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Antibiotic prophylaxis for patients undergoing elective endoscopic retrograde cholangiopancreatography

A survey of South African endoscopists and review of the literature

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Summary

Background. Antibiotic prophylaxis for endoscopic retrograde cholangiopancreatography (ERCP) is controversial. We set out to assess the current antibiotic prescribing practice among South African endoscopists who perform ERCPs, and then reviewed international guidelines and relevant studies.

Methods. Our audit of South African endoscopists who perform ERCPs took the form of a questionnaire. For the literature review a Pubmed search was performed from 1978 to March 2008, and these findings were compared with the current practice in South Africa.

Results. No specific protocols were being implemented widely in South Africa, and there was a marked difference in the practice between surgical and medical gastroenterologists, with surgeons using antibiotics more often. There was also a wide spectrum of antibiotic types that were being used.

The Pubmed search revealed only 7 randomised controlled trials, with little consensus between them as to the absolute indications for prophylactic antibiotics in ERCP.

Conclusions. Guidelines on antibiotic prophylaxis for ERCP are based on poor evidence. Varied opinions on its indications in South Africa may reflect the situation in other countries as well.

Endoscopic retrograde cholangiopancreatography (ERCP) involves cannulation of the ampulla of Vater and has diagnostic as well as therapeutic capabilities, but the number of non-therapeutic ERCPs is decreasing with time.[1] Endoscopic sphincterotomy, stone extraction and stenting are not without complications. The most widely recognised of these include bleeding, which occurs in 0.7 - 2% of patients, perforation (0.3 - 0.6%), pancreatitis (7%), cholangitis (1%) and cholecystitis (0.2 - 0.5%). Procedure-related mortality is approximately 0.2%.[2] Review of international guidelines regarding the use of prophylactic antibiotics with ERCP shows that routine use of antimicrobials is recommended for biliary obstruction and pancreatic pseudocysts. However, several studies, including a meta-analysis, fail to show any benefit.[3-6]

We set out to assess the current antibiotic prescribing practice among South African endoscopists who perform ERCPs, and then review international guidelines and relevant studies.

Methods

Our audit of South African endoscopists who perform ERCPs took the form of a questionnaire. This was distributed at the Hepato-Pancreatico-Biliary Association of South Africa Congress held during October 2007 in Johannesburg, and was also sent to all members of the South African Gastro-Enterology Society via email. The questionnaire was anonymous. Endoscopists were questioned regarding their years of experience, the monthly volume of ERCPs they perform, and their indications for antibiotic prophylaxis (for diagnostic biliary ERCP, diagnostic pancreatic ERCP, therapeutic biliary ERCP and therapeutic pancreatic ERCP). Respondents were also asked to indicate their antibiotic of preference and the number of doses administered. The results were then tabulated for comparison, and the chi-squared test was used to calculate p-values. A p-value of 0.05 was considered significant.

A Pubmed search was performed from 1978 to March 2008 using the search terms Cholangiopancreatography-Endoscopic-Retrograde Antibiotic-Prophylaxis, random* or control* or blind* or meta-analys*, all subheadings. An Internet search was also performed to identify recommendations from various international gastrointestinal societies.

Results

Thirty-nine endoscopists (22 surgeons, 16 medical gastroenterologists and 1 radiologist) responded to our questionnaire. Most had more than 6 years of experience (30/39) and performed more than 10 ERCPs per month (22/39). Approximately half of the endoscopists (19/39) were aware of ERCP antibiotic protocols, either the American Society of Gastro-Enterology (ASGE) or UK National Health Service (NHS) recommendations. The results are depicted in Table I. 'Always' implied that the endoscopist used antibiotic prophylaxis with each patient, 'selected' implied specific indications, and 'never' implied no use of antibiotic prophylaxis.

TABLE I. AUDIT RESULTS

	Surgeons (*N*=22)			Gasteroenterologists + radiologist (*N*=6+1)		
ERCP	Always	Selected	Never	Always	Selected	Never
Diagnostic biliary	**14**	**5**	**3**	**2**	**8**	**5**
Diagnostic pancreatic	**13**	**6**	**3**	**2**	**4**	**11**
Therapeutic biliary	**19**	**2**	**1**	**5**	**10**	**2**
Therapeutic pancreatic	**19**	**2**	**1**	**5**	**9**	**3**

'Always' = antibiotic prophylaxis used with each patient; 'selected' = specific indications; 'never' = no use of antibiotic prophylaxis.

No endoscopist performed sphincter of Oddi pressure studies. The *p*-value of surgeons versus other endoscopists using antibiotics for diagnostic biliary ERCP was 0.01, for diagnostic pancreatic ERCP 0.0018, for therapeutic biliary ERCP 0.012 and for therapeutic pancreatic ERCP 0.0014.

