

Antibacterial Effect of Octylcyanoacrylate against Ciprofloxacin-resistant *Pseudomonas aeruginosa* Isolates from Patients with Chronic Suppurative Otitis Media

CHUL HO JANG^{1,2}, HAEKYUN PARK², YONG BUM CHO¹, CHEOL HEE CHOI² and CHANGHUN SONG³

¹Department of Otolaryngology, Chonnam National University Medical School and

²Research Center for Resistant Cells, Chosun University Gwangju;

³JB Stem Cell Research Center, Gwangju, South Korea

Abstract. *Background:* There has been a steady increase in the number of cases of ciprofloxacin-resistant *Pseudomonas aeruginosa* (CRPA) otorrhea; this is a growing medical concern. For otological surgery in children, octylcyanoacrylate can be an alternative method of closure for surgical incisions. Recent in vitro studies have shown that octylcyanoacrylate is effective as an antimicrobial barrier. To date, there have been only rare reports on the antibacterial effect of octylcyanoacrylate against CRPA. The purpose of this study is to determine the antimicrobial effects of octylcyanoacrylate against the CRPA that was isolated from patients with chronic suppurative otitis media. *Patients and Methods:* Clinical CRPA ($n=20$) bacteria and ciprofloxacin-sensitive PA (CSPA) ($n=20$) were obtained from patients. The susceptibilities to various antibiotics were determined by disk diffusion method. *Result:* Both CSPA and CRPA were resistant to octylcyanoacrylate. *Conclusion:* Results demonstrated that octylcyanoacrylate has no antibacterial activity against CSPA and CRPA.

Tissue adhesives are a class of compounds that are known as cyanoacrylates and can bind to skin surfaces via a polymerization reaction. Tissue adhesives have good tensile strength, are bactericidal and bacteriostatic, have negligible histotoxicity and they peel off spontaneously (1, 2). Octylcyanoacrylates are a newly introduced generation of tissue adhesives. Octylcyanoacrylate has been designed to overcome the shortcomings of butylcyanoacrylates: it

forms a stronger and more flexible bond, its breaking strength is three to four times higher than that of butylcyanoacrylates and is comparable to that of a 5/0 monofilament suture (3). For otological surgery in children, octylcyanoacrylate can be an alternative method of closure for surgical incisions. Several comparative studies involving low-tension wounds of the face have shown that tissue adhesives provide a cosmetic outcome comparable to that of suturing both at 2 months and at the 1-year follow-up, while they cause less pain as measured on a visual analogue scale (4) and require less time for completion of the procedure (1, 2, 5, 6).

Ciprofloxacin is a fluoroquinolone and is available as a topical preparation. It has been shown to be effective against *Pseudomonas aeruginosa* (7-9). Ototopical ciprofloxacin in patients was curative in nearly 70% of patients with otorrhea associated with *P. aeruginosa* who were previously unresponsive to other antimicrobial agents (10-11).

As the clinical application of the ototopical ciprofloxacin solution has increased, newly evolved bacterial fluoroquinolone-resistance has also been more challenging. The resistance to fluoroquinolone is basically a reflection of mutation, which is a result of selective pressure created by the use of fluoroquinolones (12). Previous studies have reported on ciprofloxacin-resistant *P. aeruginosa* (CRPA) in chronic suppurative otitis media (13). Due to the resistance of *P. aeruginosa* and the development of resistance during therapy, the selection of an optimal treatment caused by this pathogen is often complicated.

The skin formed by octylcyanoacrylate is effective against gram-positive and gram-negative bacteria. Cyanoacrylates have been shown to have antimicrobial properties (14, 15). To date, there are only rare reports on the antibacterial effect of octylcyanoacrylate against CRPA. The purpose of this study was to determine the antimicrobial effects of octylcyanoacrylate against the CRPA that was isolated from patients with chronic suppurative otitis media.

Correspondence to: Chul Ho Jang, Department of Otolaryngology, Chonnam National University Hospital, Hakdong 8, Dongku, Gwangju, South Korea. Tel: +82 622206774, Fax number: +82 62 2206776, e-mail: chulsavio@hanmail.net

