Evidence based case report

Antibiotic treatment for spontaneous bacterial peritonitis

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A 55 year old woman, previously diagnosed with cirrhosis secondary to chronic hepatitis C infection, was admitted to our department with fever. She seemed well and had no focal symptoms or signs of infection. As ascites was present, she had paracentesis. This yielded a Gram negative clear fluid with a polymorphonuclear count of 700 cells/mm^3. We thought that secondary peritonitis was unlikely and diagnosed spontaneous bacterial peritonitis. She had had no previous episodes or prophylactic antibiotic treatment. Empirical treatment with cefotaxime (2 g every 8 hours) was started.

How did we choose our treatment?

When admitting the patient, the junior doctor had access to two main databases: the Cochrane Library, which contained no relevant information,[1] and UpToDate, which recommended intravenous cefotaxime or oral ofloxacin for patients with uncomplicated spontaneous bacterial peritonitis.[2]

On the morning after her admission, there was a lively discussion at the departmental meeting. The main question was whether the patient could have started taking oral ofloxacin, given her excellent clinical condition. Other questions were raised about the strength of the evidence supporting the standard treatment with cefotaxime and the ideal dose and duration of treatment. We therefore decided to do a systematic review of the literature on antibiotic treatment for spontaneous bacterial peritonitis.

Searching for evidence

We searched Medline (1966-December 2000) and the Cochrane Library (Issue 4, 2000) for randomised trials comparing different antibiotics for spontaneous bacterial peritonitis (table 1). Additionally, we inspected the references of all identified studies and a consensus document organised by the International Ascitic Club[3] and contacted authors by email to ask for complementary information.

Our search strategy identified 18 trials. We excluded five studies because of inadequate concealment of allocation[4–8]; two because less than 10% of the patients had spontaneous bacterial peritonitis diagnosed[9 10]; one because it lacked an antibiotic comparison[11]; and another because of missing relevant information.[12] We included nine randomised trials in the review (table 2).[13–21]

We searched for the following outcomes in the nine included studies: mortality, antibiotic effectiveness in current episode, and life threatening adverse events. None of the trials compared similar experimental and control treatments. We therefore analysed the results of each trial separately.

Assessing the evidence

Should cefotaxime be regarded as the treatment of choice?—No reliable evidence exists to place cefotaxime as the treatment of choice for spontaneous bacterial peritonitis, although this has been suggested by many authors.[3 17 22] In one trial in which 72 patients were randomised to intravenous cefotaxime or ampicillin plus tobramycin, cefotaxime had no significant benefit on mortality or fatal adverse events, although it did increase resolution of spontaneous bacterial peritonitis (table 2).[13]

What is the optimal dose and duration of cefotaxime?—Only two relevant trials were identified.[19 20] The results indicate that cefotaxime 4 g/day may be as effective as cefotaxime 8 g/day[19] in terms of mortality and resolution of symptoms. Treatment for 10 days was no more effective than treatment for five days.[20]

Are oral or intravenous antibiotics more effective?—Four trials evaluated the effects of oral and intravenous antibiotics on mortality and resolution of symptoms,[14 16 17 21] but no definite conclusions could be drawn. No significant differences were found in trials

Table 1 Search strategy used in Medline and Cochrane Library

Database	Search strategy	Results
Cochrane Library (issue 4, 2000)	((Peritonitis*.ME or peritonitis) and spontaneous) AND (Liver-cirrhosis*.ME or cirrhosis) AND (Antibiotics*.ME or antibiotic*)	14 references
Medline (1966-December 2000)	Search described for the Cochrane Library AND (Randomised-controlled-trial in PT or Controlled-clinical-trial in PT or Randomised-controlled-trials or Random-allocation or Clinical-trial in PT or Clinical trials)	15 References

Table 2 Main results of randomised clinical trials of antibiotic treatment for spontaneous bacterial peritonitis

