Sepsi da E. coli ESBL+ a partenza dalle vie biliari: alternative ai carbapenemi ?

Dr Biagetti Carlo
UO Malattie Infettive AUSL Rimini

Attualità in infettivologia 2013

Corso di Aggiornamento

con il patrocinio di

in collaborazione con

Le Infezioni Associate alle Cure Sanitarie

20 Giugno 2013
Azienda Ospedaliero-Universitaria Ferrara
Nuovo Arcispedale S. Anna - Polo Ospedaliero di Cona (Fe) - Aula Congressuale

Introduzione

- Gli enterobatteri GRAM neg ESBL+ sono caratterizzati dalla capacità di inattivare la maggior parte degli antibiotici beta lattamici, ma non i carbapenemi
- Per questo motivo negli ultimi anni ad una diffusione dei ceppi ESBL+ si è associato un aumentato consumo di carbapenemi con l'inevitabile selezione di enterobatteri produttori di carbapenemasi

Introduzione

Nuovi antibiotici

Razionalizzazione utilizzo carbapenemi

Sistema di sorveglianza

Controllo degli enterobatteri produttori di carbapenemasi in Emilia-Romagna

2011-2012

Agenzia sanitaria e sociale regionale

RegioneEmilia-Romagna

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA

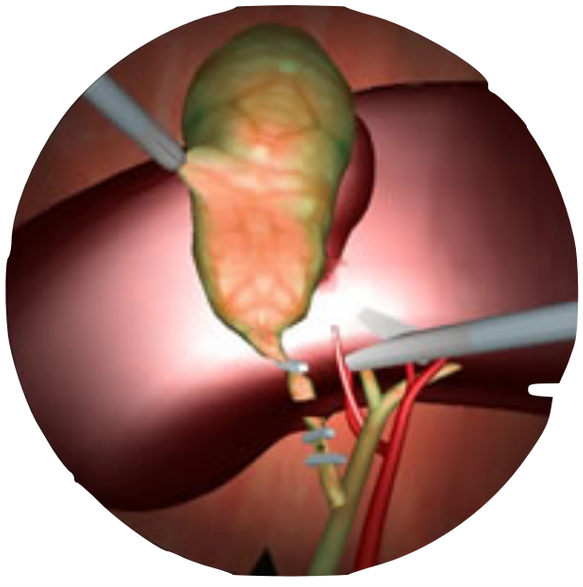
Case report

- Paziente maschio di 66 anni
- Anamnesi Pat Rem:

2003 TURV (Resezione Tumore Vescicale per via trans uretrale) con successivo follow-up neg

2010 litiasi colecisti e VBP per cui ha eseguito ERCP con sfinterotomia e bonifica endoscopica

2010 colecistectomia



Case report

- Anamnesi Pat Rec:

  da circa una settimana lamentava dolori addominali ai quadranti superiori prevalentemente post-prandiali, associati a nausea e vomito e da tre giorni febbre con puntate max a 38°C e subittero, per cui accedeva al PS

  A domicilio ha assunto solo paracetamolo

19
dom 19 maggio 2013

Case report

Infection, documented or suspected, and some of the following:
General variables
Fever (> 38.3°C)
Hypothermia (core temperature < 36°C)
Heart rate > 90/min^{-1} or more than two SD above the normal value for age
Tachypnea
Altered mental status
Significant edema or positive fluid balance (> 20 mL/kg over 24 hr)
Hyperglycemia (plasma glucose > 140 mg/dL or 7.7 mmol/L) in the absence of diabetes
Inflammatory variables
Leukocytosis (WBC count > 12,000 μL^{-1})
Leukopenia (WBC count < 4000 μL^{-1})
Normal WBC count with greater than 10% immature forms
Plasma C-reactive protein more than two SD above the normal value
Plasma procalcitonin more than two SD above the normal value
Hemodynamic variables
Arterial hypotension (SBP < 90 mm Hg, MAP < 70 mm Hg, or an SBP decrease > 40 mm Hg in adults or less than two SD below normal for age)
Organ dysfunction variables
Arterial hypoxemia (Pao_2/FIO_2 < 300)
Acute oliguria (urine output < 0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation)
Creatinine increase > 0.5 mg/dL or 44.2 μmol/L
Coagulation abnormalities (INR > 1.5 or aPTT > 60 s)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count < 100,000 μL^{-1})
Hyperbilirubinemia (plasma total bilirubin > 4 mg/dL or 70 μmol/L)
Tissue perfusion variables
Hyperlactatemia (> 1 mmol/L)
Decreased capillary refill or mottling

TC:39°C
FC:110 batt/min
GB:13000, N:86%
PCR:178
Bil tot:6.26
GPT:571
Creatinina:1.03
PT:1,2

19
dom 19 maggio 2013

Case report

Severe sepsis definition = sepsis-induced tissue hypoperfusion or organ dysfunction (any of the following thought to be due to the infection)
Sepsis-induced hypotension
Lactate above upper limits laboratory normal
Urine output < 0.5 mL/kg/hr for more than 2 hrs despite adequate fluid resuscitation
Acute lung injury with Pao_2/Fio_2 < 250 in the absence of pneumonia as infection source
Acute lung injury with Pao_2/Fio_2 < 200 in the presence of pneumonia as infection source
Creatinine > 2.0 mg/dL (176.8 μmol/L)
Bilirubin > 2 mg/dL (34.2 μmol/L)
Platelet count < 100,000 μL
Coagulopathy (international normalized ratio > 1.5)

19
dom 19 maggio 2013

Case report

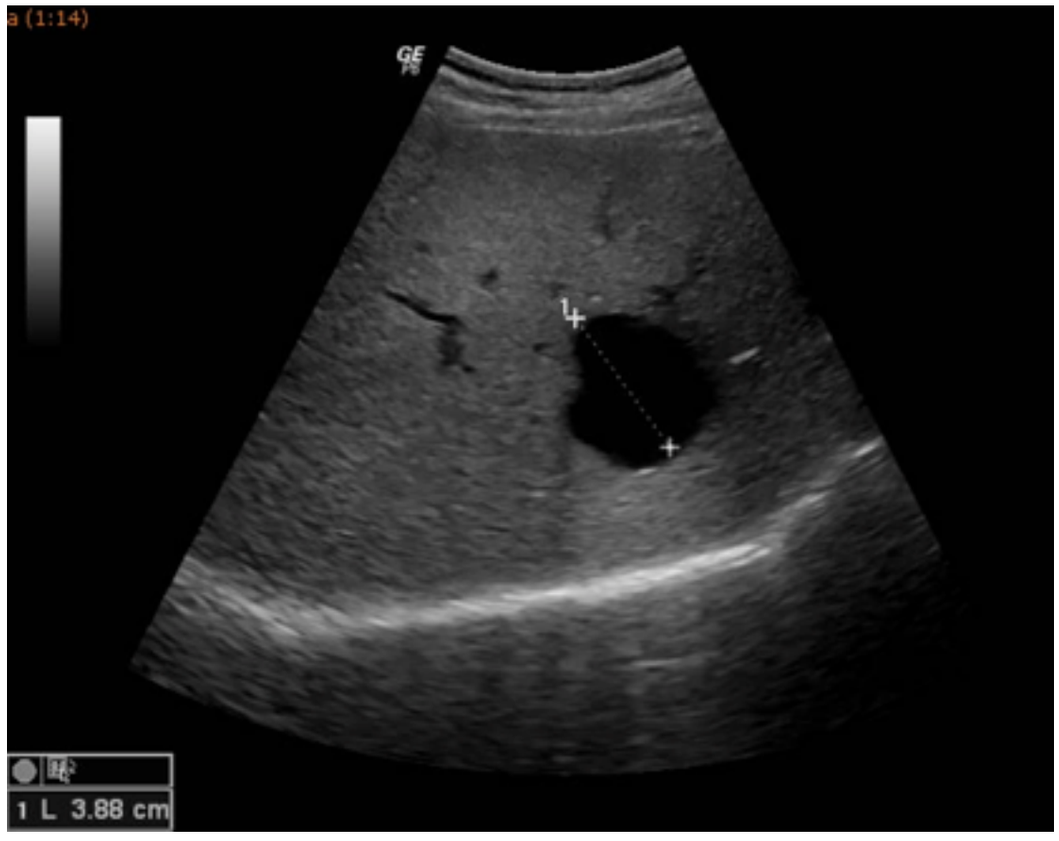
Esegue:

