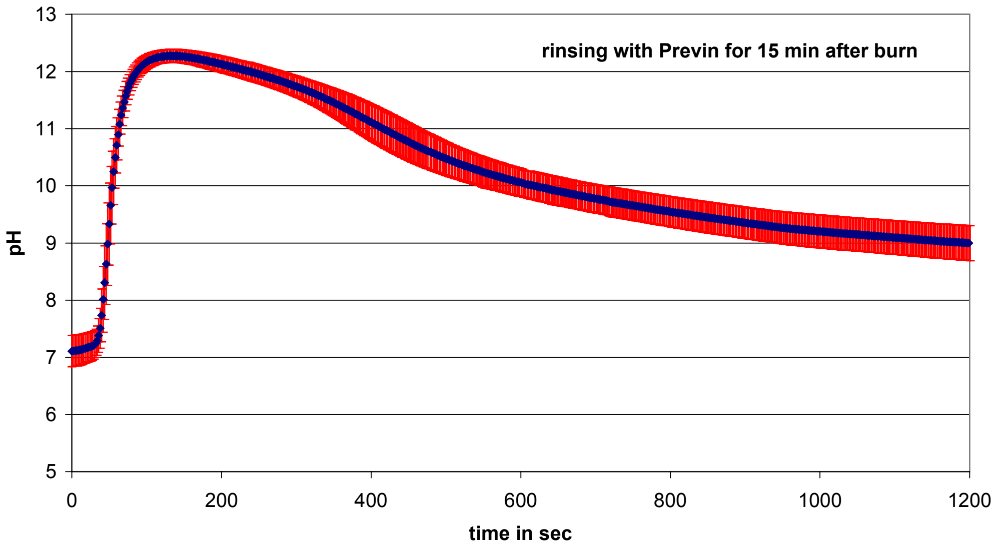

Fig. 7 Mean and standard deviation of the intracameral pH value in the rabbit eye (n=5) by rinsing treatment with Previn after alkali burning with 25 µl of 2 mol NaOH for 20 s.

As it is believed in the medical media that treatment with phosphates leads to the return of the pH in the anterior chamber to its normal level of pH 7.4, this concept was the starting point of most of the modern studies. The recommendation of rinsing [2] with sterilized saline or phosphates, advocated since 1953, has remained unchanged and it has not been actualized by a comparative study on the solutions used in the emergency treatment of chemical or thermal eye burns [2]. Rinsing, furthermore, effects a considerable cooling of the anterior eye [28] and eliminates the severe inflammatory factors resulting from chemical burns [7]. The delay in starting with rinsing therapy and its effect on the course of disease and prognosis has been dealt with in detail [12]. But up till now there have been no prospective studies on tap water as a first aid rinsing solution or special solutions in cases of chemical eye burns. We studied the effects of Diphoterine and phosphate experimentally on healthy human eyes and these solutions have been well tolerated [8]. Moreover, reports of therapeutic cases have been published after treatment with Diphoterine, describing good results [5].

There are some additional observations in this study that must be discussed. There are very small standard deviations for all ionic components in this study. This reflects the effect of ionic forces on the interaction of buffers and fluids with the burnt cornea that is not yet understood. To us the huge standard deviation of anterior chamber pH in the group rinsed with water seems to be indicative of the still unknown effects on the tissue and pH with the use of ionic components. The pH and ionic content of the anterior chamber after experimental burning is far out of the range of measuring tolerance of pH meters so that there is no doubt about the accuracy of the measurements. The initial peak of pH in the anterior chamber is highest with untreated and ionic components in all cases in which PBS seems to peak highest. As yet we do not know whether the peak or the area under the pH curve is a limiting factor of cellular survival in the biological system of the anterior chamber of the eye.