Trial	Outcome	Experimental group (No with outcome/total No)	Control group (No with outcome/total No)	Relative risk (95% CI)
Felisart 1985[13]	Death	Cefotaxime (14/37)	Ampicillin+tobramycin (10/36)	1.36 (0.70 to 2.66)
	Resolution of SBP	Cefotaxime (28/37)	Ampicillin+tobramycin (18/36)	1.51 (1.04 to 2.20)
	Fatal adverse events	Cefotaxime(0/37)	Ampicillin+tobramycin (1/36)	0.33 (0.01 to 7.93)
	Nephrotoxicity	Cefotaxime (0/37)	Ampicillin+tobramycin (1/36)	0.33 (0.01 to 7.93)
Figueiredo 1997[14]	Death	Cefixime (4/20)	Ceftriaxone (3/18)	1.20 (0.31 to 4.65)
	Resolution of SBP	Cefixime (18/20)	Ceftriaxone (17/18)	0.95 (0.79 to 1.15)
Gomez-Jimenez 1993[15]	Death	Cefonicid (11/30)	Ceftriaxone (9/30)	1.32 (0.66 to 2.64)
	Resolution of SBP	Cefonicid (27/30)	Ceftriaxone (30/30)	0.90 (0.79 to 1.03)
	Fatal adverse events	Cefonicid (1/30)	Ceftriaxone (0/30)	3.00 (0.13 to 70.83)
Navasa 1996[16]	Death	Ofloxacin (12/64)	Cefotaxime (11/59)	1.01 (0.48 to 2.10)
	Resolution of SBP	Ofloxacin (54/64)	Cefotaxime (50/59)	1.00 (0.86 to 1.16)
Rimola 1984[18]	Death	Ampicillin+tobramycin (10/18)	Ampicillin+tobramycin+neomycin+nystatin+colistin (7/18)	1.51 (0.73 to 3.10)
		Ampicillin+tobramycin (12/18)	Ampicillin+tobramycin+neomycin+nystatin+colistin (16/18)	0.79 (0.54 to 1.16)
Rimola 1995[19]	Death	Low dose cefotaxime (22/71)	High dose cefotaxime (15/72)	1.49 (0.84 to 2.63)
	Resolution of SBP	Low dose cefotaxime (51/71)	High dose cefotaxime (55/72)	0.94 (0.77 to 1.14)
Ricart 2000[17]	Death	Co-amoxiclav (3/24)	Cefotaxime (5/24)	0.60 (0.16 to 2.23)
	Resolution of SBP	Co-amoxiclav (21/24)	Cefotaxime (20/24)	1.05 (0.83 to 1.33)
Runyon 1991[20]	Death	5 days' cefotaxime (14/43)	10 days' cefotaxime (20/47)	0.77 (0.44 to 1.32)
	Resolution of SBP	5 days' cefotaxime (27/43)	10 days' cefotaxime (31/47)	0.95 (0.70 to 1.30)
Terg 2000[21]	Death	Oral+intravenous ciprofloxacin (11/40)	Intravenous ciprofloxacin (11/40)	1.0 (0.49 to 2.04)
	Resolution of SBP	Oral+intravenous ciprofloxacin (29/40)	Intravenous ciprofloxacin (29/40)	1.0 (0.76 to 1.31)

SBP=spontaneous bacterial peritonitis.

of oral ofloxacin versus cefotaxime[16] and of oral versus intravenous ciprofloxacin.[21] However, the trials were small and should be considered inconclusive. Finally, it has been suggested that patients with moderate symptoms and a positive response to a short course of intravenous antibiotics could benefit from oral treatment with quinolones.[3 21 22] The only trial investigating quinolones found no significant effect on mortality or resolution of symptoms.[21]

Outcome for patient

On the third day, cultures of the blood and ascitic fluid were negative. The patient was afebrile and doing well, and we offered to discharge her on oral ofloxacin. She was reluctant to switch to oral therapy and leave the hospital. Although she understood that one trial showed no benefit for cefotaxime over oral ofloxacin,[16] she was alarmed that we could not rule out that the risk of a death with ofloxacin might be twice as high as with cefotaxime. We tried to balance that against the risk of a severe nosocomial infection (about 2% a day).[23] The patient was unconvinced. She found the monitoring and intravenous therapy reassuring and opted for five days' treatment with cefotaxime and then oral ofloxacin. She was discharged on the sixth day after an uneventful stay.

Comment

The patient was treated in real time according to the available information.[2] A later discussion led to a systematic review. Clearly, clinicians cannot do a systematic review for every question raised in their daily experience. Nevertheless, reviewing the literature in depth enables clinicians to comprehend where practices stem from, how these are founded on evidence, and sometimes, as in this case, how frail the evidence is to support routine practices.

We found no convincing evidence concerning efficacy of antibiotics for spontaneous bacterial peritonitis, and we identified several gaps that warrant future research. For example, we found no conclusive evidence to support cefotaxime as the treatment of choice[3] or to recommend quinolones for patients with uncomplicated spontaneous bacterial peritonitis.[16] Until large, well conducted trials have been published, antibiotic treatment for spontaneous bacterial peritonitis has to be based on clinical experience.

