Intraoperative Cefuroxime in Penicillin allergy during cataract surgery

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Research Article

Keywords: cataract surgery, penicillin allergy, intracameral cefuroxime, cross reactivity, antibiotics, anaphylaxis

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Abstract

Purpose

To establish the incidence of anaphylactic reaction to intraoperative cefuroxime in patients with a self-reported penicillin allergy during cataract surgery.

Methods

A retrospective study carried out in clinical practice in North Devon District Hospital, Barnstaple, United Kingdom. It included patients who underwent cataract surgery between March 2009 and March 2020. The details of their demography, procedure carried out, record of allergies, intra-op medication were extracted from the EMR. The main outcome measures were post op allergic reaction; urticarial or anaphylactic. The data was analyzed on Microsoft Excel

Results

Overall 15764 eyes had cataract surgery between March 2009 and March 2020. 1764 [11%] of these were reported to be allergic to penicillin and 1652 [93.6%] still received intraoperative cefuroxime (intracameral +/- subconjunctival) despite their history of penicillin allergy. None of these 1652 patients developed any anaphylactic reaction.

Conclusion

Intra-operative cefuroxime during cataract surgery was well tolerated in patients with self-reported penicillin allergy in this large patient cohort. No post-operative anaphylaxis was observed.

Keywords:

cataract surgery, penicillin allergy, intracameral cefuroxime, cross reactivity, antibiotics, anaphylaxis.

Introduction

Cataract surgery has been one of the most performed surgeries in many parts of the world with postoperative endophthalmitis being one of its most dreaded complications. Various measures have been in place to reduce the risk of this including the use of intracameral cefuroxime. Montan et al detected that intracameral cefuroxime provided a 5-fold protective effect against endophthalmitis. Colleaux and Hamilton also found a significant protective effect with subconjunctival antibiotics vs
without [0.01% vs. 0.17%]. The ESCRS practice guideline of 2007 recommended the systematic use of intracameral cefuroxime.

Penicillin allergy is frequent in the general population. True type I penicillin allergy occurs in 7–23% of patients who give a history of penicillin allergy. Cross reactivity to first generation cephalosporins is estimated at 0.5%. This was once thought to be as high as 10% but that was due to a contamination of cefuroxime with penicillin during manufacture. Cross reactivity to second generation cephalosporins like cefuroxime is unlikely due a different side chain. In 2009 the Medical Defense Union (MDU) successfully defended a claim in relation to penicillin/cephalosporin cross reactivity concluding that usage of cephalosporins in the presence of a history of a rash in response to penicillin is acceptable and common practice.

Though there is good evidence that intracameral cefuroxime is safe in patients with reported penicillin allergy, there have been 2 case reports of anaphylactic reaction to intracameral cefuroxime in penicillin allergy, but no incidence rate has been reported. Hence it was of interest to audit the incidence of anaphylaxis in those patients where IC and s/c cefuroxime was administered in the presence of a patient-reported penicillin allergy.

**Methods**

This was a retrospective study carried out at North Devon District Hospital, Barnstaple. Ethical approval was not required as established best practice was retrospectively audited.

It included 15764 eyes who underwent intraocular surgery between the March 2009 - March 2020. The data were extracted using the Medisoft audit function of our EMR. Information on demography, surgery, penicillin allergy, intraoperative antibiotic and the occurrence of anaphylactic reaction or any allergic reaction was gleaned from Medisoft. This was entered and analyzed on Microsoft excel.

**Results**

There were 15,764 eyes who had cataract surgery between March 2009 and March 2020

9,137(58%) were females and 6,627(42%) males

The ages of the patients ranged between 20 and 109 with a mean age of 80.6 years. All the patients received intra-operative antibiotics with 14,530 (92.2%) receiving intracameral cefuroxime alone and a further 1106(7%) receiving subconjunctival cefuroxime either alone or in combination with intracameral cefuroxime. This is very much in line with the ESCRS endophthalmitis study group guidelines

Of the 15764 patients 1,764(11.2%) had penicillin allergy entered in their records. (Table 1)
Table 1
Antibiotic use during cataract surgery

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Total n(%)</th>
<th>Pen allergy n(%)</th>
<th>No steroid + pen allergy n(%)</th>
<th>Reaction with no steroid n(%)</th>
<th>Reaction with steroid n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.C Cefuroxime</td>
<td>14530 (92.2)</td>
<td>1533 (87)</td>
<td>1348 (96.7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>S.C Cefuroxime</td>
<td>1106 (7)</td>
<td>119 (6.7)</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>I.C Cefotaxime</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>S.C Gentamicin</td>
<td>102 (0.6)</td>
<td>94 (5.3)</td>
<td>19 (1.3)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Top Ofloxacin</td>
<td>19</td>
<td>17</td>
<td>17 (1.2)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>S.C/I.C Vancomycin</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>S.C Cefazolin</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Top Chloramphenicol</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>15764</td>
<td>1764</td>
<td>1394</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Of the 1,764 penicillin allergic patients, 1,652 (94%) still received cefuroxime – 87% IC cefuroxime and 7% SC cefuroxime +/- IC cefuroxime (Table 1). No reactions were reported in these 1,652 patients. This reflects a cross reactivity of 0.

Table 2 shows us the different antibiotics that were used in our study. As already pointed out above an overwhelming majority (93.7%) of the penicillin allergic patients received cefuroxime, 5.3% received gentamicin and the rest received topical ofloxacin and some vancomycin.