Our study is the first experimental study made on the eye dealing with the effect of tap water as a therapeutic emergency rinsing solution in chemical eye burns com-

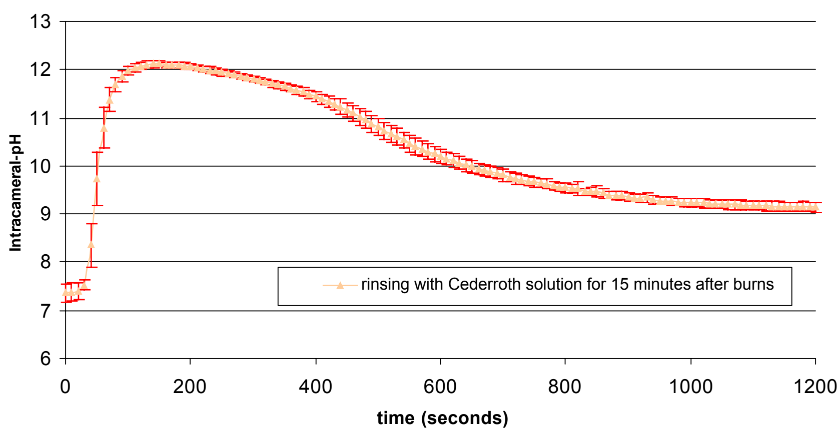

Fig. 8 Mean and standard deviation of the intracameral pH changes of the rabbit eye (n=5) after chemical burning with 2 mol NaOH for 20 s and rinsed with Cederroth Eye Wash solution.