- due coppie di emocolture
- inizia terapia e.v. con Amoxicillina+clavulanato 2 g
- ECO addome

19
dom 19 maggio 2013

Case report

Esiti di colecistectomia. Strie iperecogene in corrispondenza delle diramazioni biliari intraepatiche e dell'epato-coledoco in relazione ad aerobilia, non valutabili per calibro le vie biliari medesime.
Fegato nei limiti morfovolumetrici, con steatosi di II grado, areole ipoecogene perilari in relazione a parenchima risparmiato. Formazione liquida a profili lobulati con diametro di 38 mm all'VIII segmento. Pancreas, milza e reni nei limiti (cisti parapieliche al polo inferiore del rene dx). Non calcoli né idronefrosi.

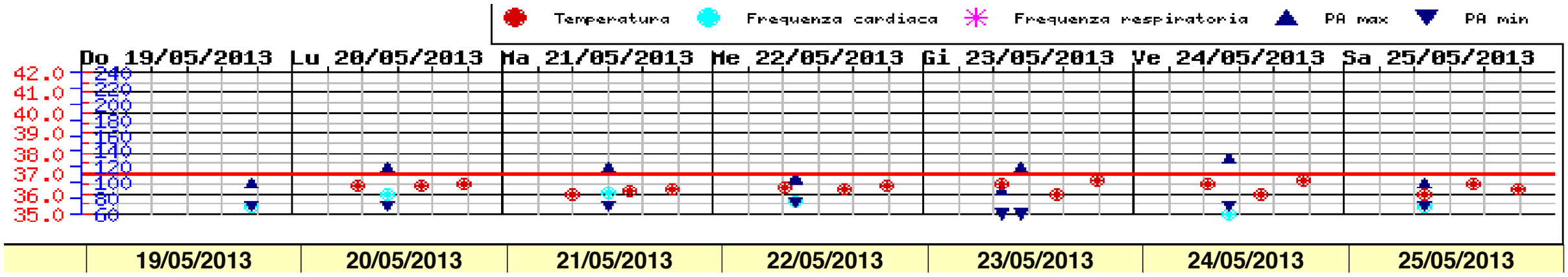


19
dom 19 maggio 2013

Case report

- V. chirurgica: non indicazioni chirurgiche
- ricoverato in Malattie Infettive

  All'ingresso (10 h dopo l'inizio della terapia antibiotica) il paziente è apirettico con parametri vitali nella norma, persiste la sintomatologia addominale.



Case report

Confermare la terapia con Amoxicillina+clavulanto ?

A quale dosaggio ?

Case report

The 2013 update of the World Society of Emergency Surgery (WSES)

Sartelli *et al. World Journal of Emergency Surgery* 2013, **8**:3
http://www.wjes.org/content/8/1/3

WORLD JOURNAL OF EMERGENCY SURGERY

REVIEW Open Access

2013 WSES guidelines for management of intra-abdominal infections

Appendix 5. Antimicrobial therapy for biliary IAI in stable, non-critical patients presenting with no ESBL-associated risk factors (WSES recommendations)

Community-acquired biliary IAIs
Stable, non-critical patients
No risk factors for ESBL
AMOXICILLIN/CLAVULANATE
Daily schedule: 2.2 g every 6 hours (2-hour infusion time)
OR (in the event of patients allergic to beta-lactams)
CIPROFLOXACIN
Daily schedule: 400 mg every 8 hours (30-minute infusion time)
+
METRONIDAZOLE
Daily schedule: 500 mg every 6 hours (1-hour infusion time)

Case report

Nel sospetto di colangite/ascesso epatico:

Enterobacteriacee 70%

Enterococchi: 14%

Bacteroides:10%

Clostridium 7%

- amoxi+clavulanato 1 g ogni 8 h

  pipera+tazo 4.5 g ogni 8h

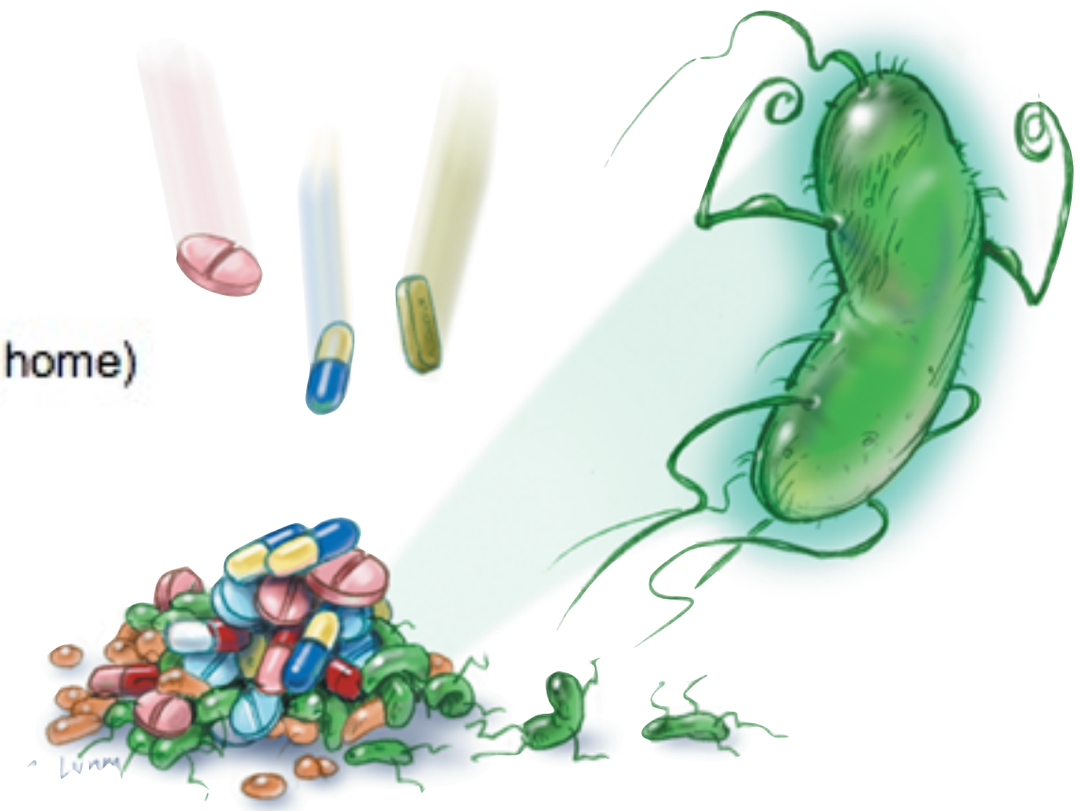
  ceftriaxone 2g ogni 24 o ciprofloxacina/levofloxacina 750mg+ metronidazolo 30mg/kg in tre dosi

