

# Single-dose intra-procedural ceftriaxone during endoscopic ultrasound fine-needle aspiration of pancreatic cysts is safe and effective: results from a single tertiary center

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## Abstract

**Background** Endoscopic ultrasound (EUS) with fine-needle aspiration (FNA) is universally used for the investigation and diagnosis of pancreatic cystic lesions (PCL). Infectious complications following EUS-FNA of PCL are rare. Antibiotic prophylaxis to reduce the risk of infection is recommended; however, there is no consensus on the optimal regimen or route of administration. Potential advantages of a single-dose intravenous (IV) antibiotic over a prolonged oral regimen include simplicity, guaranteed delivery and fewer antibiotic related adverse events, but there are only limited data to support this. We aimed to investigate the safety and efficacy of a single 1 g dose of IV ceftriaxone in preventing infectious complications following EUS-FNA of PCL.

**Methods** A retrospective analysis was conducted of EUS-FNA of PCL procedures performed at our center. We reviewed patient medical records for any presentation to a hospital in our district within 30 days of the procedure. An infectious complication was defined as fever/rigors, or bacteremia, or abdominal pain accompanied by imaging or laboratory results suggestive of infection, within 30 days of the procedure. Data collection included patient demographics, procedural data and outcome.

**Results** EUS-FNA of 204 PCL (mean size 18.0 mm) was performed. Successful fluid aspiration was achieved in 94% of cases. Single-dose IV ceftriaxone was given in 146/204 (72%) cases. Four patients had a complication (pancreatitis n=1, post-procedural pain n=3). No infectious complications and no IV antibiotic-related adverse events were identified.

**Conclusion** A single dose of IV ceftriaxone appears to be a safe, effective and convenient intervention for preventing infectious complications after FNA.

**Keywords** Endoscopic ultrasound, fine-needle aspiration, antibiotics, infectious complications

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## Introduction

Endoscopic ultrasound (EUS) with fine-needle aspiration (FNA) is universally used for the investigation and diagnosis of pancreatic cystic lesions (PCL). Infectious complications (i.e. fever, infected cyst or bacteremia) following EUS-FNA

are uncommon, with a reported incidence of 0-6% in various studies [1-6]. Furthermore, prospective data from studies that used antibiotic prophylaxis suggest a very low risk (0-1.4%) of infectious complications [7-9]. However, whilst the incidence is low, post-FNA infection can result in readmission to hospital and adverse patient experience.

Although antibiotic prophylaxis to reduce the risk of infection is recommended by both the American Society of Gastrointestinal Endoscopy and the European Society of Gastrointestinal Endoscopy, there is no consensus on the optimal regimen or route of administration [1,10]. Previous studies reported on the use of single-dose intravenous (IV) regimens, such as ciprofloxacin, or piperacillin/tazobactam, while commonly used 3-5 day oral regimens include ciprofloxacin or amoxicillin/clavulanic acid [7,11]. Potential advantages of a single-dose IV antibiotic over a prolonged oral regimen include simplicity, guaranteed delivery and potentially fewer antibiotic related adverse events; however, there are only limited data to support this.

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Conflict of Interest: None

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Ceftriaxone is a third-generation semisynthetic cephalosporin with a long half-life. It is administered IV or intramuscularly, with an overall excellent safety profile, and has a broad spectrum of activity against Gram-positive, Gram-negative aerobic, and some anaerobic bacteria [12,13]. Ceftriaxone is well-established as the drug of choice for surgical prophylaxis [14,15].

We herein aimed to establish the safety and efficacy of a single-dose intraprocedural antibiotic (1 g IV ceftriaxone) in preventing infectious complications following EUS-FNA of PCL.

## Patients and methods

### Design

We conducted a single-center retrospective analysis of the safety and efficacy of single-dose IV antibiotics during EUS-FNA of PCLs. The study was approved by the local human research and ethics committee (HREC LNRSSA/15/WMEAD/121).

### Patients

Patients who underwent ambulatory EUS-FNA of PCLs at our hospital between March 2006 and December 2015 were identified through an endoscopy reporting database program (ProVation MD, version 5 - ProVation Medical Inc. USA; or Endoscribe - Health Communication Network, Australia).

