Concise Practice Point

Intraoperative Antimicrobial Prophylaxis in Elective Cataract Surgery Patients with Penicillin Allergy

The ROYAL COLLEGE of OPHTHALMOLOGISTS

Introduction

The true prevalence of IgE-mediated allergy in those self-identifying as penicillin allergic sits at less than 1%[1] and cross-reactivity between penicillins and cephalosporins has been reported in up to 10% of these patients for first and second-generation cephalosporins, such as cefuroxime[2].

There is a lack of evidence for significant cross-reactivity of intracameral cefuroxime in penicillin allergic patients. This has led to significant variation in intraoperative antimicrobial prophylaxis for cataract surgery in this setting. An online survey of UK surgeons in 2019 looking specifically at their use of intracameral cefuroxime (ICC) found more than 80% of respondents gave ICC in penicillin-allergy patients without a history of anaphylaxis and almost a third did so even if there was a history of anaphylaxis[3]. There has not always been as much confidence in ICC use.[4]. There appears to be greater consensus from authorities in Europe. For example, the French Agency for Safety of Health Products validated ICC as early as 2011 for prophylaxis in intraocular surgery[5]. Furthermore, patients in Sweden are only denied ICC if they report a distinct allergy to cephalosporins, but notably, not penicillin[6].

In this Concise Practice Point, we critically appraise published evidence to produce evidence-based recommendations on this varied area of practice.

Methods

A literature search was conducted using PUBMED. The search was performed on all fields using the search terms, “penicillin”, “allergy”, “cataract surgery” and “cefuroxime” in August 2021. References of cited publications were examined to identify further relevant articles. Summarised results, references and further evidence considered can be found in the appendices.

Recommendations

1	Take a thorough allergy history to determine whether or not the patient has a history of possible anaphylaxis
2	If there is a confirmed or suspicion of possible anaphylaxis to penicillin, intracameral moxifloxacin should be considered as an alternative
3	If there is no confirmed or suspicion of possible anaphylaxis to penicillin, based on the evidence we have considered, we recommend proceeding with intracameral cefuroxime (ICC)
4	It is important to note that informed consent necessitates making patients aware of any and all material risks, as highlighted by the case of Montgomery vs Lanarkshire Health Board[7]. As such, a discussion must be had with the penicillin allergy patient in which their options and associated risks are discussed and clearly documented
5	Any adverse drug reactions must be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) via the Yellow Card scheme, in addition to an in-house incident report as per local policy[8]

A decision algorithm summarising these recommendations is presented below

Decision Algorithm: approach to antimicrobial prophylaxis for elective cataract surgery patient reporting penicillin allergy

Take an allergy history

Does the history fit with possible anaphylaxis to penicillin?

Example symptoms to elicit from history:

- Breathing difficulty / wheeze
- Loss of consciousness / light-headedness
- Hospitalisation / told to carry adrenaline auto-injector (EpiPen)

Yes

Consider alternatives and discuss these with the patient e.g.

1. Intracameral moxifloxacin 0.1ml of 0.5mg/0.1ml made up in-house: discuss sourcing this with local pharmacy department.
2. Intracameral 0.1ml of preservative-free topical 0.5% moxifloxacin preparation (e.g. Vigamox, Alcon): if in-house preparation not possible and acknowledge that topical preparations of antibiotics are not routinely tested for pyrogens hence this represents a theoretical risk of adverse reaction with intraocular use.
3. Subconjunctival gentamicin: warn the patient against adverse effects including discomfort, conjunctival toxicity, retinal toxicity and toxic myopathy of the extraocular muscles.

Keep patient in department for 30-minute period of observation post-op

Counsel the patient that while the evidence base is slightly limited compared with cefuroxime, this must be balanced against risk of anaphylaxis. Reassure them that there is still well-documented efficacy and safety from clinical studies.

No

Proceed with intracameral cefuroxime 1mg/0.1ml

Counsel the patient that while there is a theoretical risk of cross-reactivity and anaphylaxis, there is a well-documented good safety profile from clinical studies.