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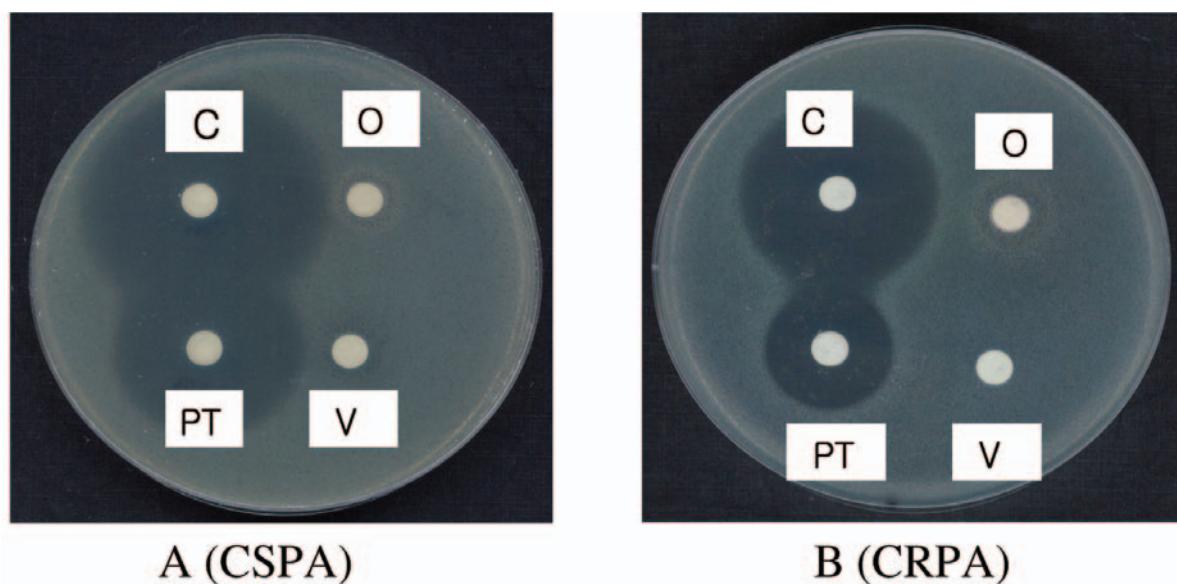


Figure 1. The susceptibilities to antibiotics and octylcyanoacrylate were determined for ciprofloxacin-sensitive (A) and ciprofloxacin-resistant *Pseudomonas aeruginosa* (B) by disk diffusion method. CSPA: ciprofloxacin-sensitive *Pseudomonas aeruginosa*, CRPA: ciprofloxacin-resistant *Pseudomonas aeruginosa*, O: octyl-cyanoacrylate, V: vancomycin, C: ceftazidime, PT: piperacillin-tazobactam.

Table I. Antibacterial effect of octyl-cyanoacrylate compared to antibiotics.

	Vancomycin	Ceftazidime	PT	Octyl-cyanoacrylate
CSPA	–	6 +	5 +	–
CRPA	–	5+	4 +	–

–, No inhibition; 1+, <3 mm zone of inhibition; 2+, 3-5 mm; 3+, 5-7 mm; 4+, 7-10 mm; 5+, 10-13 mm; 6+, 13 mm<; PT, piperacillin-tazobactam; CSPA, ciprofloxacin-sensitive *Pseudomonas aeruginosa*; CRPA, ciprofloxacin-resistant *Pseudomonas aeruginosa*.

Patients and Methods

The bacterial cultures used in this study were obtained from the otorrhea in chronic suppurative otitis media (CSOM) patients. Clinical CRPA ($n=20$) bacteria and ciprofloxacin-sensitive *P. aeruginosa* (CSPA) bacteria ($n=20$) were obtained from patients at the Chonnam National University Hospital in Gwangju City, South Korea (March 2006 through May 2007). The susceptibilities to various antibiotics were determined by disk diffusion method according to the guidelines of the Clinical Laboratory Standards Institute (16). Bacterial inoculates were seeded on plates containing Muller-Hinton medium for the CRPA and CSPA. All the bacteria were seeded. After inoculation, a small filter paper impregnated with 20 μ l (64 μ g/ml) of antibiotics, or 20 μ l of octylcyanoacrylate were gently pressed and evenly distributed on the agar plates. The tested antibiotics were vancomycin (SamjinPharm. Co, Seoul, South Korea), ceftazidime (KunwhaPharm. Co, Seoul, South Korea) and piperacillin-tazobactam (Tazocin; Weith Korea, Inc. Seoul, South Korea). The plates were incubated overnight. The antibacterial activity was then assessed by sampling the inhibition zones when they were present. The inhibition zones were measured by virtue of the difference in contrast between the bacterial lawn and that surrounding the disk or well where the bacterial growth had been prevented.

Results

Table I shows the mean size of all the inhibition zones on the study plates. Figure 1 shows that there is no antibacterial effect of octylcyanoacrylate against CSPA nor CRPA.

However, both CSPA and CRPA were sensitive to tazocin and ceftazidime.

Discussion

This study shows the antibacterial effect of octylcyano-acrylate against the CRPA and CSPA that were isolated from CSOM patients. The antibacterial effect of cyanoacrylate varies according to the speed of degradation (17, 18). *In vitro* studies have shown that cyanoacrylate homologues are increasingly bacteriotoxic in order of their decreasing chain length (19).

The exact mechanism of the antimicrobial effect of cyanoacrylate is unclear, but it is likely to be a cell wall mechanism because the sensitivities are restricted to gram-positive organisms. A possible explanation could be the

strong electronegative charge on the polymer that could react with the cell wall of gram-positive organisms that have a positive charge. The gram-negative organisms would be relatively unaffected because of their lipopolysaccharide membrane, which insulates the cell wall (14). To the best of the authors' knowledge, this is the first study on the antibacterial activity of octylcyanoacrylate against the CRPA that was isolated from the otorrhea in patients with chronic suppurative otitis media.