### Procedure

Westmead Hospital is a tertiary referral center for the Western Sydney local health district, with an annual EUS case volume of over 600. Two consultant gastroenterologists with extensive EUS experience, or their advanced endoscopy fellows under direct supervision, performed all EUS procedures. Procedures were performed under conscious sedation using midazolam, fentanyl, and propofol. Standard EUS-FNA technique was used in all cases. The choice of FNA needle size was at the discretion of the endoscopist: generally, a 19 G or 22 G needle was used for a trans-gastric approach and a 22 G or 25 G for a trans-duodenal approach. Whenever possible cysts were drained to dryness. The decision to administer periprocedural antibiotics (1 g IV ceftriaxone) for non-penicillin allergic patients, or to prescribe oral antibiotics (3-5 days of amoxicillin/clavulanic acid or ciprofloxacin) on discharge from the endoscopy unit was at the discretion of the consultant performing the procedure. Patients were monitored for 1-2 h following the procedure prior to discharge. Analysis of fluid amylase and carcinoembryonic antigen were performed in the hospital pathology lab. Cytology was reported by a specialist cytologist.

### Data collection

Data collection included patient demographics, procedural data and outcome. We reviewed the patient's endoscopy report, their computerized medical records and any presentation to a hospital in our district within 30 days of the procedure. In our health district, computerized medical record software (Powerchart), which includes procedure reports, admission and discharge letters, imaging studies and all laboratory data, has been available since 2006.

### Complications

An infectious complication was defined as fever/rigors, or bacteremia, accompanied by clinical symptoms such as abdominal pain, nausea and vomiting, or by radiological or laboratory evidence of an abdominal infection, all within 30 days of the procedure. Pancreatitis was defined as a  $\geq 3$ -fold elevation in amylase or lipase, or typical findings on computed tomography accompanied by an appropriate clinical scenario.

### Statistical analysis

Continuous data are presented as mean + standard deviation or median + interquartile range (IQR). Categorical data are presented as frequencies. The association between categorical variables was assessed using the chi-square or the Monte Carlo exact test, as needed.

## Results

### Patients

One hundred eighty-four patients (mean age 63 years, 60% female), underwent EUS+FNA of 204 PCLs (median size 20 mm, IQR 16-30) between March 2006 and December 2015. Single-dose IV ceftriaxone was given in 146 procedures, oral antibiotics for 3-5 days were given in 23 procedures and in 35 procedures periprocedural antibiotics were inadvertently omitted (Fig. 1).

### PCLs

The main indications for the procedure included evaluation of newly diagnosed PCL (84%), or surveillance of known PCL (16%). Cyst types were serous (23%), mucinous (14%), intraductal papillary mucinous neoplasms (40%), cystic tumors (17%), or undetermined (6%). Cysts were located in the pancreatic head (31%), neck (12%), body (38%), or tail (12%). Morphologically, cysts were also classified as simple (61%), oligocystic (25%), polycystic (9%), or suspected cystic