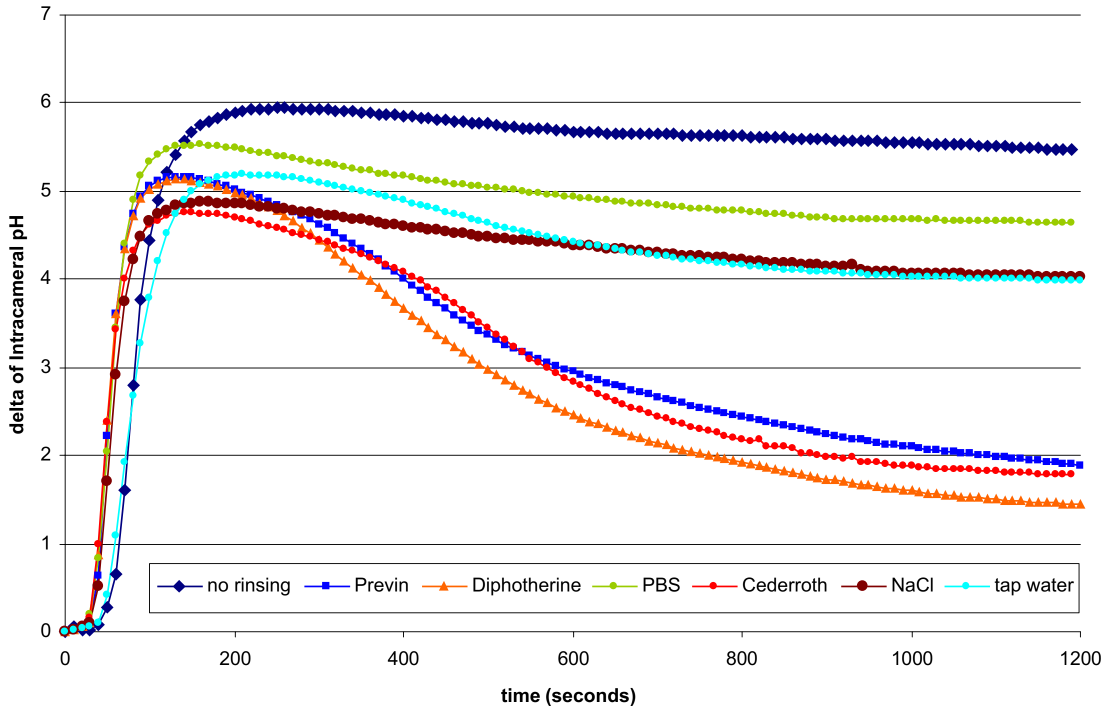

Fig. 9 Comparison of all rinsing fluids for 15 min of rinsing. The data all start from the same point called 'normalized data' using the individual starting point for each substance as zero: delta pH is given in this plot (*n*=5 measurements per substance). The normalized data show that the efficiency of rinsing fluids is somewhat different in this respect compared with Fig. 10 and can be described ranging from non-neutralizing to neutralizing: phosphate buffer (PBS), tap water, saline solution and Previn, Cederroth Eye Wash Solution, and Diphoterine. These last three solutions proved to be highly significantly more effective in lowering pH for all observations >250 s compared with untreated cases and rinsing with water, saline and PBS solution (p<0.001, comparative *t* test).

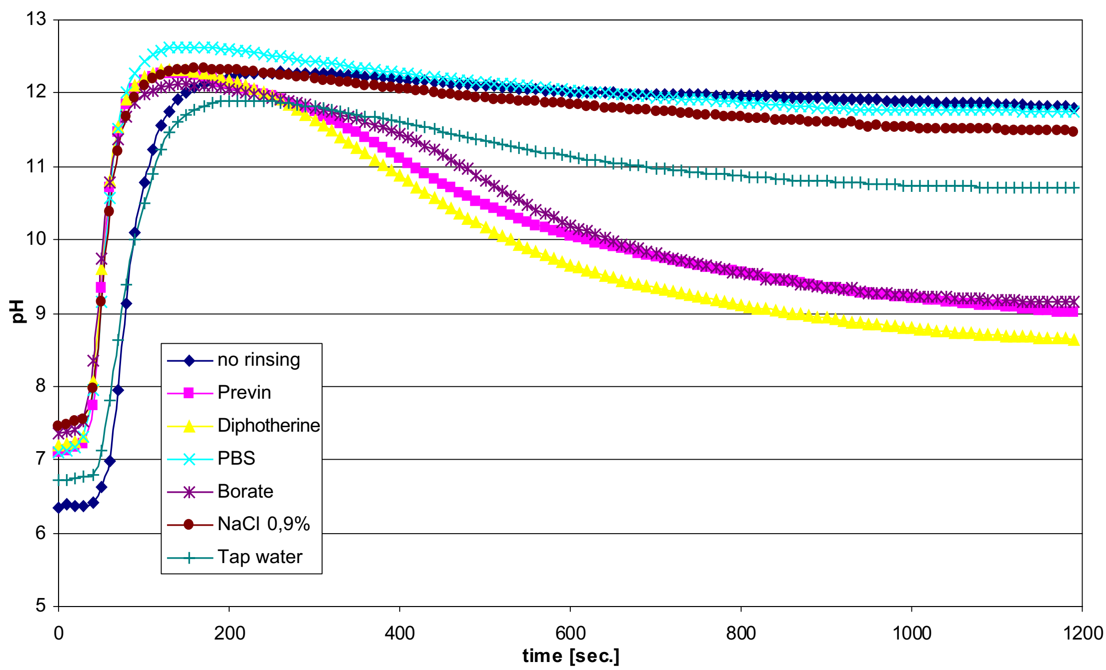

Fig. 10 Comparison of all rinsing fluids in an original data diagram (*n*=5 measurements per substance). The efficiency of rinsing fluids must be described on the basis of the upper curves in the zone later than 400 s after initial burning. Non-neutralizing in the aqueous humor in this setting are phosphate buffer (PBS), tap water, and saline. The three following solutions showed buffering qualities: Cederroth Eye Wash Solution (Borate), Previn and Diphoterine. The results of these three were highly significantly more effective in lowering pH for all observations >250 s compared with untreated eyes and with treatment with water, saline and PBS solution (p<0.001, comparative *t* test).

pared with the special rinsing solutions. Unless eyes of recently deceased rabbits are considerably different from living eyes concerning circulation and starting pH, the neutralization curves that we found in most cases are similar to those that Kompa et al. published in a report on living rabbits' eyes [8].

