Long-term Management of Severe Ocular Surface Injury Due to Methamphetamine Production Accidents

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Purpose: The aim of this study was to report the clinical features and management of patients with ocular surface damage during methamphetamine production accidents.

Methods: This is a retrospective noncomparative interventional case series of 5 patients with methamphetamine production–related ocular injuries referred to the Cincinnati Eye Institute between 1999 and 2014.

Results: Four of 5 cases were white young men with severe bilateral ocular injury and extremely poor vision. All except 1 eye (9 of 10) were diagnosed with total or near-total ocular surface failure. Limbal stem cell transplantation was performed in 8 of 10 eyes. Keratolimbal allograft was followed by penetrating keratoplasty in 7 of 10 eyes. Ocular surface stability was achieved in 7 of 10 eyes after keratolimbal allograft. Postoperative visual acuity was better than 20/200 in 4 of 10 eyes; the rate of rejection of penetrating keratoplasty was also 3 out of 10 eyes.

Conclusions: Methamphetamine-related accidents can lead to severe bilateral ocular injuries. Although stem cell transplantation procedure success is guarded in most of these patients because of severe conjunctival inflammation and accompanying ocular comorbidities, as well as personality issues, compliant patients can achieve good visual function with ocular surface transplantation and subsequent keratoplasty.

Key Words: methamphetamine, ocular surface, keratolimbal allograft, chemical injury

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methamphetamine type stimulants are the second most widely used class of illicit drugs worldwide.1 Particularly, methamphetamine production and use has had a tremendous surge in the last 2 decades all across the globe.

This is because the drug can be easily made in small clandestine laboratories, with fairly low-cost over-the-counter ingredients such as pseudoephedrine. However, methamphetamine production involves other dangerous ingredients such as anhydrous ammonia (in fertilizer), lye (sodium hydroxide), swimming pool cleaner (hydrochloric acid), red phosphorous (in matches), ethyl ether (engine starter fluid), and lighter fluid (butane).2

Each year, the number of methamphetamine laboratory incidents grows according to the Drug Enforcement Administration.3 In a study performed in Iowa, almost 10% of patients admitted in a burn unit in a period of 16 months had facial and ocular injuries related to methamphetamine production accidents.4 These accidents typically occur from an explosion caused by mixing of flammable liquid ingredients, caustic agent spills, or propane gas container explosions. Recently, the so-called “shake-and-bake” has emerged as a rough new method where the raw materials are mixed in 2-L soda bottles. Hence, the chances of accidents are tremendously higher, and this could be translated into a substantial increase in the number of methamphetamine-related chemical injuries.

In the largest retrospective analysis of methamphetamine-associated burns, the face was the most frequently injured area with 70% involvement. Ocular surface burns were diagnosed in nearly 20% of cases in that study.5

To the best of our knowledge, there is only one short report specifically focusing on ocular injuries due to methamphetamine-related burns in the literature.4 Lee et al6 also mentioned 3 cases of ocular injury due to anhydrous ammonia injuries associated with methamphetamine production in a letter.

We sought to review a series of cases with ocular injury due to methamphetamine-manufacturing accidents, which were referred to the Cincinnati Eye Institute for treatment. The focus of this study was to report the long-term management and outcomes of these patients.

PATIENTS AND METHODS

This is a retrospective chart review study of 5 patients with methamphetamine production–related ocular injuries between January 1999 and May 2014. After obtaining approval from the ethics committee, the patients’ records fitting the inclusion criteria were reviewed. The inclusion criteria comprised all methamphetamine production–related ocular injuries that were referred to the Cincinnati Eye Institute.
Institute’s cornea clinic for evaluation and management, with a minimum of 1-year follow-up.

The parameters assessed included demographics, the causative chemical agent according to patient statements, presenting features before management, indications for ocular surface procedure, preoperative Snellen best spectacle-corrected visual acuity (BSCVA), intraoperative and postoperative complications and the course of the disease including postoperative BSCVA and ocular surface stability up to the last follow-up. Ocular surface stability was determined based on the presence or absence of late fluorescein staining (conjunctival epithelium on the cornea). The ocular surface condition was classified as stable, partially failed, or totally failed. A stable ocular surface had an intact corneal epithelium devoid of conjunctivalization or inflammation. A partially failed ocular surface was defined as an eye with areas of abnormal conjunctival epithelium on the cornea and regions of normal looking cornea. Total ocular surface failure or visually significant failure was defined as total compromise of the ocular surface with complete corneal conjunctivalization and/or inflammation substantially impacting the patient’s vision.

