

Cluster of Postinjection Abscesses Related to Corticosteroid Injections and Use of Benzalkonium Chloride

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Benzalkonium chloride (BC) is an unreliable disinfectant. A matched case-control study and environmental investigation were conducted to determine the cause of and risk factors for a cluster of postinjection abscesses at a private medical clinic where BC was used as a disinfectant. Twenty-eight case-patients who had an abscess at the injection site were matched with 126 control patients who had received an intramuscular injection at the clinic on the same day. Risk factors for abscess development in a multivariable logistic model were corticosteroid injection and being female. All case-patients had received a corticosteroid injection from a multidose vial. Cultures of abscesses from 20 of 23 case-patients grew *Pseudomonas aeruginosa*. Cultures of BC prepared at the clinic also grew *P aeruginosa*, suggesting that BC was the source of infection. Injection site cleaning with BC did not appear to be the route of infection since use of BC at the time of injection was not associated with abscess development. A more likely route of infection was injection of contaminated corticosteroid from multidose vials that could have been inoculated with pseudomonads via needle puncture after vial septa were wiped with contaminated BC. Benzalkonium chloride should not be used to clean injection vial septa or injection sites.

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Benzalkonium chloride is an unreliable disinfectant: Gram-negative organisms (eg, pseudomonads) often are resistant to benzalkonium chloride, and benzalkonium chloride's efficacy is diminished when substances that adsorb the compound (eg, cotton balls or gauze) are immersed in it.¹⁻³ The use of benzalkonium chloride in hospitals has been discouraged by the Centers for Disease Control and Prevention since 1976.⁴

In spring 1995, several patients at a private medical clinic in New Mexico began complaining of pain and swelling at the injection site after receiving intramuscular (IM) corticosteroid injections. *Pseudomonas aeruginosa* was later cultured from several patients' abscesses, and the clinic discontinued these corticosteroid injections. The clinic had been using cotton balls soaked in alcohol or benzalkonium chloride to clean injection sites and injection-vial septa. The Office of Epidemiology of the New Mexico Department of Health (NMDOH) initi-

ated an investigation to determine whether use of benzalkonium chloride was the cause of this cluster of postinjection abscesses and to identify other risk factors for abscess development among clinic patients.

Methods

Epidemiologic Investigation

We defined a case as a patient with an abscess at the injection site that drained pus spontaneously or surgically following an injection at the clinic during January-June 1995. Case-patients were identified through the clinic, local surgeons, and patients' attorneys.

We conducted a matched case-control study to identify risk factors for postinjection abscess development in patients receiving IM injections at the clinic. Through interviews with case-patients and review of

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their medical charts, we identified the day on which each of the case-patients received the injection associated with their abscess. All other patients receiving IM injections on those days served as controls. We reviewed medical records and interviewed case- and control-patients using a standard questionnaire. The questionnaire requested information regarding demographic factors, clinical signs and symptoms, and potential risk factors.

The following potential risk factors for abscess formation were assessed: age; sex; body mass index [BMI = weight in kg/(height in m)²] in adults; presence of selected health conditions that affect the immune response—regular use of steroids, diabetes, chemotherapy or radiation therapy for cancer at the time of the injection, or other immunosuppressive conditions; injection site (gluteal versus deltoid); type of medication received (corticosteroid versus other); type of vial (multidose versus single-dose); individual administering injection; and type of disinfectant used to clean the injection site and injection-vial septum (benzalkonium chloride versus alcohol). The disinfectant used at the time of injection was assumed to be whichever disinfectant the person administering the injection had normally used during the months when case-patients received injections. All intramuscular injections were given by five clinic employees who were very consistent in their use of either benzalkonium chloride or alcohol as a disinfectant during that time period: Four reported using the same disinfectant 100% of the time, and one reported using the same disinfectant 80% of the time.

We calculated odds ratios (ORs) for each risk factor with respect to abscess development in accordance with a frequency matched design in which cases were matched with controls by injection date. Because of small cell sizes for some injection dates, we calculated conditional maximum likelihood estimates of the ORs using an exact estimation approach. We also assessed the independent contribution of risk factors when considered simultaneously in a conditional logistic regression model. The statistical software packages StatXact 3 for Windows and LogXact were used for the statistical analyses.^{5,6} Statistical significance was defined as a *P* value < .05.

The investigation was conducted under the authority of the New Mexico Public Health Act; therefore, approval from an institutional review board was not sought. Consent was obtained from each patient before proceeding with the telephone interview.