Randomised trials of spontaneous bacterial peritonitis need to include several hundred patients in order to have sufficient power. Recruitment of sufficient patients should be possible given the relatively high prevalence of cirrhosis complicated by ascites and the incidence of spontaneous bacterial peritonitis in these patients.[3 23] Future trials should also examine long term outcomes, recurrence rate, long term survival, and the development of resistant pathogens, particularly with quinolones.

This paper was based on the results of a systematic review recently published in the Cochrane Library.[24]

Contributors: KSW formulated the problem, designed the protocol, searched the literature, participated in the data collection and analysis, and wrote the paper. MB collaborated in data collection and analysis and commented on the final draft. MP helped in the data collection and provided details from the patient. LL coordinated and supported the protocol design, data analysis, and interpretation and helped in writing the paper. KSW and LL are the guarantors.

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A medical mishap

What came first and what seems worse

Clinical mishaps are likely to be overlooked and buried—or concealed by sympathetic patients, relatives, or colleagues. Mine was very public, the talk of the hospital. Doctors came from far and wide to admire it, and if it wasn't photographed for a textbook it should have been. As an exchange student in the United States, I was asked to do a tuberculin test on a patient with mysterious shadows in her lungs. Tuberculin came in twin packs labelled "first strength" and "second strength." I misunderstood the instructions and used the wrong one. The patient had an extreme response—a black carbuncle on her arm the size of a plum. Everyone was kind about it, particularly the victim. In those days patients entering teaching hospitals cost-free did not expect them to be risk-free. But they did expect their experience to be exotic. This certainly was. The reaction was construed as of great diagnostic significance, not that we ever made a diagnosis.

Nowadays, I suppose I might be sued, the incident reported, and somebody might tell the manufacturer that their labelling was inherently ambiguous. Sometimes first strength means weaker than second, sometimes stronger. Think of football teams. Thirty seven years later, I cannot remember which pack was which. Anyway, read instructions carefully. Twice. If you write them, keep them simple. Even better, keep the stronger stuff somewhere separate.

As a young doctor, I buried the usual complement of patients—through ignorance, misdiagnosis, or oversight, but not, I comfort myself, through neglect. I lost plenty of sleep, but never worrying about, or regretting, clinical decisions. Decades later, however, I still squirm when remembering what should be best controlled and least excused—things said or not said rather than what was done or not done:

As a house surgeon, I clerked an anxious patient with varicose veins. She was scheduled at the end of a long operating list and was preceded by a patient who would either be opened and shut or involved in heroic surgery. My patient was warned we might not get to her, and so it happened. Cancelling or postponing operations was rare in those days. As he began stitching up the previous patient, the registrar released me from helping and sent me up to the ward to apologise: "Guarantee her a place on the next list. Best coming from you, Hugh." Little did he know. After that first case, however, varicose veins seemed superficial and trivial.

Tired and dishevelled, I made for the lift after checking that my theatre pyjamas weren't bloody. It was Friday evening. Outside the ward visitors waited their cue to enter. Inside there was bustle and excited anticipatory chatter. Supper had just finished and was being cleared up. Except for my patient. In accordance with custom, she was laid out like a corpse in a sepulchre—in shroud-like theatre garb, with curtains half drawn, and "Nil to eat or drink" exhibited over the bed.

"I'm very sorry we can't do your operation today," I explained. "You are guaranteed a place on the very next list."

She gazed at me in silent, anguished terror.

"Anyway," I said, trying to be helpful and make conversation, "now you can eat and drink. . . ."

Her countenance failed to change.

Just as I realised the implications, I added, ". . .and be merry."

"Yes," she said melodramatically, "for tomorrow we die," and burst into tears.

An unwritten role of hospital nurses is mopping them up after doctors have been. What was said could not be unsaid. I stood looking at her, tired, hungry, at a loss what to say, the situation beyond my control.

She had her operation on the next list and didn't die. Somehow that did not really make amends.

Hugh Tunstall-Pedoe *professor of cardiovascular epidemiology, University of Dundee*

We welcome articles up to 600 words on topics such as *A memorable patient, A paper that changed my practice, My most unfortunate mistake,* or any other piece conveying instruction, pathos, or humour. If possible the article should be supplied on a disk. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for "Endpieces," consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.