  se il paziente è in gravi condizioni: carbapenemi

Case report

Fattori di rischio per ESBL+

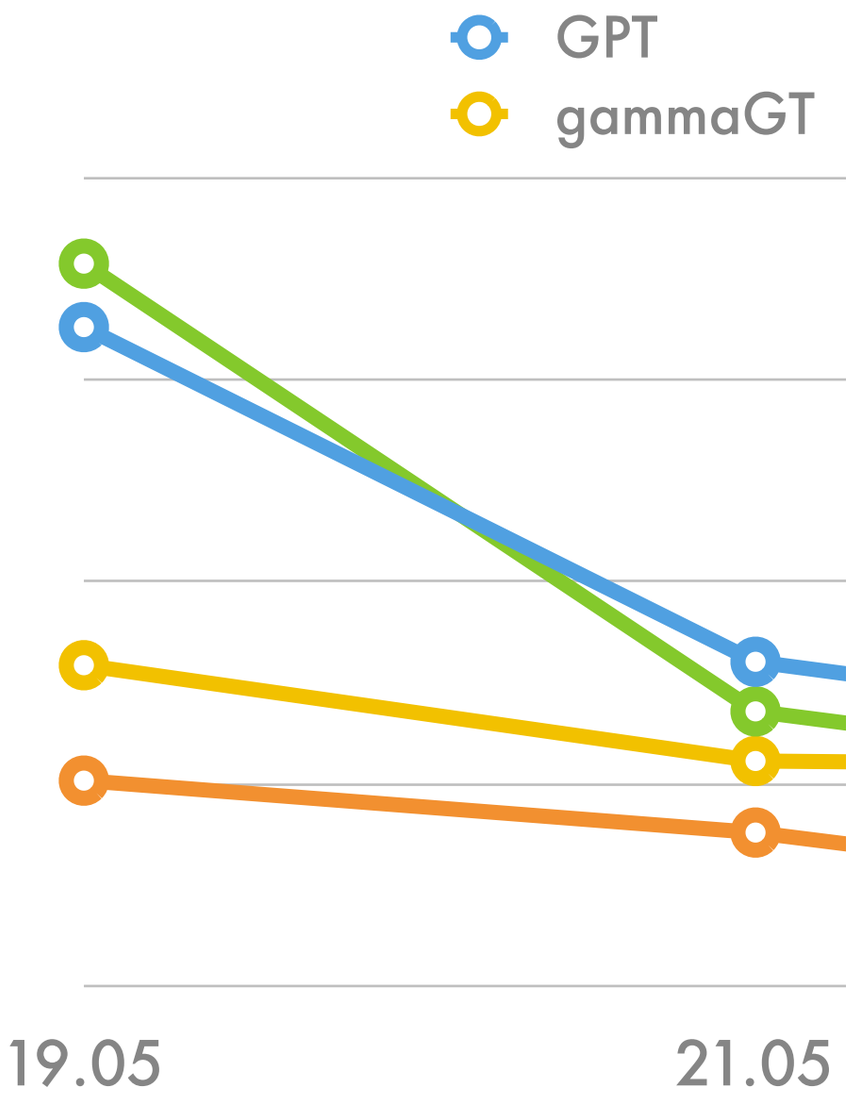
- Length of hospital stay
- Length of ICU stay
- Presence of central venous or arterial catheters
- Emergency abdominal surgery
- Presence of a gastrostomy or jejunostomy tube
- Gut colonization
- Low birth weight
- Prior administration of any antibiotic
- Prior residence in a long-term care facility (eg, nursing home)
- Severity of illness
- Presence of a urinary catheter
- Ventilatory assistance
- Hemodialysis



21
mar 21 maggio 2013

Case report

Abbiamo mantenuto amoxi+clavulanato 1g x 3/die



22
mer 22 maggio 2013

Case report

3 giorni dopo...

1 Escherichia coli

ANTIBIOTICI	I	MIC
Amikacina	S	<=2
Amoxicillina/ac. clavulanico	**R**	16
Nitrofurantoina	S	<=16
Cefepime	**R**	8
Cefotaxima	**R**	>=64
Ceftazidima	**R**	16
Ciprofloxacina	**R**	>=4
ESBL	+	Pos
Fosfomicina	S	<=16
Gentamicina	S	<=1
Imipenem	S	<=0,25
Meropenem	S	<=0,25
Piperacillina/Tazobactam	S	<=4
Trimetoprim/sulfametoxazolo	S	<=20