Table 2
Penicillin allergy and choice of antibiotics

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefuroxime</td>
<td>1652 (93.7%)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>94 (5.3%)</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>17 (0.096%)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1 (0.05%)</td>
</tr>
<tr>
<td></td>
<td>1764 (100%)</td>
</tr>
</tbody>
</table>

Discussion
In our study we found 11.2% (1764) of our patients had penicillin allergy recorded. This is a little higher than the incidence of 5–10% in previous papers\textsuperscript{18–20}. It has also been reported in one study that the percentage of patients with a true hypersensitivity reaction is only about 5–10% of the self-reported cases with 0.01–0.04% of all patients having true anaphylaxis\textsuperscript{18}.

Of the penicillin allergic patients 94% still received cefuroxime. 84.3% of the 94% had also not received any intra-operative steroid. We thought this was relevant to point out as steroids giving the anti-inflammatory effects of steroids. With majority of our patients not getting intra-op steroids, there is good indication of truly absent reaction in these patients.

It is interesting to note that a patient being penicillin allergic changed the surgeon’s standard choice of antibiotic in only 6% of these allergic to penicillin (Table 2). Subconjunctival gentamicin was the antibiotic that was most used when cefuroxime was avoided in these patients. Other antibiotics used were topical ofloxacin, subconjunctival and intracameral vancomycin. In a study done after the ESCRS endophthalmitis study 67% of doctors in the UK said they did not consider penicillin allergy a contraindication to intracameral cefuroxime\textsuperscript{21}. In NDDH penicillin allergy was not considered a contraindication to intracameral cefuroxime in 87% of those allergic to penicillin and we have no recorded adverse event.

It has been suggested that most of the cross reactivity is with the 1st generation cephalosporins and that with the 2nd generation cephalosporins the cross reactivity with penicillin is negligible\textsuperscript{21}. This is closer to what we have found in this study with cefuroxime being a second generation cephalosporin.

The abundance of lymphoid tissue in the subconjunctival space compared to the immune privileged anterior chamber means a higher risk of triggering a sensitivity reaction in a sensitized patient but no cross reactivity was seen in the 119 penicillin allergic patient who received cefuroxime. (Table 1) The cross reactivity of penicillin and sub conjunctival cefuroxime has also been found to be low in previous studies\textsuperscript{22,23} and in our study this was zero(0).

In the patients who had penicillin allergy recorded we looked at what type of reaction they had recorded (Table 3) We found that 30.5% said they had a rash, 2.6% said they had anaphylactic/ respiratory symptoms with penicillin. Extrapolating this to the whole data we find a self-reported anaphylaxis rate of about 0.3%, this is slightly higher than suggested in previous studies which was 0.2% in one study\textsuperscript{24} and 0.01–0.04% in another\textsuperscript{11}. 
Table 3
Penicillin allergic reaction type and choice of antibiotic

<table>
<thead>
<tr>
<th>Reaction type</th>
<th>IC/SC cefuroxime</th>
<th>Gentamicin</th>
<th>Other</th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>514</td>
<td>21</td>
<td>3</td>
<td>538</td>
<td>(30.5%)</td>
</tr>
<tr>
<td>More severe than a rash/but no anaphylaxis</td>
<td>192</td>
<td>15</td>
<td>4</td>
<td>211</td>
<td>(12.0%)</td>
</tr>
<tr>
<td>Anaphylaxis/respiratory symptoms</td>
<td>28</td>
<td>16</td>
<td>2</td>
<td>46</td>
<td>(2.6%)</td>
</tr>
<tr>
<td>Not recorded</td>
<td>918</td>
<td>44</td>
<td>7</td>
<td>969</td>
<td>(54.9%)</td>
</tr>
</tbody>
</table>

1,764 (100%)

It was also interesting that almost 55% did not have their specific reaction recorded either because they could not recall having a penicillin allergy or it was not explored further. This prompted one of our recommendations which was for more detailed medical records.

This has been a large retrospective study covering over 10 years involving different surgeons and we have found that the risk of anaphylactic reaction from intracameral cefuroxime which is the recommended intraoperative antibiotic for cataract surgery in those allergic to penicillin is negligible and in fact 0 in our study.

**Declarations**

**Financial Disclosure**

None to disclose

**Public/private disclosure**

None to disclose

**PRESENTATION:** As a poster at ESCRS 2nd to 4th October 2020

**ACKNOWLEDGEMENTS**

We would like to thank Mike Dyne from Medisoft who helped us pull the data off Medisoft audit suite.

**VALUE STATEMENT**

WHAT WAS KNOWN
• Previous literature has alluded to a low cross reactivity between penicillin and cefuroxime
• 67% of doctors in the UK did not consider penicillin allergy a contraindication for intracameral cefuroxime following the ESCRS endophthalmitis study

WHAT THIS PAPER ADDS

• In 87% of cases, penicillin allergy was not considered a contraindication to administering intracameral cefuroxime during cataract surgery
• There was 0% cross reactivity between cefuroxime and penicillin in this study as such penicillin allergy should not be considered a contraindication for giving intracameral cefuroxime in cataract surgery.
• We found it safe to administer cefuroxime in penicillin allergic patients as the risk of cross reactivity was 0% in our study

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COMPETING INTEREST

The authors declare that we have no financial nor non-financial interests to disclose.

AUTHOR CONTRIBUTION

All authors contributed to the study. Conception and supervision by Achim Nestel. Material preparation, data collection and analysis were performed by Oluwaniyi Eke, and Umair Arain. The first draft of the manuscript was written by Oluwaniyi Eke and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

References