The preferred antibiotic was piperacillin and tazobactam (14/39), followed by gentamicin (8/39), cephalosporins (6/39), ciprofloxacin (4/39) and co-amoxiclavulanic acid (3/39). Of the endoscopists 30 administered the antibiotic as a single dose before the procedure, 5 preferred a 24-hour course, 3 gave antibiotics for 48 hours and 1 did so for 5 days. All but 3 of the endoscopists administered the antibiotics via the intravenous route.

The recommendations of various gastrointestinal/endoscopic societies are summarised in Table II.

The Pubmed search yielded 44 results, of which 14 were clinical trials. Of these trials only 2 were randomised, double-blind, placebo-controlled trials (Table III) and 5 were randomised controlled trials (Table IV). Three trials compared different antibiotic regimens and 4 were not applicable to this topic.

Discussion

Currently there are 102 gastroenterologists registered with the Health Professions Council of South Africa, consisting of 26 surgical and 76 medical gastroenterologists. The 39 doctors who responded to our questionnaire are probably an accurate representation of the endoscopists who perform ERCPs. The results of our questionnaire demonstrate that South African endoscopists do not follow any consistent antibiotic protocol, and that there is also a significant difference in antibiotic usage between surgeons and non-surgeons. It is postulated that surgeons use antibiotics more often because they are more likely to deal with cases of severe pancreatic sepsis and this may influence their prescribing habit. There appears to be no adherence to evidence-based medicine or guidelines in South Africa in this regard. Review of the current literature did not identify a similar national audit of this nature, and we wonder whether the varied antibiotic practice we identified here does not also occur in other countries.

The question arises as to whether or not prophylactic antibiotics are required with ERCP. Experimental studies have shown that bacterial regurgitation from bile into the hepatic venous blood flow, which creates bacteraemia, is directly proportional to biliary pressure, in other words to the degree of obstruction.[11] For this reason decompression alone will effectively either prevent or resolve established cholangitis, although in all likelihood patients with established cholangitis will already be on antibiotics, making prophylactic antibiotics irrelevant.[12] Cotton *et al.* demonstrated in an 11-year audit of their unit that a high rate of technical success in relieving biliary obstruction reduced the incidence of septic complications as well as the use of prophylactic antibiotics.[13] It is a well-recognised fact that endoscopic procedures result in bacteraemia, and ERCP is associated with a bacteraemia rate as high as 14%.[14] However, studies have shown that organisms isolated on blood or bile cultures and those cultured from the endoscope or the irrigation system are often the same.[6,14,15] Proper disinfection of the endoscope should therefore decrease the frequency of bacteraemia. Routine surveillance cultures of endoscopes should be instituted, but it must be kept in mind that infectious complications can still occur, particularly with *Pseudomonas aeruginosa*.[16] It has been suggested that even a single confirmed *Pseudomonas* infection following ERCP should be investigated with an epidemiological study.[17]

Our Pubmed search illustrated the conflicting evidence for the use of prophylactic antibiotics. Van den Hazel *et al.*[7] and Byl *et al.*[8] used similar cohorts (patients with an obstructed biliary duct) and came to opposite conclusions. However, the duration of the prophylaxis used in Byl *et al.*'s study was up to 7 days or until the obstruction was relieved. Only two of the controlled trials concluded that there was a benefit in using prophylaxis in an obstructed biliary system.[9,10] Previously patients at high risk of infective endocarditis, including those with a previous history of infective endocarditis, prosthetic heart valves, cyanotic heart conditions and surgically created shunts or conduits, were thought to require antibiotic cover.[9] However, the current recommendation of the American Heart Association is that antibiotic prophylaxis is not required with any gastrointestinal endoscopic procedure.[18,19] Currently patients who have had a synthetic vascular graft placed within 1 year of the proposed ERCP procedure should receive prophylaxis.[20] Patients who have a prosthetic orthopaedic joint do not require antibiotic prophylaxis.[21]

In our opinion, and after analysis of current literature, the only patients who should receive antibiotic prophylaxis are those who have complex biliary obstruction that is unlikely to be resolved by one ERCP procedure, and probably patients with pancreatic pseudocysts that are not drained. Others are those at high risk of bacterial endocarditis or who have had a synthetic vascular graft within the past year.