S=Sensibile, R=Resistente, I=Intermedio

Apirettico, persisitono dolori addominali

Case report

Continua amoxi+clav

Cambia terapia

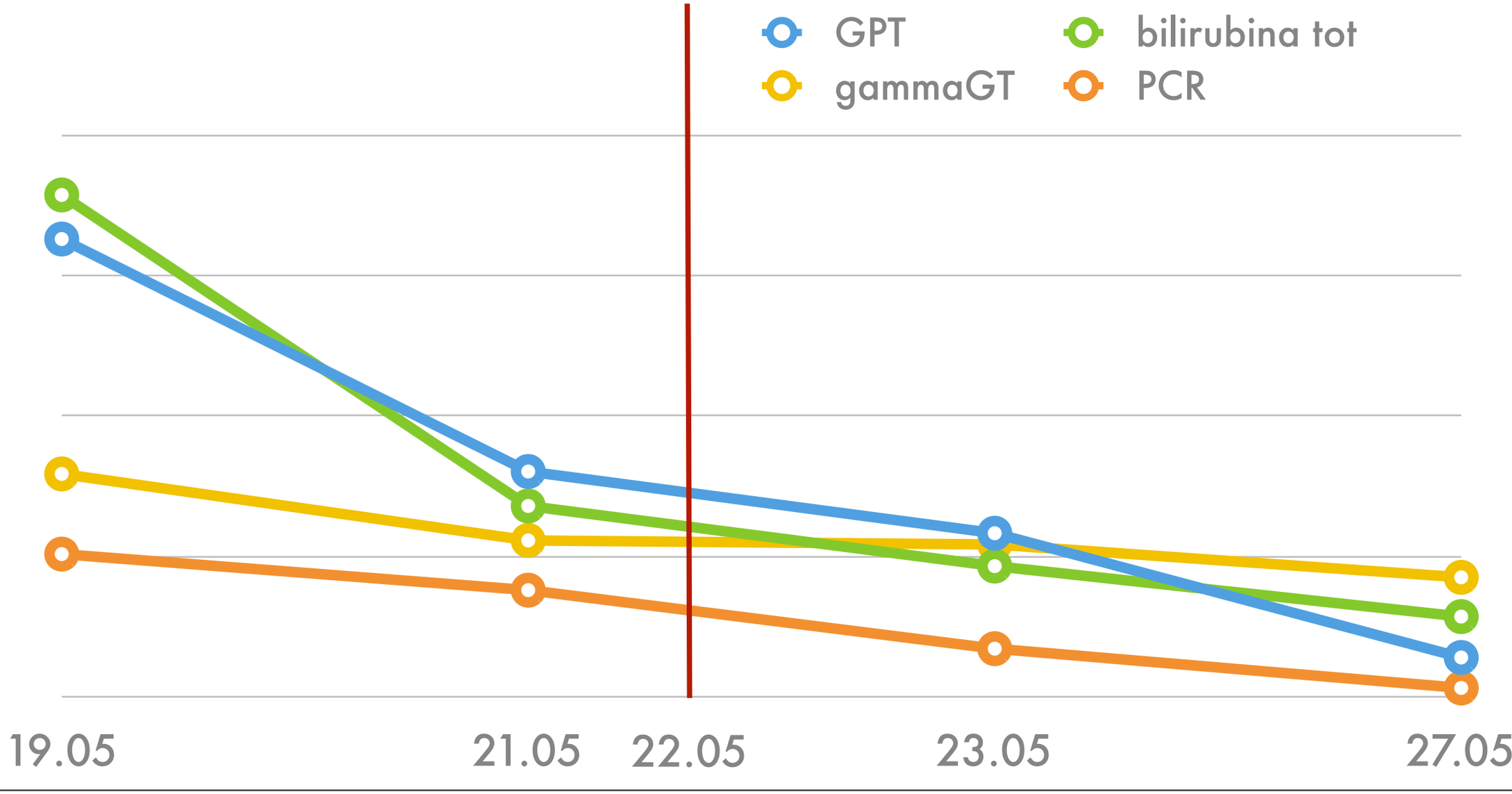
Pipera +tazo

Carbapenemi

22
mer 22 maggio 2013

Case report

Siamo passati a pipera+tazo 4.5 x 3/die



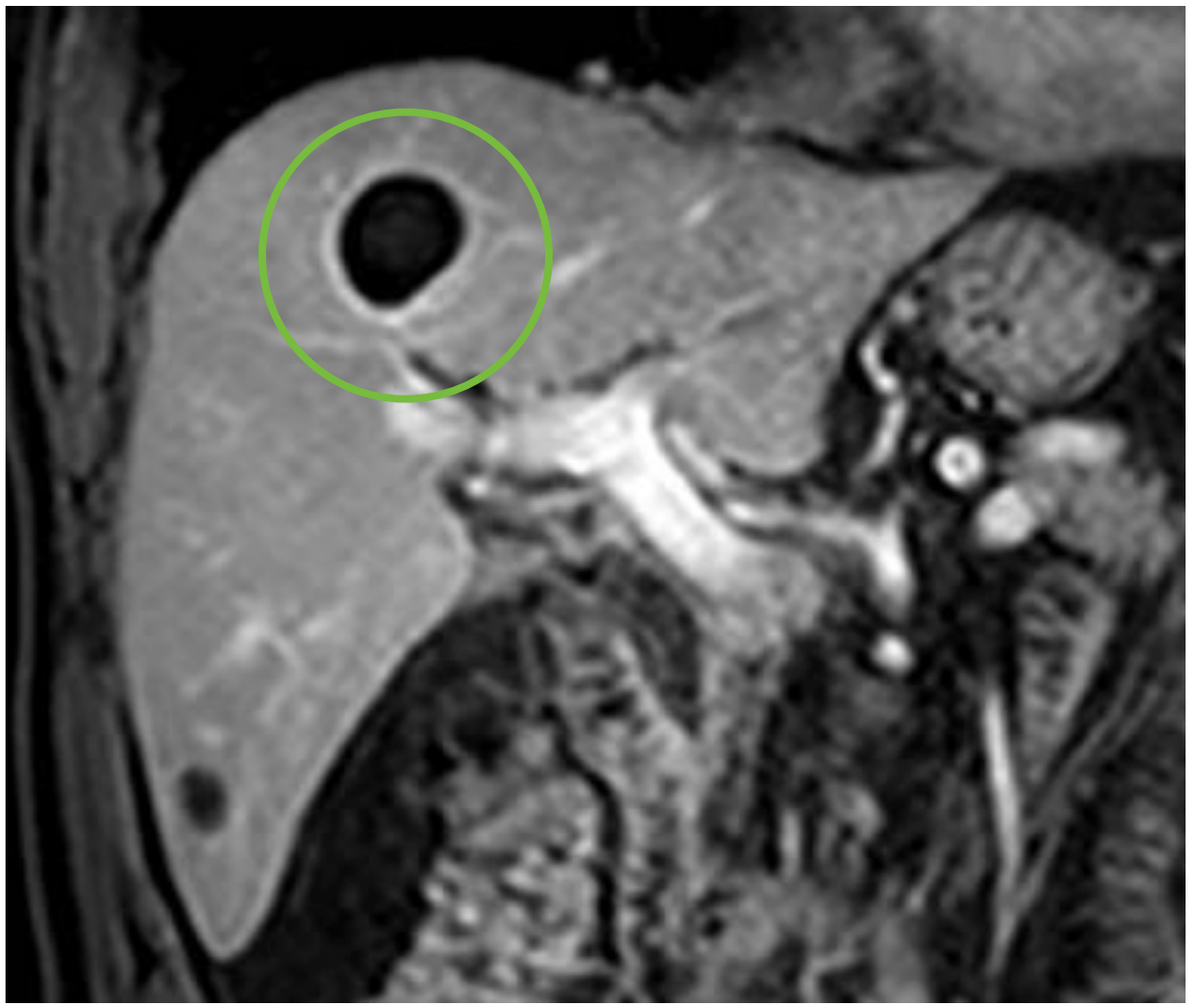
27
lun 27 maggio 2013

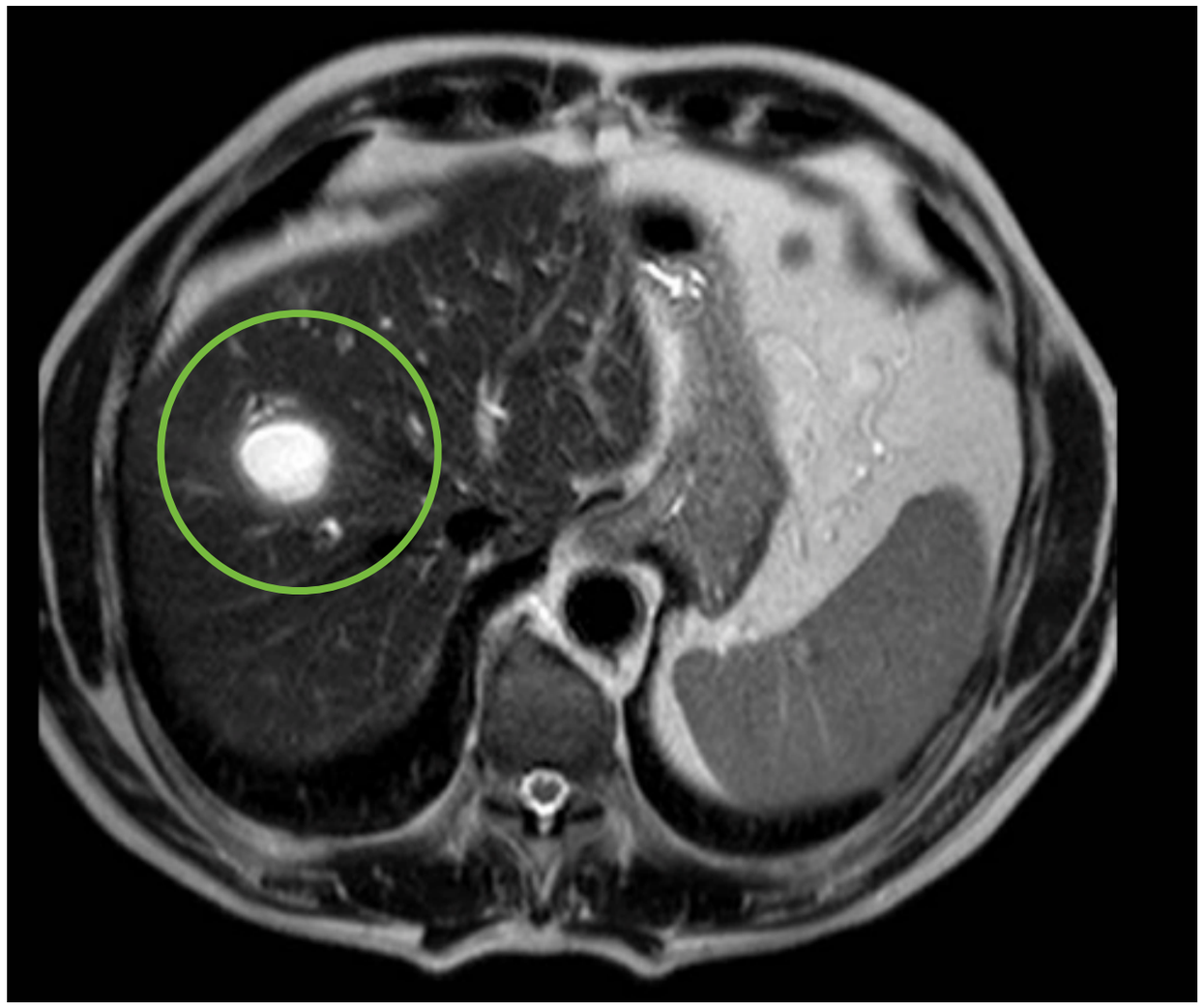
Case report

Colangio RMN

In rapporto al quesito clinico, è evidente almeno una formazione litiasica nel terzo distale del coledoco con diametro trasverso di 6 mm e craniocaudale di 1 cm, più alcuni difetti di riempimento craniali a questo, compatibili con fango biliare.
Nelle vie biliari intraepatiche di sn altra formazione litiasica di 5 X 3 mm.
Nell'VIII segmento formazione rotondeggiante di 32 mm, centralmente liquida con cercine solido che assume MdC, in prima ipotesi compatibile con lesione ascessuale intraepatica.
Cisti epatiche semplici in VIII e VI segmento.
Nei limiti la milza, il pancreas (dotto pancreatico non dilatato), i surreni e i reni (cisti parapieliche bilaterali, maggiori a destra).
Non versamento, non linfoadenomegalie.

Case report





28
mar 28 maggio 2013

Case report

ERCP

Incanulazione VBP, multipli passaggi con cestello di Dormia, lavaggi e multipli passaggi con pallone di Fogarty con estrazione di multipli calcoli.

Eseguita toilette completa

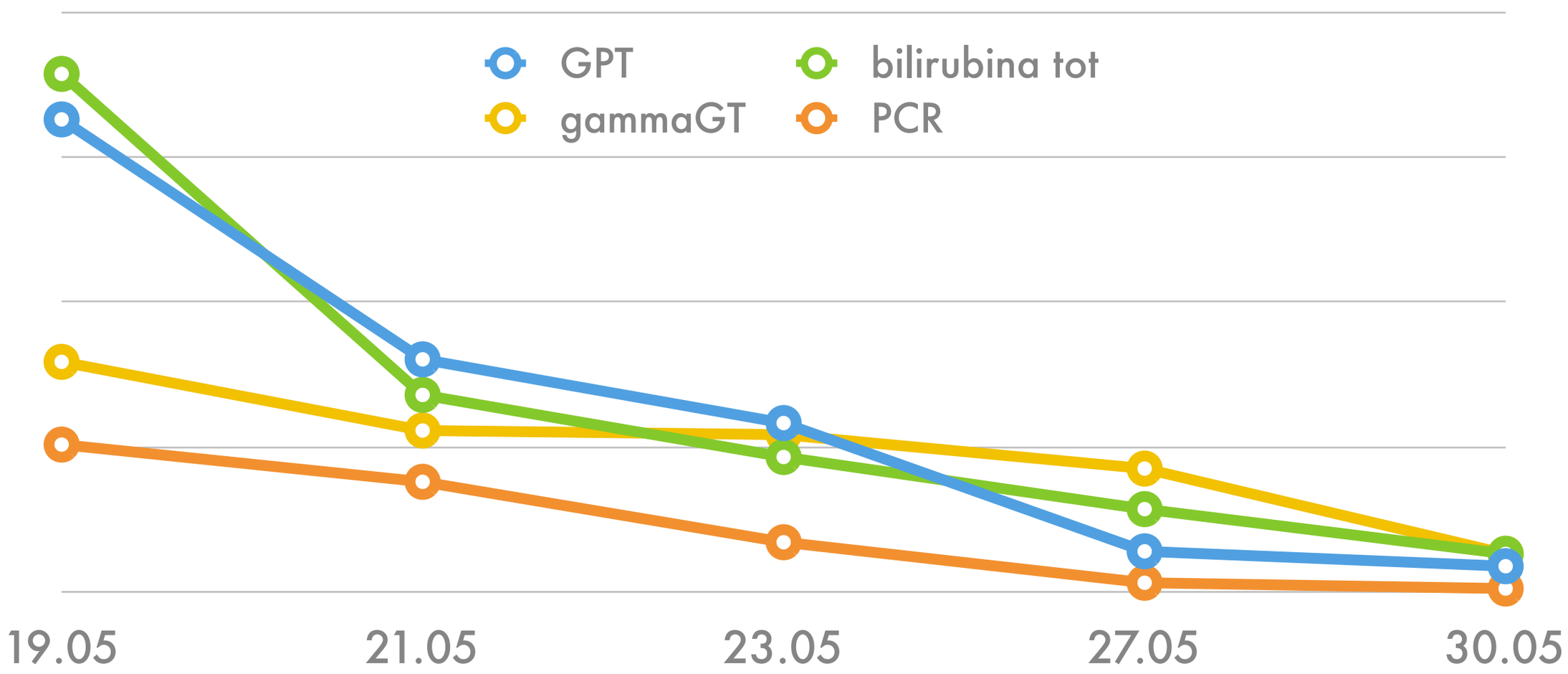