Discussion

The most suitable intracameral antimicrobial alternative to ICC is moxifloxacin (ICM), for which large retrospective studies from the Aravind Eye Care System and elsewhere provide strong support.[15,16] This option has many appealing features for the patient with penicillin allergy; it is molecularly distinct, can be injected undiluted from a commercial preparation, it is not toxic to the eye and it has proven efficacy in preventing endophthalmitis.[17]

Appendix 1: Key Papers

Author	Methodology	Key Message	Strengths	Limitations
LaHood et al[9]	Literature search in which a range of antimicrobial agents via varying routes for antimicrobial prophylaxis in penicillin-allergy patients are explored.	They place the key fork in the decision process at whether or not a patient is suspected of being anaphylactic to penicillin. If so, they suggest use of intracameral moxifloxacin (ICM) and if not, to stick with ICC.	The suggestions made were all backed up with evidence and a neutral stance is maintained.	None identified
Promelle et al[10]	Assessment of tolerability of ICC in penicillin-allergy.	ICC is safe in this cohort since no cases of anaphylaxis were encountered out of 40 eyes of 40 patients.	Prospective study and a reasonable number were recruited and analysed.	Diagnostic purity bias since patients underwent pre-operative subcutaneous cefuroxime testing and those with a positive result were denied ICC.
Svetozarskiy et al[11]	Systematic review in which they collate reported adverse reactions to ICC.	Listed adverse reactions include: toxic anterior segment syndrome (TASS), serous retinal detachment (RD) with macular oedema, retinal haemorrhagic infarction and anaphylaxis. A proportion of the serous RD cases and all the retinal haemorrhagic infarction cases relate to instances of above-treatment dose injection.	None identified	Irvine Gass syndrome remains an important differential diagnosis of post-op macular oedema.
Mitra et al[12]	Retrospective case notes review of penicillin-allergy patients receiving subconjunctival cefuroxime for prophylaxis.	Out of the 36 cases given cefuroxime, none had any issues.	An enquiry as to the exact nature of penicillin allergy was performed and included facial swelling, tongue involvement and loss of consciousness.	The sub-conjunctival route is not the mainstream choice of delivery.
Myneni et al[13]	Incidence of post-op endophthalmitis (POE) was examined over an 8-year period.	Out of 50 cases of ICC given to those with penicillin allergy, no adverse reactions occurred.	Prospective study	Diagnostic purity bias since none of these patients reported a history of anaphylaxis to penicillin.
Mesnard et al[14]	Case series	5 patients developed POE despite receiving ICC, one in the setting of posterior capsular rupture. This serves as an important reminder of the fact that while it comes close, ICC is still not quite the silver bullet that we need for safe and universal prophylaxis.	None identified	None identified