Conclusion

Guidelines on antibiotic prophylaxis for ERCP are based on poor evidence, and there is inconsistent usage in South Africa, which may reflect the situation in other countries as

TABLE II. SUMMARY OF SOCIETY GUIDELINES

Society	Recommendation	Suggested antibiotic
ASGE	**'All patients undergoing ERCP for known or suspected biliary obstruction or known pancreatic pseudocyst should receive antibiotics along with adequate drainage of the biliary obstruction or cyst'**	**'Antibiotics that cover biliary flora such as enteric gram-negative organisms, enterococci and possibly pseudomonns are recommended'**
NHS	**'Antibiotic prophylaxis is recommended for all patients undergoing ERCP with evidence of biliary stasis or pancreatic pseudocyst'**	**Oral ciprofloxacin or parenteral gentamicin (or parenteral quinolone, cephalosporin or ureidopenicillin)**
ESGE	**'Antibiotic prophylaxis is recommended for patients who are likely to undergo therapeutic ERCP if there has been previous biliary sepsis, bile duct obstruction or pancreatic pseudocyst'**	**Ciprofloxacin 750 mg orally 60 - 90 min before the procedure OR gentamicin 120 mg intravenously just before the procedure OR parenteral quinolone, cephalosporin or ureidopenicillin**
CAG	**'Biliary obstruction with possible sepsis is another high-risk situation, especially with instrumentation, and even average risk patients deserve prophylaxis'**	**Ampicillin 2 g & gentamicin 1.5 mg/kg not exceeding 120 mg intravenously within 30 min of starting; 6 h later, ampicillin 1 g intravenously or IMI**
GESA	**'Antibiotic prophylaxis is recommended for selected patients'**	**Ciprofloxacin oral 750 mg or IV 200 mg 2 h before procedure OR Piperacillin 4.5 g IV 30 min before procedure OR piperacillin + tazobactam 4.5 g IV 30 min before procedure OR ticacillin ± clavulinic acid 3.1 g 30 min before procedure**

ASGE = American Society of Gastro-Enterology; NHS = UK National Health Services; ESGE = European Society for Gastro-Enterology; CAG = Canadian Association of Gastroenterology; GESA = Gastro-Enterology Society of Australia.

TABLE III. RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIALS

Author	Method of study	Author's conclusions
Van den Hazel *et al.*[7]	**Group I: single-dose piperacillin 4 g 30 min before ERCP (*N*=270) Group II: placebo 30 min before ERCP (*N*=281) Inclusion criteria: suspected biliary tract stones, or distal CBD stricture**	**Single-dose prophylaxis with piperacillin is not associated with a clinically significant reduction in the incidence of acute cholangitis after ERCP**
Byl *et al.*[8]	**Group I: piperacillin 4 g TDS just before ERCP until biliary obstruction relieved, or maximum of 7 days (*N*=34) Group II: placebo TDS from just before ERCP until obstruction relieved, or maximum of 7 days (*N*=34) Inclusion criteria: age >18 years, cholestasis, ERCP for ultrasonically suspected bile duct stone/stricture**	**Antimicrobial prophylaxis significantly reduces the incidence of septic complications**

CBD = common bile duct.

TABLE IV. RANDOMISED CONTROLLED TRIALS

Author	Method of study	Author's conclusions
Llach *et al.*[4]	**Group I: clindamicin 600 mg and gentamicin 80 mg 1 h before ERCP (*N*=31) Group II: control (*N* =30) *Inclusion criteria:* consecutive patients referred for ERCP**	**Prophylactic administration of clindamicin and gentamicin does not reduce the incidence of bacteraemia and cholangitis**
Lorenz *et al.*[5]	**Group I: single-dose cefuroxime 1.5 g 30 min before ERCP (*N*=49) Group II: control (*N*=50) *Inclusion criteria:* consecutive patients with bile duct obstruction or pancreatic duct stenosis**	**Rates of bacteraemia and septicaemia between two groups not statistically significant**
Raty *et al.*[9]	**Group I: single-dose ceftazidime 2 g 30 min before ERCP Group II: control *Inclusion criteria*: all consecutive patients for ERCP**	**Antibiotic prophylaxis effectively decreases the risk of pancreatitis and cholangitis**
Niederau *et al.*[10]	**Group I: single-dose cefotaxime 2 g 15 min before ERCP (*N*=50) Group II: control (*N*=50) *Inclusion criteria*: consecutive patients to undergo therapeutic or complicated diagnostic ERCP**	**Prophylactic antibiotics can reduce the incidence of bacteraemia and septicaemia**
Sauter *et al.*[6]	**Group I: single-dose cefotaxime 2 g 15 min before ERCP (*N*=50) Group II: control (*N*=50) *Inclusion criteria:* unselected consecutive ERCP patients**	**The frequency of cholangitis following ERCP was not significantly reduced by antibiotic prophylaxis**

well. Overuse seems to be occurring, and we suspect that this is probably the case in other countries. National audits would be helpful in elucidating the magnitude of the problem.

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