WITHOUT TIP

30
gio 30 maggio 2013

Case report

Apirettico, asintomatico,10° gg di terapia antibiotica

ECO addome: lesione ascessuale di 2 cm



Case report

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ANTIBIOTICI	I	MIC
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Nitrofurantoina	S	<=16
Cefepime	**R**	8
Cefotaxima	**R**	>=64
Ceftazidima	**R**	16
Ciprofloxacina	**R**	>=4
ESBL	+	Pos
Fosfomicina	S	<=16
Gentamicina	S	<=1
Imipenem	S	<=0,25
Meropenem	S	<=0,25
Piperacillina/Tazobactam	S	<=4
Trimetoprim/sulfametoxazolo	S	<=20

S=Sensibile, R=Resistente, I=Intermedio

30
gio 30 maggio 2013

Case report

Dimesso con terapia domiciliare

Bactrim F 1 cp ogni 8 ore

15
sab 15 giugno 2013

V. di controllo

ECO addome: ascesso 1.5 cm

Esami ematici: ok

Discussione

1. Prima di parlare di antibiotici...

Discussione

Discussione

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2012;10:1157–1161

LIVER, PANCREAS, AND BILIARY TRACT

Delayed and Unsuccessful Endoscopic Retrograde Cholangiopancreatography Are Associated With Worse Outcomes in Patients With Acute Cholangitis

MOUEN A. KHASHAB, ALI TARIQ, USMAN TARIQ, KATHERINE KIM, LUCIA PONOR, ANNE MARIE LENNON, MARCIA I. CANTO, AHMET GURAKAR, QILU YU, KERRY DUNBAR, SUSAN HUTFLESS, ANTHONY N. KALLOO, and VIKESH K. SINGH

Division of Gastroenterology and Hepatology, Department of Medicine, The Johns Hopkins Hospital, Baltimore, Maryland