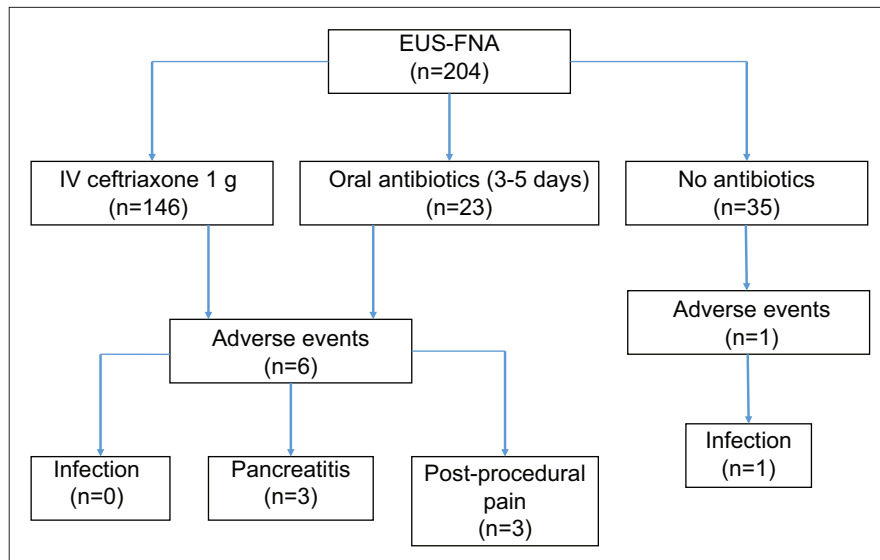


Figure 1 Study flowchart

tumor (5%). Fluid type was recorded as clear/watery (62%), thick/viscous (30%), turbid (5%), or pus (3%).

## Procedure

EUS+FNA was attempted in 204 PCLs. Fluid was successfully aspirated in 191/204 (94%) of the cases. Most commonly, a 22 G needle was used (72%) followed by 19 G (17%) and 25 G (11%). An average of 1.3 passes were made (range 1-5). A summary of the descriptive data is presented in Table 1.

A total of 6 (3%) procedure-related complications were recorded in patients receiving antibiotics. Three patients had post-procedure pancreatitis (2 patients that received an oral regimen and 1 patient who received IV ceftriaxone), and 3 patients had postoperative pain that was resolved in all cases with conservative management. No infectious adverse events were encountered and no antibiotic-related adverse events were recorded in patients receiving periprocedural antibiotics. In the group of patients who did not receive antibiotics (n=35), there was one case (3%) of an infectious complication. Table 2 summarizes the complications and outcomes.

Since our study spanned nearly a decade of clinical practice, we also analyzed the results according to years. We compared the results from procedures performed up to and including 2010 to those performed between 2011 and 2015. We found no differences in the indications, percentage of procedures where antibiotics were administered, the type of antibiotics given and the rate of complications (Table 3). We also found no differences in the study endpoints when comparing different cyst types, although the numbers for each group in this comparison were very small and hence it is difficult to draw conclusions.

## Discussion

EUS+FNA of PCLs has an overall favorable safety profile. However, compared to EUS+FNA of solid lesions, it appears to have a higher risk of infectious complications [1,10]. Current data demonstrate a low risk of infectious complications; however, most studies are retrospective and differ in design, patient characteristics and the use of antibiotics.

In a large retrospective study by Lee *et al* [16], 603 FNA were performed and only 1 patient developed an infectious complication. Antibiotics (fluoroquinolones, ampicillin, vancomycin, or gentamicin) were given at the discretion of the endoscopists and usually in cases of large cysts or incomplete drainage. However, this was not associated with a reduction in infectious complications. In a more recent study, Guarenir *et al* [17] reported on 1 case of cyst infection and 3 cases of antibiotic-related adverse events in a cohort of 88 patients who were given periprocedural antibiotics. In this study, multiple antibiotic regimens were used (levofloxacin in 78 cases, ciprofloxacin plus metronidazole in 3 cases, vancomycin plus gentamicin in 2 cases, piperacillin-tazobactam in 2 cases, and single-dose amoxicillin-clavulanate plus metronidazole, ampicillin, or doxycycline in 3 cases).

There are few prospective studies reporting on infectious complications in patients following EUS-FNA of PCLs. Barawi *et al* [2] reported no infectious complications in EUS-FNA of 108 lesions. In a study by Tarantino *et al* [7], 298 patients received a single dose of piperacillin/tazobactam followed by 3-5 days of oral antibiotics. Four patients (1.3%) developed fever following the procedure. Finally, Marinos *et al* [11] reported no infectious complications in a cohort of 85 EUS-FNA cases that were given a single IV dose of piperacillin/tazobactam or ciprofloxacin. While the results of these studies are encouraging, complex regimens involving parenteral antibiotics hours in advance of the procedure or oral courses