There is a major discussion point in comparing the original data with the normalized data as presented in Figs. 9 and 10. There is a possible dependency of the initial pH peak on the starting point of pH 6.34 to 7.45. This in fact seems to be doubtful because the changes from the initial starting point to the somewhat later measured peak are related to the concentrations of OH^- and H+ ions in order of magnitudes that have no relation to the initial values. The concentration of the 2 mol NaOH is so high that the trauma and diffusion via the corneal stroma will raise the pH in the anterior chamber independent of any initial pH between 6 and 8. Regarding decreasing pH values later on, we believe that the initial pH does not have any effect due to the enormous dilution or buffering by the huge amounts of fluids that we applied in all our cases. Nevertheless, we present the normalized data to get some sort of idea of the absolute scale of changes (Fig. 10).

Tap water is available in most places and has the property of dilution with low osmolarity compared with the corneal stroma and intraocular milieu. Schrage et al. measured the osmolarity of the healthy cornea of the rabbit eye as being 420 mosmol/l [30]. Rinsing with tap water leads to increased water influx into the cornea by ion exchange from the ionic loaded cornea after burning toward the hypo-osmolar water. To protect the cornea from swelling the application of hyperosmolar solutions prevents water entry into the cornea [12].The advice that the ANSI Standard gives for the usage of tap water in the emergency treatment of chemical eye burns is that it remains safe as long as the accident occurs in a place where no preparations have been made for an emergency and where no therapeutic rinsing solutions for the treatment of eye burns are at hand. However, these recommendations are not acceptable as soon as the accident happens in a place where such burns must be expected, such as in factories or laboratories. Here, care must be taken that special rinsing systems are available, including guaranteed and tested therapeutic rinsing solutions.

Our measurements of alkali burns show clear results in the equation of OH ions for Previn, Diphoterine, and Cederroth Eye Wash Solution in the experiments on ex vivo corneas and in vitro. This is confirmed in our preparatory study for these experiments on alkaline burns, which was published in 2004 [31]. The results of our ex vivo study on the animal eye, which comes close to the real process of a chemical eye burn, supported these results and confirmed that best efficiency was achieved by Diphoterine followed by Cederroth Eye Wash Solution and Previn. In this setting of alkaline eye burns these solutions are to be preferred to tap water in the emergency treatment of a freshly burnt eye. On the other hand, tap water proved to be preferable to phosphates or the physiological saline solution in this setting.

In severe eye burns as simulated here the ANSI recommendation of 15 min of rinsing is useful in order to lower the intraocular pH toward a level below pH 9 in cases of alkali eye burns by application of Previn, Cederroth Eye Wash solution, and Diphoterine. All other special eye wash solutions fail in this aspect. In normal cases, as published in the INRS report [3], the eye burning period is shorter and the damage not as severe. Therefore, the strict recommendation of 15 min rinsing for severe eye burns seems reasonable to us and gives a good and safe outline in cases of unknown history of severe eye burns.

Recommendation

In chemical eye burns we generally recommend a prompt rinsing with agents of high neutralizing capacity as emergency treatment. In our experiments on the most severe eye burns a period no less than 15 min was required to return the pH to normal. There is even a description in the literature that shorter rinsing times produce good clinical results [3] (not tested here) with a quantity no less than 1,000 ml of one of the high activity therapeutic solutions such as Diphoterine, Previn and Cederroth Eye Wash Solution. These solutions, with their varying osmolarities, can equalize the destructiveness of the substance that causes the burn on the eye's surface in a better way than phosphates or physiological saline solution, which did not show any therapeutic activity in the model of severe alkali eye burns used in this study. Rinsing with tap water had an intermediate position on the scale of efficiency, but was much less effective in this experiment than the amphoteric or buffering solutions.

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