Discussione

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Table 1. Characteristics of the Study Population and ERCP Procedures

Variable	Value
Mean age, *y* (range)	60 (16–97)
Female, n (%)	43 (48)
Prior history of acute cholangitis, n (%)	28 (32)
Fever at presentation, n (%)	70 (80)
SIRS at presentation, n (%)	46 (51)
Benign etiology, n (%)	66 (74)
Mean CCI (range)	5 (1–11)
Presented with concomitant acute pancreatitis, n (%)	7 (8)
Coagulopathy, n (%)	17 (19)
Mean (range) preprocedural bilirubin level	6 (0.5–27)
Altered mental status, n (%)	4 (4)
Positive blood cultures, n (%)	31 (42.5)[a]
Mean time between admission and ERCP, *h* (range)	38.5 (0.35–167)
ERCP within 24 h, n (%)	38 (42.2)
ERCP within 24–48 h, n (%)	23 (25.6)
ERCP within 48–72 h, n (%)	16 (17.8)
ERCP >72 h, n (%)	13 (14.4)
Pus seen during ERCP, n (%)	17 (20)
Stent placed, n	54
Biliary sphincterotomy performed, n	52
Failed ERCP, n (%)	7 (8)
Post-ERCP pancreatitis, n (%)	3 (3)
Post-sphincterotomy bleeding, n (%)	1 (1)

CCI, Charlson comorbidity index; SIRS, systemic inflammatory response syndrome.
[a]Among 73 patients who had blood cultures obtained.

Discussione

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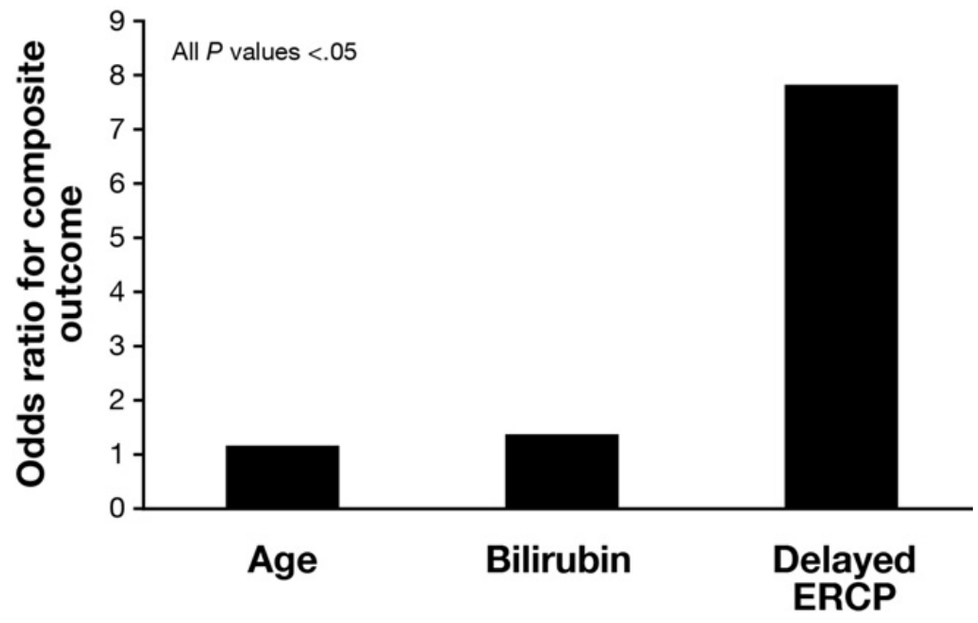

Figure 2. Multivariate analysis: independent predictors of composite clinical outcome (death, ICU, and/or persistent organ failure).

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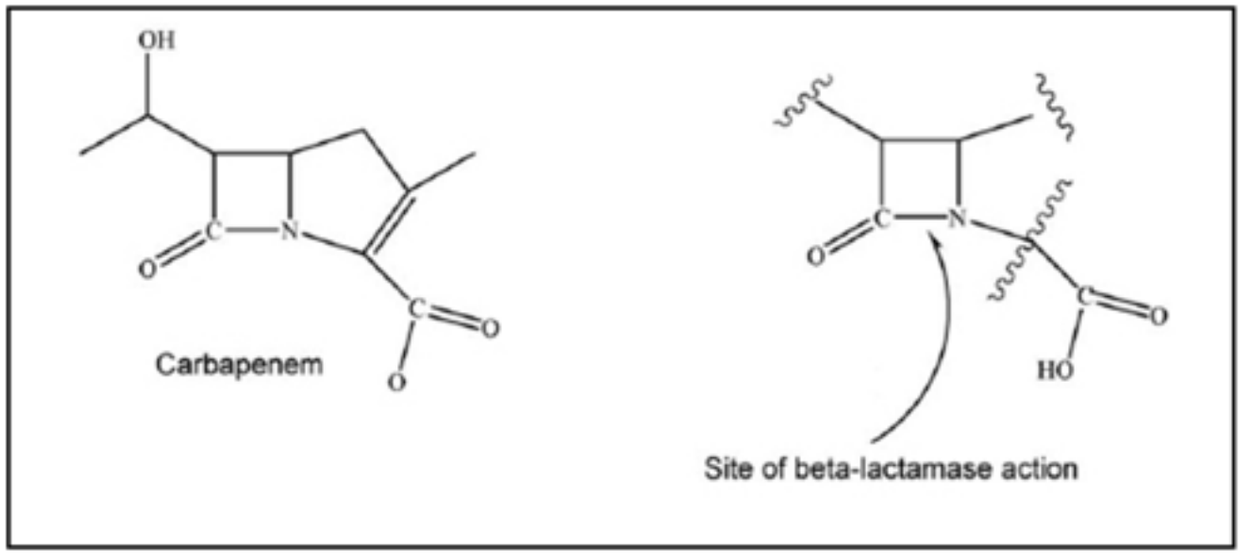
Discussione

2. Solo carbapenemi per ESBL +



Discussione

MAJOR ARTICLE

Cefepime Therapy for Monomicrobial Bacteremia Caused by Cefepime-Susceptible Extended-Spectrum Beta-Lactamase–Producing *Enterobacteriaceae*: MIC Matters

Nan-Yao Lee,[1,2] Ching-Chi Lee,[1,2] Wei-Han Huang,[4] Ko-Chung Tsui,[5,8] Po-Ren Hsueh,[6,7,a] and Wen-Chien Ko[1,2,3,a]

[1]Department of Internal Medicine, [2]Center for Infection Control, National Cheng Kung University Hospital and Medical College, and [3]Department of Medicine, National Cheng Kung University Medical College, Tainan; [4]Department of Clinical Pathology, Buddhist Tzu-Chi General Hospital, Hualien; [5]Department of Clinical Pathology Cathay General Hospital, and Departments of [6]Laboratory Medicine and [7]Internal Medicine, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei; and [8]Fu-Jen Catholic University School of Medicine, New Taipei City, Taiwan