Environmental and Laboratory Investigation

We asked clinic staff to prepare a stock solution of benzalkonium chloride in the same manner as was done before its use was discontinued prior to our investigation. Cultures were taken of cotton balls soaked in this solution. Other environmental samples from the clinic were benzalkonium chloride concentrate (17% Zephiran[®] Chloride), tap water, cotton balls soaked in alcohol,

hand washes used by clinic personnel, swabs from the tops of eight opened multidose vials, and samples from the contents of two of these vials. All cultures were performed by NMDOH's Scientific Laboratory Division (SLD) using standard methods.^{7,8}

The clinic returned unopened vials of triamcinolone acetonide (TA), the most common corticosteroid used at the clinic, to the manufacturer (Steris Laboratories, Inc, Phoenix, AZ) for sterility testing. An opened vial of TA and 18 opened multidose vials of other injectable medications (eg, estrogen, testosterone, vitamin B₁₂, vaccines) from the clinic were sent to the US Food and Drug Administration (FDA) laboratory in Denver, Colorado for sterility testing.

Laboratory records were obtained for all case-patients whose abscesses were cultured. All available patient isolates were sent to SLD for identification confirmation using standard methods⁸ and for further categorization using the Microbial Identification System (MIS), which categorizes isolates based on fatty acid methyl esters of the cell wall.⁹ Patient isolates were also sent to the University of New Mexico Health Science Center, Molecular Epidemiology Laboratory for DNA fingerprint analysis using pulse-field gel electrophoresis.¹⁰

Results

Epidemiologic Investigation

A total of 28 patients met the case definition; none had more than one abscess. The 28 case-patients received the injections associated with their abscesses during a 2-month period (April 20–June 22, 1995). Case-patients ranged in age from 13.6 to 79.8 years (mean = 43.2); 23 (82.1%) were female.

All case-patients had been given a corticosteroid injection to relieve allergy symptoms: Twenty-four (85.7%) received triamcinolone acetonide (TA) (dose range: 30–80 mg), three (10.7%) received methylprednisolone acetate (dose: 80 mg), and for one case-patient, whether TA or triamcinolone diacetate was given could not be determined. For two patients, we could not determine whether the injection of methylprednisolone or another injection given at the same time was the one associated with abscess formation. These case-patients were excluded from analyses involving medication. Abscesses began draining (spontaneously or surgically) a median of 75.5 (range: 32–211) days after the injection. Five (17.9%) case-patients were hospitalized for 1–13 days (median = 2 days).

We interviewed 126 (90%) of the 140 patients who had received IM injections on the same days that case-patients received the injection associated with their abscess. No significant differences with respect to sex, mean age, or proportion receiving a corticosteroid injection existed between the 14 control patients who could not be interviewed and the 126 patients who participated in the study.

When we compared case- and control-patients, abscess formation was not associated with immunosup-

TABLE 1.—Comparison of Risk Factors for Abscess Formation in Case- and Control-Patients

Potential Risk Factor	Case		Control		OR* (95% CI)†
	n	%	n	%	
Sex: female	28	82.1	126	50.8	5.1 (1.7, 19.2)
BMI‡: ≥30	27	7.4	107	17.8	0.4 (0.0, 1.8)
Site: gluteal	28	100.0	119	82.4	Undef (1.3, Undef)
Medication: corticosteroid	26	100.0	126	48.4	Undef (5.9, Undef)
Type of vial: multidose	28	100.0	126	86.5	Undef (1.2, Undef)
Disinfectant used: BC	25	36.0	107	43.9	0.5 (0.2, 1.5)

BC = benzalkonium chloride, Undef = undefined

*Conditional maximum likelihood estimate of odds ratio; case- and control-patients matched on injection date.

†Exact 95% confidence interval.

‡Body mass index; only calculated for adults.

pressive conditions, age, or the person administering the injection. Being female, corticosteroid injection, injection from a multidose vial, and injection in the gluteal muscle were significantly associated with abscess formation (Table 1). When we adjusted the effects of the risk factors listed in Table 1 with a conditional logistic regression model, the effects of injection site and type of vial were inestimable in the model due to lack of variation between case- and control-patients within too many matched case-control groups. We removed these two risk factors and constructed a model with the remaining variables (Table 2). Only receipt of corticosteroid (OR = 17.8) and being female (OR = 7.4) were significantly associated with abscess formation.

Environmental and Laboratory Investigation

Cultures from cotton balls soaked in the demonstration benzalkonium chloride solution from the clinic grew *P aeruginosa*. The solution was prepared monthly by mixing approximately one part Zephiran® Chloride (17%) and two parts commercial normal saline in a glass canister and adding cotton balls. The canister was washed with soap between batches of benzalkonium chloride. None of the other environmental samples collected from the clinic were contaminated with *P aeruginosa*.

Unopened vials of TA passed standard sterility tests conducted by the manufacturer. The FDA found no evidence of microbial contamination in 1 opened, multidose vial of TA or in the 18 opened, multidose vials of other injectable medications.

The abscesses of 23 case-patients were cultured; laboratory records showed that 20 (87.0%) grew *P aeruginosa*, and one grew *Pseudomonas fluorescens/putida*. We obtained *P aeruginosa* isolates from three case-patients: All isolates were confirmed to be *P aeruginosa* by SLD. Isolates from two patients were identified as the same strain by MIS and pulse-field gel electrophoresis.