Appendix 2: References

1. Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma and Immunology; American College of Allergy, Asthma and Immunology; Joint Council of Allergy, Asthma and Immunology. Drug allergy: an updated practice parameter. Ann Allergy Asthma Immunol. 2010 Oct;105(4):259-273.
2. British National Formulary bnf.nice.org.uk/drug/cefuroxime.html
3. Kim, J. and Patton, N., Intracameral antibiotics in cataract surgery: current evidence base. Eyes News, Aug/Sep 2019, Vol 26 No. 2
4. Gore, D.M., Angunawela, R.I. and Little, B.C., 2009. United Kingdom survey of antibiotic prophylaxis practice after publication of the ESCRS Endophthalmitis Study. Journal of Cataract & Refractive Surgery, 35(4), pp.770-773.
5. AFSSAPS French agency for safety of health Products.[Antibioprophylaxis in ocular surgery. Recommendations]. J FrOphtalmol 2011;34:431—4.
6. Barry et al. European Society of Cataract and Refractive Surgeons (ESCRS) Guidelines for Prevention and Treatment of Endophthalmitis Following Cataract Surgery: Data, Dilemmas and Conclusions 2013.
7. Montgomery v Lanarkshire Health Board [2015] SC 11 [2015] 1 AC 1430.
8. The Medicines and Healthcare products Regulatory Agency. yellowcard.mhra.gov.uk/the-yellow-card-scheme/
9. LaHood BR, Andrew NH, Goggin M. Antibiotic prophylaxis in cataract surgery in the setting of penicillin allergy: A decision-making algorithm. Surv Ophthalmol. 2017 Sep-Oct;62(5):659-669. doi: 10.1016/j.survophthal.2017.04.004. Epub 2017 Apr 22. PMID: 28438590.
10. Promelle V, Jany B, Drimbea A, Jezraoui P, Milazzo S. Tolerability of intracameral cefuroxime during cataract surgery in case of penicillin allergy. J Fr Ophtalmol. 2015 Apr;38(4):283-7. doi: 10.1016/j.jfo.2014.11.005. Epub 2015 Apr 1. PMID: 25840617.
11. Svetozarskiy SN, Andreev AN. Oslozhneniia vnutrikamernogo vvedeniia tsefuroksima v khirurgii katarakty [Complications of intracameral cefuroxime in cataract surgery]. Vestn Oftalmol. 2018;134(5):104-110. Russian. doi: 10.17116/oftalma2018134051104. PMID: 30499547.
12. Mitra, A. and McElvanney, A., 2006. Prophylactic subconjunctival cefuroxime during cataract surgery in patients with a penicillin allergy. Annals of Ophthalmology, 38(4), pp.293-295.
13. Myneni, J., Desai, S.P. and Jayamanne, D.G.R., 2013. Reduction in postoperative endophthalmitis with intracameral cefuroxime. Journal of Hospital Infection, 84(4), pp.326-328.
14. Mesnard, C., Beral, L., Hage, R., Merle, H., Fares, S. and David, T., 2016. Endophthalmitis after cataract surgery despite intracameral antibiotic prophylaxis with licensed cefuroxime. Journal of Cataract & Refractive Surgery, 42(9), pp.1318-1323.
15. Haripriya A, Chang DF, Namburar S, Smita A, Ravindran RD. Efficacy of Intracameral Moxifloxacin Endophthalmitis Prophylaxis at Aravind Eye Hospital. Ophthalmology. 2016 Feb;123(2):302-308. doi: 10.1016/j.ophtha.2015.09.037. Epub 2015 Oct 30. PMID: 26522705.
16. Arshinoff SA, Modabber M. Dose and administration of intracameral moxifloxacin for prophylaxis of postoperative endophthalmitis. J Cataract Refract Surg. 2016 Dec;42(12):1730-1741. doi: 10.1016/j.jcrs.2016.10.017. PMID: 28007104.
17. Herrinton LJ, Shorstein NH, Paschal JF, et al. Comparative effectiveness of antibiotic prophylaxis in cataract surgery. Ophthalmology. 2016;123(2):287e94