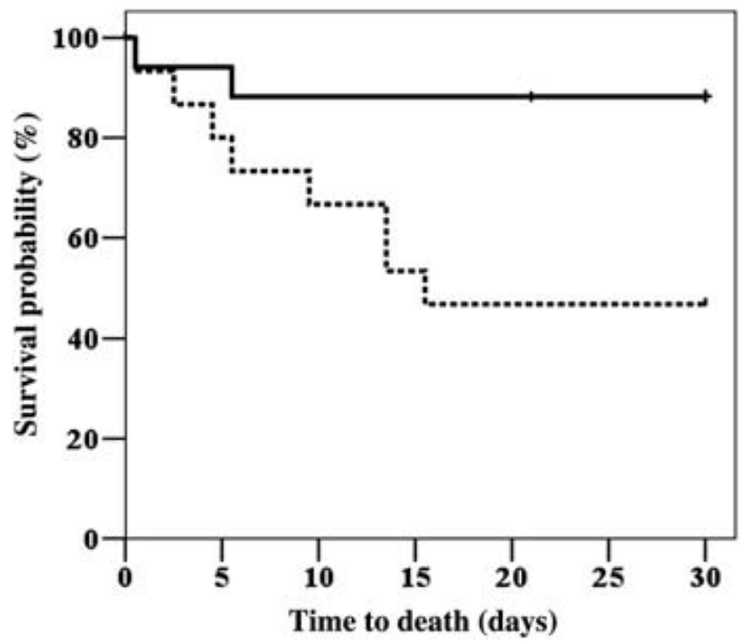


Figure 3. Kaplan-Meier survival analysis curves for patients with bacteremia caused by extended-spectrum ß-lactamase–producing organisms; bacteremia treated using a carbapenem (solid line) vs cefepime (broken line; log-rank test, $P = .016$).

Discussione

Impact of empirical treatment in extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella spp.bacteremia. A multicentric cohort study.

BMC Infectious Diseases 2012, **12**:245 doi:10.1186/1471-2334-12-245

BMC Infectious Diseases

BioMed Central
The Open Access Publisher

Cases of ESBL producing Enterobacteriaceae (ESBL-E) bacteremia collected from 2003 through 2008 in 19 hospitals in Spain. Statistical analysis was performed using multivariate logistic regression.

We analyzed 387 cases ESBL-E bloodstream infections. The main sources of bacteremia were urinary tract (55.3%), biliary tract (12.7%), intra-abdominal (8.8%) and unknown origin (9.6%). Among all the 387 episodes, *E. coli* was isolated from blood cultures in 343 and in 45.71% the ESBL-E was multidrug resistant. Empirical antibiotic treatment was adequate in 48.8% of the cases and the in hospital mortality was 20.9%. In a multivariate analysis adequacy was a risk factor for death [adjusted OR (95% CI): 0.39 (0.31-0.97); P = 0.04], but not in patients without severe sepsis or shock. The class of antibiotic used empirically was not associated with prognosis in adequately treated patients.

Discussione

BMC Infectious Diseases

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	Death (n = 81)	Survival (n = 306)	p	RR (95 % CI)
Presentation				
Sepsis severe or shock	57 (70.4)	68 (22.5)	<0.001	4.9 (3.2-7.51)
Adequate empirical therapy	34 (42)	164 (53.6)	0.04	0.69 (0.47-1.02)
Adequate change for definitive therapy	29 (32.1)	109 (35.6)	0.33	0.88 (0.58-1.34)

A multivariate analysis selecting patients without severe sepsis or shock showed that adequate empirical therapy was not associated with mortality in this group, but it was associated with mortality in patients with severe sepsis or shock (adjusted OR, 0.42; 95% CI, 0.19–0.92; P = 0.03).

Discussione

BMC Infectious Diseases

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- Questo è lo studio più ampio sull'outcome delle batteriemie da ESBL-E . Le sepsi da enterobatteri produttori di ESBL hanno una mortalità piuttosto elevata (nello studio in questione intorno al 26%)

- Il ruolo dei β-lattamici + inibitore non è ben definito nel trattamento delle sepsi da germi ESBL produttori. Nello studio in questione il trattamento con questi farmaci non si è dimostrato inferiore a quello con carbapenemi, quando gli isolati erano sensibili e in caso di sepsi gravi.

- L'uso di questi farmaci nella terapia empirica è difficile da stabilire, macertamente questi farmaci ed altri (fluorochinoloni) hanno un ruolo nel trattamento degli isolati sensibili all'antibiogramma (de-escalating strategy)

Discussione

Outcome of bacteraemia due to extended-spectrum β-lactamase-producing *Escherichia coli*: Impact of microbiological determinants

Jesús Rodríguez-Baño [a,b,*], Jesús Mingorance [d], Natalia Fernández-Romero [d], Lara Serrano [a], Lorena López-Cerero [a], Alvaro Pascual [a,c], The ESBL-REIPI Group [e]

Table 2 Univariate association between microbiological determinants and 30-day mortality among patients with bacteraemia due to ESBL-producing *E. coli*.

Variable	Category	No. of patients who died/ No. in the category (%)	RR (95% CI)	*p*
Phylogroup	A	12/55 (21.8)	Ref.	
	B1	14/55 (25.5)	1.16 (0.59—2.29)	0.6
	B2	9/30 (30)	1.37 (0.65—2.88)	0.3
	D	12/51 (23.5)	1.07 (0.53—2.17)	0.2
Ciprofloxacin-resistance	No	12/62 (19.4)	Ref.	
	Yes	35/129 (27.1)	1.40 (0.78—2.50)	0.2
Amoxicillin—clavulanate-resistance	No	23/118 (19.5)	Ref.	
	Yes	24/73 (32.9)	1.68 (1.03—2.75)	0.03

Variables not shown: *papG*, *papGIII*, *sfaD/E*, *afaB/C*, *hlyA*, *cnf1*, *cdtB*, and *svg* (all present in <15 cases).
[a] Eight isolates were excluded because they produced ESBLs from 2 different groups (7) or a TEM ESBL (1).

"surrogate markers for higher virulence of subgroups"

Discussione

MAJOR ARTICLE

β-Lactam/β-Lactam Inhibitor Combinations for the Treatment of Bacteremia Due to Extended-Spectrum β-Lactamase–Producing *Escherichia coli*: A Post Hoc Analysis of Prospective Cohorts