Discussion

Contaminated benzalkonium chloride has been implicated as the source of infection in several nosocomial outbreaks over the past 40 years^{2,11-16} and was also the most likely source of infection in this cluster of abscesses. Benzalkonium chloride solution from the clinic grew *P aeruginosa* as did the majority of abscesses, whereas other environmental samples and unopened vials of TA were not contaminated. The canister containing benzalkonium chloride solution was not disinfected between batches, and once contaminated, could have contaminated successive batches. Two strains of *P aeruginosa* were identified among three patient isolates and *P putida/fluorescens* was isolated from one patient's abscess, suggesting that the canister may have become contaminated with several *Pseudomonas* strains and species. Unfortunately, the isolate from the benzalkonium chloride solution was discarded before it could be compared with patient isolates.

Contaminated benzalkonium chloride could have led to abscesses in patients via two main pathways. First, use of contaminated benzalkonium chloride solution at the time of injection could have contaminated the hands of the person administering the injection, the skin of the patient at the injection site, and/or the needle used for the injection. Any of these factors could have resulted in infection in patients. Second, the contents of multidose vials could have become contaminated when vial septa were wiped with contaminated benzalkonium chloride and punctured with a needle. Injection of contaminated medication could cause infection, regardless of the disinfectant used at the time of injection. We found that use of benzalkonium chloride on patients at the time of the injection was not a risk factor for abscess development. More than half of the case-patients received injections from clinic personnel who used alcohol to clean injection sites and vial septa. These findings suggest that the first pathway was not a significant contributing factor to infection in patients and that the second pathway (contamination of multidose vials) is a more significant explanation for this cluster of abscesses.

TABLE 2.—Multivariable Analysis of Risk Factors for Abscess Formation

Potential Risk Factor	Adjusted OR*	Exact 95% CI†
Sex: female	7.4	1.6–69.1
Body mass index‡: > 30	0.2	0.0–1.3
Medication: corticosteroid	17.7	2.7–undefined
Disinfectant used: BC	0.6	0.1–2.5

BC = benzalkonium chloride

*Conditional maximum likelihood estimate of odds ratio; case- and control-patients matched on injection date.

†Exact 95% confidence interval.

‡Only calculated for adults.

The clinic did not record from which vial each patient received an injection; thus it was impossible to determine whether case-patients were associated only with injections withdrawn from vials that had been wiped previously with benzalkonium chloride. The one opened vial of TA available for testing was not contaminated with *Pseudomonas* spp. The vial may not have been wiped with benzalkonium chloride, however, and the vial was cultured several months after it was opened, allowing sufficient time for any present organisms to have died.

Receiving a corticosteroid injection was a strong risk factor for abscess development in persons receiving IM injections at the clinic (Tables 1 and 2). All case-patients received a corticosteroid injection compared with 48.4% of control-patients. Corticosteroids were the only medication associated with abscess development, although at least nine other medications from multidose vials also were used at the clinic. This outcome may have been due to the immunosuppressive effects of pharmacologic dosages of glucocorticoids (eg, TA and methylprednisolone).¹ Corticosteroid injections have been involved in other nosocomial outbreaks,^{15,16} including a cluster of abscesses following IM injection of methylprednisolone in New Mexico in 1978.¹⁷

All case-patients received corticosteroid injections from multidose vials administered in the gluteal muscle. To try to separate the effects of these highly associated variables, we first limited the analysis to patients receiving medications from multidose vials and then to patients receiving injections in the gluteal muscle only. Corticosteroid injection remained a strong, statistically significant risk factor for abscess development in both of these models (exact 95% confidence interval = [4.18, undefined] and [3.45, undefined], respectively), whereas injection site was no longer significant in the first model, and vial type was no longer significant in the second. These results suggest that corticosteroid injection was the most important risk factor of the three; vial type and injection site may have appeared as risk factors only because of their association with corticosteroid injections.

Being female was a risk factor for postinjection abscess development even when controlling for body mass index

in the logistic model. Females also were more likely than males to develop abscesses following injections of methylprednisolone in the 1978 cluster of abscesses in New Mexico mentioned earlier.¹⁷ Reasons for this difference between males and females were not clear.

Although benzalkonium chloride has been documented as a significant nosocomial infection liability for many years, this cluster of abscesses illustrates that some health-care providers remain unaware of the dangers of using it as a disinfectant or skin antiseptic. The use of benzalkonium chloride at this clinic may not be an isolated incident; 12% of respondents of a country-wide survey of hospital epidemiologists reported that benzalkonium chloride was in use for skin disinfection at their hospital.¹⁸ Given the unreliability of benzalkonium chloride as a disinfectant and antiseptic^{1–4,11–16} and the availability of more efficacious products,⁴ benzalkonium chloride should not be used to clean injection vial septa or the skin of patients before injections. Given the potential for contamination of multidose vials, health care providers should consider using single-dose vials of injectable medications when possible, especially when administering corticosteroids.

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