**Table 1** Patient lesions and procedural characteristics

Mean age, years	63
Male sex	40%
Indication	
Evaluation of new PCL	84%
Follow up of PCL	16%
Sonographic diagnosis	
SCA	23%
MCN	14%
IPMN	40%
Cystic tumor	17%
Indeterminate	6%
Mean number of passes (range)	1.3 (1-5)
Needle size	
19 G	17%
22 G	72%
25 G	11%
Median cyst size (IQR)	20 (16-30)
Location	
Head	31%
Neck	12%
Body	38%
Tail	12%
Uncinate	7%
Cyst morphology	
Simple	61%
Oligocystic	25%
Polycystic	9%
Cystic tumor	5%
Mean fluid volume (mL)	2.7 (1-14)
Fluid appearance	
Clear	62%
Viscous	30%
Turbid	5%
Pus	3%
Cytology results	
Non-diagnostic	54%
Normal cells	33%
Malignant/atypical cells	13%

PCL, pancreatic cystic lesion; SCA, serous cyst adenoma; MCN, mucinous cyst neoplasm; IPMN, intrapapillary mucinous neoplasm; IQR, interquartile range

after the procedure increase the complexity of the procedure and may result in non-adherence.

IV ceftriaxone is well-established and frequently used as the drug of choice for surgical prophylaxis [14,15]. It has an excellent safety profile and can be administered as a single IV

**Table 2** Complications in patients receiving intravenous ceftriaxone (n=146)

None	142 (97.2%)
Pancreatitis	1 (0.7%)
Non-specific post-procedural pain	3 (2.1%)
Infection	0 (0%)
Antibiotic-related adverse events	0 (0%)

**Table 3** Comparison between procedures performed up to and including 2010 and those performed between 2011 and 2015

Procedure year	2006-2010	2011-2015	P-value
N	64	140	
Indication			
Cyst follow up	8%	19%	0.059
Initial evaluation	92%	81%	
Antibiotics given			
Yes	81%	83.5%	0.65
No	19%	16.5%	
Type of antibiotic			
Oral 3-5 days	12%	14.4%	0.65
IV ceftriaxone single dose	88%	85.6%	
Complications	3.2%	2.9%	0.89

dose during the procedure, making it an attractive alternative to more complex parenteral and oral regimens previously described. It is also less likely to contribute to the possible future development of complex antibiotic resistance. Although our study was not powered to perform a comparison of complications between the IV ceftriaxone regimen and the oral regimen, or the cases, which did not receive any antibiotics, encouragingly we had no infectious complications and no antibiotic-associated adverse events.

This study has a number of limitations. A retrospective analysis is prone to biases. The patients referred to our endoscopy unit for EUS are generally from our local health district. On discharge following EUS-FNA, all patients are routinely advised to contact us and seek medical treatment if they feel unwell in the days following the procedure. They are provided with a copy of the procedure report, which contains instructions and a telephone number for contacting our center in the event of any complications or re-presentation to medical services. We recognize that theoretically this may occur outside our local health district or in private rooms; however, we believe it is not very likely. We relied on medical records to detect complications following EUS-FNA. We elected not to contact the patients directly, since we believed there would be significant recall bias. Our sample size was not large enough to perform any comparative analysis. However, since the therapeutic intervention reported here has not been previously reported to our knowledge and the body of evidence in this area is lacking, we believe our results are important and will present physicians

## Summary Box

### What is already known:

- Infectious complications following endoscopic ultrasound fine-needle aspiration (EUS-FNA) are uncommon, with a reported incidence of 0-6%
- Both the American and the European Societies of Gastrointestinal Endoscopy recommend antibiotic prophylaxis following EUS-FNA of pancreatic cystic lesions to reduce the risk of infection
- There is no consensus on the optimal antibiotic regimen or route of administration
- Previous reports used complex antibiotic regimens

### What the new findings are:

- In this retrospective analysis, single-dose IV ceftriaxone was effective for the prevention of infectious complications following EUS-FNA of pancreatic cysts
- There were no antibiotic-associated adverse events with this regimen
- This offers clinicians a simple and safe alternative to more complex and prolonged antibiotic regimens

performing EUS-FNA with an additional, non-inferior alternative for the prevention of infectious complications.