RESULTS

The mean age of patients was 29.6 ± 4 years at the time of injury. Four of 5 cases were white young men, who had severe bilateral ocular injuries and were referred to us with extremely poor vision. There was only 1 female patient among our cases, who was also white. Injuries were unanimously bilateral, however with asymmetrical severity of involvement. All but 1 patient could identify the particular chemical substance by which the injury occurred. All of the identified chemicals were alkaline in nature, the most common being anhydrous ammonia (40%). All of the patients gave a false history on initial admission. Plumbing was the most common falsely reported activity during which the accident happened. However, each patient eventually gave the history of a methamphetamine production accident. The patients were referred to us for treatment between 3 months and 3 years after the causative accident. The injuries were extremely damaging to the ocular surface. Nine of 10 eyes were diagnosed with total ocular surface failure, manifested as total conjunctivalization/neovascularization of the cornea with late fluorescein surface staining, inflammation, and scarring of the ocular surface, as well as symblepharon, ankyloblepharon, and foreshortening of fornices. In addition to ocular surface abnormalities, 5/10 had cataracts and 3/10 had high intraocular pressure at initial assessment visits. Preoperative visual acuity (VA) was very poor in most eyes with 9/10 of eyes having BSCVA of counting finger at 3 feet or less.

The mean follow-up time was 30.6 ± 24 months (range, 12–59 months). Indications for surgical intervention included ocular surface failure and corneal opacity in all eyes. All of the patients had total ocular surface failure with 100% surface late staining, complete scarring and conjunctivalization. Previous treatments such as amniotic membrane or buccal mucosal grafts were ineffective in cases that underwent those procedures.

Keratolimbal allograft (KLAL) was performed in 8/10 of eyes. Penetrating keratoplasty (PK) followed KLAL in 7/10 eyes. Ocular surface stability was achieved in 7/10 of eyes after KLAL. Postoperative VA was better than 20/200 in 4/10 of eyes. Keratolimbal graft rejection occurred in 3/10; the rate of rejection of PK was also 3/10.

There was no intraoperative complication in any of eyes undergoing KLAL or PK. The major postoperative complication was KLAL or PK rejection. There were 2 KLAL and 1 PK rejection episodes. In 1 case, KLAL rejection was initially resolved with medical treatment, but eventually, the graft progressively failed. The other 2 cases of rejection (1 KLAL and 1 PK) were not responsive to medical treatment and failed rapidly.

Table 1 summarizes the key parameters of interest in 5 patients. Three of our cases (6 eyes) had poor compliance. Two of them had poor follow-up as well. The 2 patients who were more compliant (4 eyes) achieved much better visual outcomes between 20/40 and 20/300. The poor visual outcome in 2 of our patients is most likely because of lack of follow-up. Figure 1 illustrates pre- and post-op images of a 28-year-old lady with bilateral ocular injury due to methamphetamine production accident.

DISCUSSION

Previous studies in the past decade estimated that between 2% and 4% of burn unit admissions in hospitals located in endemic regions of the United States were methamphetamine related, and the numbers are estimated to rise.7,8

Since the upsurge of methamphetamine-related accidents in the last 2 decades, investigators have noticed significant differences in the forms and severities of injuries caused by this type of accident. It was observed that methamphetamine burn patients have significantly more fluid loss than the same percentage of body surface involvement in patients with non–methamphetamine-related burns. Also, despite the younger age, the mortality with comparably sized burns was significantly higher.7

Ocular injuries are commonly reported in methamphetamine-manufacturing accidents.5 In predominately farming regions of the United States where the problem is endemic, as high as 60% of burns involve ocular injury.9

Similar to previous reports on severity of injuries in this group of patients,7,9 ocular injuries are routinely very severe. In our cases, injuries were invariably bilateral and had severely compromised vision. One reason could be the nature of the hazard; these accidents not only cause chemical injury but also damage tissues by thermal burn and traumatic force of the explosion. Moreover, the primary causative agent was frequently reported to be an alkali. One of the key ingredients for so-called “dry cooking of meth” is anhydrous ammonia. This alkaline substance is primarily used in farming to develop fertilizers. Most of our patients reported working with anhydrous ammonia when the accident occurred, similar to previous reports.6,9

Bloom et al reported anhydrous ammonia as the most common cause of chemical injury with 40% of cases of all chemical injuries in a tertiary hospital in southern Illinois;
Interestingly, 75% of which were injured during manufacturing of methamphetamine.

The authors also found that anhydrous ammonia exerts a combined thermal-chemical effect on tissues resulting in considerably greater damage to the tissue compared with non-methamphetamine-related chemical injuries. This might explain the disproportionate severity of injuries seen in multiple studies in those who had methamphetamine production accidents.

Another possible reason that could explain the extent of the damage is delay in reporting the incident and especially seeking primary medical care. The patients tended to give false histories and were generally less compliant with medications and follow-ups.

Oral immunosuppressive medications are the mainstay of management of stem cell transplantation after the procedure. Our patients received our systemic immunosuppressive protocol. This regimen consists of tacrolimus, mycophenolate mofetil, and a short course of oral prednisone (3 months or less). Dose adjustment is required for tacrolimus based on blood levels taken each month;