Appendix 3: Further Reading

1. Centers for Disease Control and Prevention cdc.gov/antibiotic-use/community/pdfs/penicillin-factsheet.pdf
2. Kelkar P, Li J. Cephalosporin allergy. N Engl J Med 2001; 385: 804–9.
3. Anne S, Reisman R. Risk of administering cephalosporin antibiotics to patients with histories of penicillin allergy. Ann Allergy Asthma Immunol 1995; 74: 167–70.
4. Endophthalmitis Study Group. "European Society of Cataract & Refractive Surgeons: Prophylaxis of postoperative endophthalmitis following cataract surgery: Results of the ESCRS multicenter study and identification of risk factors." J Cataract Refract Surg 33 (2007): 978-988.
5. "Managing an outbreak of postoperative endophthalmitis", Ophthalmic Services Guidance July 2016, The Royal College of Ophthalmologists
6. "Cataracts in adults: management", NICE guideline 2017 (nice.org.uk/guidance/ng77)
7. Olson, R.J., 2021. The ESCRS postoperative endophthalmitis prospective trial 15 years later. Journal of Cataract & Refractive Surgery, 47(7), pp.839-841.
8. Urain, escrs.org/amsterdam2020/programme/free-papers-details.asp?id=36892
9. Qureshi, ascrs.confex.com/ascrs/18am/meetingapp.cgi/Paper/41799
10. Nanavaty, M.A. and Wearne, M.J., 2010. Perioperative antibiotic prophylaxis during phaco-emulsification and intraocular lens implantation: national survey of smaller eye units in England. Clinical & experimental ophthalmology, 38(5), pp.462-466.
11. Çakır, B., Celik, E., Aksoy, N.Ö., Bursalı, Ö., Uçak, T., Bozkurt, E. and Alagoz, G., 2015. Toxic anterior segment syndrome after uncomplicated cataract surgery possibly associated with intracamaral use of cefuroxime. Clinical Ophthalmology (Auckland, NZ), 9, p.493.
12. Le Dû, B. and Pierre-Kahn, V., 2014. Macular oedema after phacoemulsification and suspicion of overdose of cefuroxime: about 6 cases. French Journal of Ophthalmology, 37 (3), pp. 202-210.
13. Xiao, H., Liu, X. and Guo, X., 2015. Macular edema with serous retinal detachment post-phacoemulsification followed by spectral domain optical coherence tomography: a report of two cases. BMC Research notes, 8(1), pp.1-5.
14. Faure, C., Perreira, D. and Audo, I., 2015. Retinal toxicity after intracameral use of a standard dose of cefuroxime during cataract surgery. Documenta Ophthalmologica, 130(1), pp.57-63.
15. Aslankurt, M., Çekiç, O., Andı, Í. and Dursun, O., 2016. Transient macular edema after standard dose of intracameral cefuroxime injection during phacoemulsification. Canadian Journal of Ophthalmology, 51(5), pp.e141-e142.
16. Andreev, A.N. and Svetozarskiy, S.N., 2018. Serous retinal detachment after phacoemulsification with intracameral cefuroxime (a case-control report). Vestnik oftalmologii, 134(3), pp.73-77.
17. Villada, J.R., Vicente, U., Javaloy, J. and Alió, J.L., 2005. Severe anaphylactic reaction after intracameral antibiotic administration during cataract surgery. Journal of Cataract & Refractive Surgery, 31(3), pp.620-621.
18. Moisseiev, E. and Levinger, E., 2013. Anaphylactic reaction following intracameral cefuroxime injection during cataract surgery. Journal of Cataract & Refractive Surgery, 39(9), pp.1432-1434.
19. Lin, P.F., Naveed, H., Eleftheriadou, M., Purbrick, R., Ghanavati, M.Z. and Liu, C., 2021. Cataract service redesign in the post-COVID-19 era. British Journal of Ophthalmology, 105(6), pp.745-750.

20. Díez, M.R., De la Rosa, G., Pascual, R., Girón, C. and Arteta, M., 2009. Prophylaxis of postoperative endophthalmitis with intracameral cefuroxime: a five years' experience. Archivos de la Sociedad Espanola de Oftalmologia, 84(2), pp.85-89.

21. Chang DF, Braga-Mele R, Henderson BA, Mamalis N, Vasavada A, Committee ACC. Antibiotic prophylaxis of postoperative endophthalmitis after cataract surgery: results of the 2014 ASCRS member survey. J Cataract Refract Surg. 2015;41(6):1300e5

22. Witkin, A.J., Chang, D.F., Jumper, J.M., Charles, S., Eliott, D., Hoffman, R.S., Mamalis, N., Miller, K.M. and Wykoff, C.C., 2017. Vancomycin-associated hemorrhagic occlusive retinal vasculitis: clinical characteristics of 36 eyes. Ophthalmology, 124(5), pp.583-595.

23. Jenkins C, McDonnell P, Spalton D. Randomised single blind trial to compare the toxicity of subconjunctival gentamicin and cefuroxime in cataract surgery. Br J Ophthalmol. 1990;74(12):734e8

24. McDonald HR, Schatz H, Allen AW, et al. Retinal toxicity secondary to intraocular gentamicin injection. Ophthalmology. 1986;93(7):871e7]

25. Green K, Chapman J, Cheeks L. Ocular toxicity of subconjunctival gentamicin. Lens Eye Toxic Res. 1991;9(3e4):439e46

26. Moshirfar M, Feiz V, Vitale AT, Wegelin JA, Basavanthappa S, Wolsey DH. Endophthalmitis after uncomplicated cataract surgery with the use of fourth-generation fluoroquinolones: a retrospective observational case series. Ophthalmology. 2007;114(4):686e91.

Authors: Vishal Shah, Hasan Naveed, Pei-Fen Lin

The Royal College of Ophthalmologists
18 Stephenson Way, London NW1 2HD

T. 020 7935 0702
contact@rcophth.ac.uk rcophth.ac.uk