Cyanoacrylates work *via* an exothermic polymerization reaction that forms a strong bond within minutes after contact with a fluid or basic medium (19). This technology immediately became popular in multiple surgical specialties but it is especially attractive to pediatric surgeons due to the speed of application. The advantages of octylcyanoacrylate compared with suture include its ease of use, faster application and decreased pain. Further wound care is reduced because it serves as its own barrier dressing and, since it spontaneously falls off, no follow-up is required for removal. For otologic surgery in children, octylcyanoacrylate can be an alternative method of closure for surgical incisions. However, it would be better to take precautions for wound closure using octylcyanoacrylate in CRPA- or CSPA-positive patients since results showed that octylcyanoacrylate has no antibacterial activity against CSPA nor CRPA.

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References

- 1 Quinn JV, Drzewiecki A, Li MM, Stiell IG, Sutcliffe T, Elmslie TJ and Wood WE: A randomized controlled trial comparing a tissue adhesive with suturing in the repair of pediatric facial lacerations. *Ann Emerg Med* 22: 1130-1135, 1993.
- 2 Bruns TB, Simon HK, McLaren DJ, Sullivan KM, Wood RJ and Anand KJ: Laceration repair using a tissue adhesive in a children's emergency department. *Pediatrics* 99: 673-675, 1996.
- 3 Howell JM, Bresnahan KA, Stair TO, Dhindsa HS and Edwards BA: Comparison of effects of suture and cyanoacrylate tissue adhesive on bacterial counts in contaminated lacerations. *Antimicrob Agents Chemother* 39: 559-560, 1995.
- 4 Huskisson EC: Visual analogue scales. In: *Pain Measurement and Assessment*. Melzack R (ed.). New York, NY, Raven Press, pp. 33-37, 1983.
- 5 Simon HK, McLaren DJ, Bruns TB, Zempsky WT, Wood RJ and Sullivan KM: Long-term appearance of lacerations repaired using a tissue adhesive. *Pediatrics* 99: 193-195, 1997.
- 6 Simon HK, Zempsky WT, Bruns TB and Sullivan KM: Lacerations against Langer's lines: to glue or suture? *J Emerg Med* 16: 185-189, 1998.
- 7 Force RW, Hart MC, Plummer SA, Powell DA and Nahata MC: Topical ciprofloxacin for otorrhea after tympanostomy tube placement. *Arch Otolaryngol* 121: 880-884, 1995.
- 8 Tutken A, Ozagar A, Koc A, Batman C, Cuneys U and Schitoglu MA: Treatment of chronic ear disease: topical ciprofloxacin vs. topical gentamicin. *Arch Otolaryngol* 121: 1414-1416, 1995.
- 9 Ikeda K and Takasaka T: *In vitro* activity of ototopical drops against middle ear pathogens. *Am J Otol* 14: 170-171, 1993.
- 10 Wintermeyer SM, Hart MC and Nahata MC: Efficacy of ototopical ciprofloxacin in pediatric patients with otorrhea. *Otolaryngol Head Neck Surg* 116: 450-453, 1997.
- 11 Miles Inc. Package Information. 1993. Cipro (Ciprofloxacin). Miles Inc., West Haven, CT, USA.
- 12 Sheang WH, Chen YC, Wang JT, Chang SC, Luh KT and Hsieh WC: Emerging fluoroquinolone-resistance for common clinically important gram-negative bacteria in Taiwan. *Diagn Microbiol Infect Dis* 43: 141-147, 2002.
- 13 Jang CH and Park SY: Emergence of ciprofloxacin-resistant pseudomonas in chronic suppurative otitis media. *Clin Otolaryngol Allied Sci* 29: 321-323, 2004.
- 14 Quinn JV, Osmond MH, Yurack JA and Moir PJ: N-2-Butylcyanoacrylate: risk of bacterial contamination with an appraisal of its antimicrobial effects. *J Emerg Med* 13: 581-585, 1995.
- 15 Quinn J, Maw J, Ramotar K, Wenckebach G and Wells G: Octylcyanoacrylate tissue adhesive *versus* suture wound repair in a contaminated wound model. *Surgery* 122: 69-72, 1997.
- 16 National Committee for Clinical Laboratory Standards. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, 5th ed. M7-A5. Wayne, PA: National Committee for Clinical Laboratory Standards, 2000.
- 17 Eiferman RA and Snyder JW: Antibacterial effect of cyanoacrylate glue. *Arch Ophthalmol* 101: 958-960, 1983.
- 18 Jandinski J and Sonins S: *In vitro* effects of isobutylcyanoacrylate on four types of bacteria. *J Dent Res* 50: 1557-1558, 1971.
- 19 Bernard L, Doyle J, Friedlander SF, Eichenfield LF, Gibbs NF and Cunningham BB: A prospective comparison of octylcyanoacrylate tissue adhesive (dermabond) and suture for the closure of excisional wounds in children and adolescents. *Arch Dermatol* 137: 1177-1180, 2001.

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