### TABLE 1. Key Features of Management and Follow-up of 5 Cases of ocular Injury Due to Methamphetamine Explosion

| Eye No | Preoperative VA | Previous Surgical Treatments | Surgical Management | KLAL Failure/Rejection Cause | PK Rejection/Failure Cause |
|--------|-----------------|-----------------------------|---------------------|-----------------------------|---------------------------|
| 1      | HM              | Amniotic membrane grafts (twice) and lensectomy | 1. KLAL 2. PK (3 mo after KLAL) | Acute KLAL rejection initially resolved by medical therapy later recurred as progressive graft failure secondary to glaucoma manifested by corneal edema | None |
| 2      | LP              | Amniotic membrane grafts (twice), tube shunts and Lensectomy | 1. KLAL 2. PK (6 mo after KLAL) | Progressive KLAL failure Secondary to glaucoma manifested by epithelial irregularity | PK failure secondary to hypotony manifested by corneal edema |
| 3      | CF at 3 ft      | None                        | 1. KLAL 2. PK (3 mo after KLAL) | None | None |
| 4      | HM              | None                        | KLAL | KLAL rejection due to stopping steroid drops by the patient manifested by neovascularization | PK failure due to stopping steroid drops by the patient manifested by corneal edema |
| 5      | LP              | Amniotic membrane graft     | KLAL | None | None |
| 6      | LP              | Amniotic membrane graft     | None | None | None |
| 7      | 20/300          | None                        | 1. KLAL 2. PK | None | None |
| 8      | CF 2 ft         | None                        | 1. KLAL 2. PK | None | None |
| 9      | HM              | Tarsorrhaphy                | 1. KLAL 2. PK + sectoral KLAL | Sectoral KLAL failure manifested by limbal injection and neovascularization because of noncompliance; Difluprednate drop hourly was started and systemic mycophenolate mofetil dosage was increased; Outcome was undetermined | PK rejection manifested by endothelial rejection line because of noncompliance |
| 10     | HM              | Tarsorrhaphy                | None | None | None |

| Additional Procedures | VA in Last Follow-up | Ocular Surface Condition in Last Follow-up | Total Follow-up, mo | Compliance |
|-----------------------|----------------------|---------------------------------------------|---------------------|------------|
| 1                     | Secondary IOL, tube shunt | 20/60 | Stable | 56 | Compliant |
| 2                     | Secondary IOL, tube shunt, pars plana vitrectomy/retinal detachment repair, repeat PK (twice) | 20/300 | Stable | | |
| 3                     | Phaco                | 20/125 | Stable | 14.3 | Poor follow-up and noncompliant |
| 4                     | Phaco, repeat PK     | HM | Total surface failure | 12 | Noncompliant |
| 5                     | Symblepharon lysis, buccal membrane graft | HM | Stable | | |
| 6                     | Tube shunt, phaco    | LP | Total surface failure | | |
| 7                     | Tube shunt, phaco    | 20/40 | Stable | 59 | Compliant |
| 8                     | Tube shunt, phaco    | 20/50 | Stable | | |
| 9                     | Inferior sectoral KLAL | 20/200 | Partial surface failure | 12 | Noncompliant |
| 10                    | None                 | HM | Total surface failure | | |

CF, counting fingers; HM, hand motions; LP, light perception.

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Cornea

Likewise, the ocular injuries and often occurred due to nonhealing corneal epithelial defect.

tacrolimus is usually tapered off at 12 to 18 months. Mycophenolate mofetil was continued for our patients for the minimum of 24 to 36 months considering the remaining inflammation and tolerance to the medication.

Topical prednisolone was continued 4 times daily for the first 3 months and tapered by 1 drop per month until a proper maintenance dose was achieved. Topical cyclosporine was continued twice daily during the follow-up period, and topical fluoroquinolone was stopped after the epithelium was healed. We start postoperative topical management of PK as early as 4 hours after surgery with cyclosporine 0.05% 2 times daily, prednisolone acetate 1% 4 times daily, and a fourth-generation fluoroquinolone 4 times per day.

This study has its limitations. It is very likely that our patients have been the most severely affected cases of methamphetamine-related accidents; however, some other unidentified cases may be missed because they have refused to give the correct history. However, most of the previous studies reported poor follow-up, and thus their data are collected from much shorter follow-ups and none has reported the outcome of treatment.

It has been shown that the average methamphetamine patient’s hospital stay cost is 60% more than other non-methamphetamine-related burn patients. Likewise, the costs of ophthalmic care could be comparatively higher in such patients.

Those who had such injuries are typically young individuals who have nearly lost sight in both eyes. The severity of the damage is extreme and often multiple ocular procedures and regular long-term follow-ups with several ophthalmic subspecialties are required to increase the chance of a better visual outcome. The cost of health care becomes even more challenging because most of these patients are uninsured. Although appropriate emergent care is the key to management of all chemical/thermal injuries, it is important to address future care by timely referral of the patients for tailored long-term management.

In summary, methamphetamine-related accidents typically lead to severe bilateral ocular injuries and often blindness. Although stem cell transplantation’s success is limited in most of these patients because of severe conjunctival inflammation and accompanying ocular morbidity, this procedure is of great value in long-term management, particularly in compliant patients. In one of our patients, the preoperative VA of counting fingers at 2 feet reached functional vision of 20/40 five years after transplantation. The 2 of our cases (4 eyes), who had good compliance, did very well in long-term follow-up compared with the rest of the cases with very poor compliance and/or follow-up.

Although it is difficult to draw a solid conclusion with few numbers of cases, we observed that the outcomes of the management in our cases were highly related to the degree of compliance.

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