In conclusion, EUS-FNA of pancreatic cystic lesions is safe. A single dose of intraprocedural IV ceftriaxone is a convenient, safe and effective intervention to prevent infectious complications following FNA. These results can serve as a platform to design a multicenter randomized control trial that can further investigate the role of antibiotic prophylaxis during EUS-FNA of PCLs.

## References

1. Early DS, Acosta RD, Chandrasekhara V, et al; ASGE Standards of Practice Committee. Adverse events associated with EUS and EUS with FNA. *Gastrointest Endosc* 2013;**77**:839-843.
2. Barawi M, Gottlieb K, Cunha B, Portis M, Gress F. A prospective evaluation of the incidence of bacteremia associated with EUS-guided fine-needle aspiration. *Gastrointest Endosc* 2001;**53**:189-192.
3. Levy MJ, Norton ID, Wiersema MJ, et al. Prospective risk assessment of bacteremia and other infectious complications in patients undergoing EUS-guided FNA. *Gastrointest Endosc* 2003;**57**:672-678.
4. Janssen J, König K, Knop-Hammad V, Johanns W, Greiner L. Frequency of bacteremia after linear EUS of the upper GI tract with and without FNA. *Gastrointest Endosc* 2004;**59**:339-344.
5. O'Toole D, Palazzo L, Arotçarena R, et al. Assessment of complications of EUS-guided fine-needle aspiration. *Gastrointest Endosc* 2001;**53**:470-474.
6. Wiersema MJ, Vilmann P, Giovannini M, Chang KJ, Wiersema LM. Endosonography-guided fine-needle aspiration biopsy: diagnostic accuracy and complication assessment. *Gastroenterology* 1997;**112**:1087-1095.
7. Tarantino I, Fabbri C, Di Mitri R, et al. Complications of endoscopic ultrasound fine needle aspiration on pancreatic cystic lesions: final results from a large prospective multicenter study. *Dig Liver Dis* 2014;**46**:41-44.
8. Williams DB, Sahai AV, Aabakken L, et al. Endoscopic ultrasound guided fine needle aspiration biopsy: a large single centre experience. *Gut* 1999;**44**:720-726.
9. Bournet B, Miguères I, Delacroix M, et al. Early morbidity of endoscopic ultrasound: 13 years' experience at a referral center. *Endoscopy* 2006;**38**:349-354.
10. Polkowski M, Larghi A, Weynand B, et al. Learning, techniques, and complications of endoscopic ultrasound (EUS) -guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline 2012:190-205.
11. Marinos E, Lee S, Jones B, Corte C, Kwok A, Leong RW. Outcomes of single-dose peri-procedural antibiotic prophylaxis for endoscopic ultrasound-guided fine-needle aspiration of pancreatic cystic lesions. *United European Gastroenterol J* 2014;**2**:391-396.
12. Brogden RN, Ward A. Ceftriaxone. A reappraisal of its antibacterial activity and pharmacokinetic properties, and an update on its therapeutic use with particular reference to once-daily administration. *Drugs* 1988;**35**:604-645.
13. Richards DM, Heel RC, Brogden RN, Speight TM, Avery GS. Ceftriaxone. A review of its antibacterial activity, pharmacological properties and therapeutic use. *Drugs* 1984;**27**:469-527.
14. Geroulanos S, Marathias K, Kriaras J, Kadas B. Cephalosporins in surgical prophylaxis. *J Chemother* 2001;**13** Spec No 1:23-26.
15. Gorbach SL. The role of cephalosporins in surgical prophylaxis. *J Antimicrob Chemother* 1989;**23**(Suppl D):61-70.
16. Lee LS, Saltzman JR, Bounds BC, Poneris JM, Brugge WR, Thompson CC. EUS-guided fine needle aspiration of pancreatic cysts: a retrospective analysis of complications and their predictors. *Clin Gastroenterol Hepatol* 2005;**3**:231-236.
17. Guarner-Argente C, Shah P, Buchner A, Ahmad NA, Kochman ML, Ginsberg GG. Use of antimicrobials for EUS-guided FNA of pancreatic cysts: a retrospective, comparative analysis. *Gastrointest Endosc* 2011;**74**:81-86.