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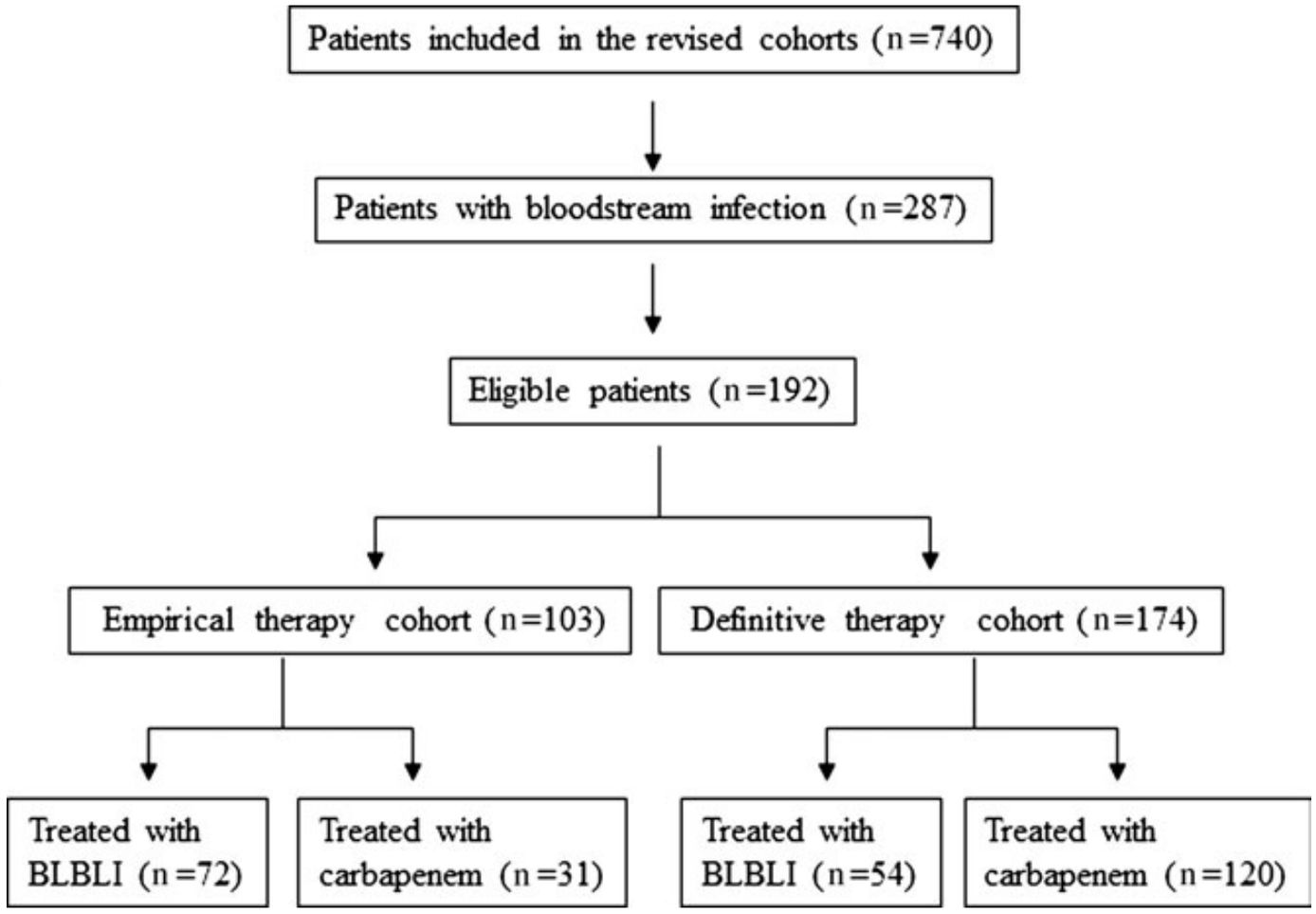
- Pot hoc analysisis di pazienti inseriti in 6 studi pubblicati
- Criteri di inclusione : eta > 17 anni, batteriemia monomicrobica da ESBL-EC, terapia con BLBLI o carbapenemi ≥48 ore
- Epirical therapy cohort (ETC) pazienti che hanno incominciato BLBLI o carbapenemico in momoterapia entro 24 h dalla esecuzione delle emocolture
- Definitive therapy Cohort (DTC) pz che hanno ricevuto una terapia efficace con BLBLI o carbapenemi in monoterapia per ≥ 50% della durata totale della terapia



37 AMC 22 IMP
35 PTZ 8 MEP
1 ETP

Discussione

Characteristics of Patients With Bloodstream Infections (BSIs) Caused by Extended-Spectrum b-Lactamase–Producing Escherichia coli, According to Therapy

	Empirical Therapy Cohort			Definitive Therapy Cohort		
Characteristic	BLBLI (n = 72)	Carbapenem (n = 31)	*P*	BLBLI (n = 54)	Carbapenem (n = 120)	*P*
Age, median y (IQR)	69 (59–80)	60 (52–78)	.1[b]	67 (56–83)	70 (55–78)	.3[b]
Male sex	29 (40.3)	11 (35.5)	.6	34 (63)	70 (58.3)	.5
Nosocomial acquisition	26 (36.1)	24 (77.4)	<.001	18 (33.3)	67 (55.8)	.006
Charlson index, median, (IQR)	2 (1–5)	2 (1–5)	.6[b]	2.5 (1–5)	3 (1–5)	.5[b]
Cancer	21 (31.9)	11 (35.5)	.7	15 (27.8)	43 (35.8)	.2
Immunosuppression	5 (6.9)	5 (16.1)	.1[c]	3 (5.6)	15 (12.5)	.1
Neutropenia	2 (2.8)	3 (9.7)	.1[c]	0	7 (5.8)	.1[c]
Urinary or biliary tract as source	52 (72.2)	18 (58.1)	.1	42 (77.8)	79 (65.8)	.1
ICU admission	7 (9.9)	2 (6.7)	.7[c]	4 (7.4)	18 (15.4)	.1
Severe sepsis or shock at presentation	14 (19.4)	9 (29.0)	.2	8 (14.8)	32 (26.7)	.08
Pitt score, median (IQR)	1 (0–2)	1 (0–2)	.7[b]	1 (0–2)	1 (1–2)	.04[b]
CTX-M enzyme	57 (80.3)	25 (86.2)	.4	43 (82.7)	95 (81.2)	.8

•Dosaggi dei farmaci . > 90% of patients in each group received the following intravenous doses (or adjusted equivalent in the case of renal failure):
•PTZ 4500 mg/6 h
•AMC, 1200 g/8 h
•imipenem, 500 mg/6 h; meropenem , 1 g/8 h, and ertapenem, 1 g/24 h.

Discussione

	Empirical Therapy Cohort			Definitive Therapy Cohort		
	BLBLI (n = 72)	Carbapenem (n = 31)	*P*	BLBLI (n = 54)	Carbapenem (n = 120)	*P*
Mortality, no. of deaths						
Day 7	2 (2.8)	3 (9.7)	.1[c]	1 (1.9)	5 (4.2)	.6[c]
Day 14	7 (9.7)	5 (16.1)	.3	3 (5.6)	14 (11.7)	.2
Day 30	7 (9.7)	6 (19.4)	.1	5 (9.3)	20 (16.7)	.1
Hospital stay after BSI , median (IQR), d	12 (8–28)	13 (9–25)	.7[b]	13 (8–22)	13 (10–25)	.04[b]

Mortality at 30 Days in Patients Who Received Empirical TherapyWith an Active b-Lactam/b-Lactam Inhibitor, According to Minimum Inhibitory Concentration of the Antimicrobial Used

	Minimum Inhibitory Concentration, mg/L				
Antimicrobial	≤1	2	4	8	16
Piperacillin-tazobactam	0/10	0/8	1/4	2/6	1/7
Amoxicillin-clavulanate	…	…	1/12	2/25	…

Discussione

Table 4. Cox Regression Analysis of Associations Between Different Variables and Mortality in the Definitive Therapy Cohort

	Crude Analysis		Adjusted Analysis	
Variable	HR (95% CI)	*P*	HR (95% CI)	*P*
Male sex	1.2 (.46–2.29)	.9	…	…
Age[a]	1.00 (.97–1.02)	.9	…	…
Nosocomial BSI	0.99 (.45–2.22)	.9	…	…
Charlson index[a]	1.02 (.88–1.28)	.7	…	…
Neutropenia	1.78 (.88–13.32)	.5	…	…
High-risk source[b]	2.07 (.94–4.54)	.06	…	…
Pitt score[a]	1.49 (1.26–1.78)	<.001	1.38 (1.12–1.70)	.002
Severe sepsis or shock[c]	3.64 (1.66–7.99)	.001	2.10 (.87–5.05)	.09
Empirical therapy with BLBLI	0.56 (.18–1.73)	.3	…	…
Inappropriate empirical therapy	1.76 (.78–3.93)	.1	…	…
Definitive therapy with BLBLI[d]	0.66 (.24–1.76)	.4	0.76 (.28–2.07)	.5

Abbreviations: BLBLI, β-lactam/β-lactamase inhibitor association; BSI, bloodstream infection; CI, confidence interval; HR, hazard ratio.

[a] Per unit.

[b] Other than urinary and biliary tract.

[c] At presentation.

[d] Reference: definitive therapy with carbapenem.

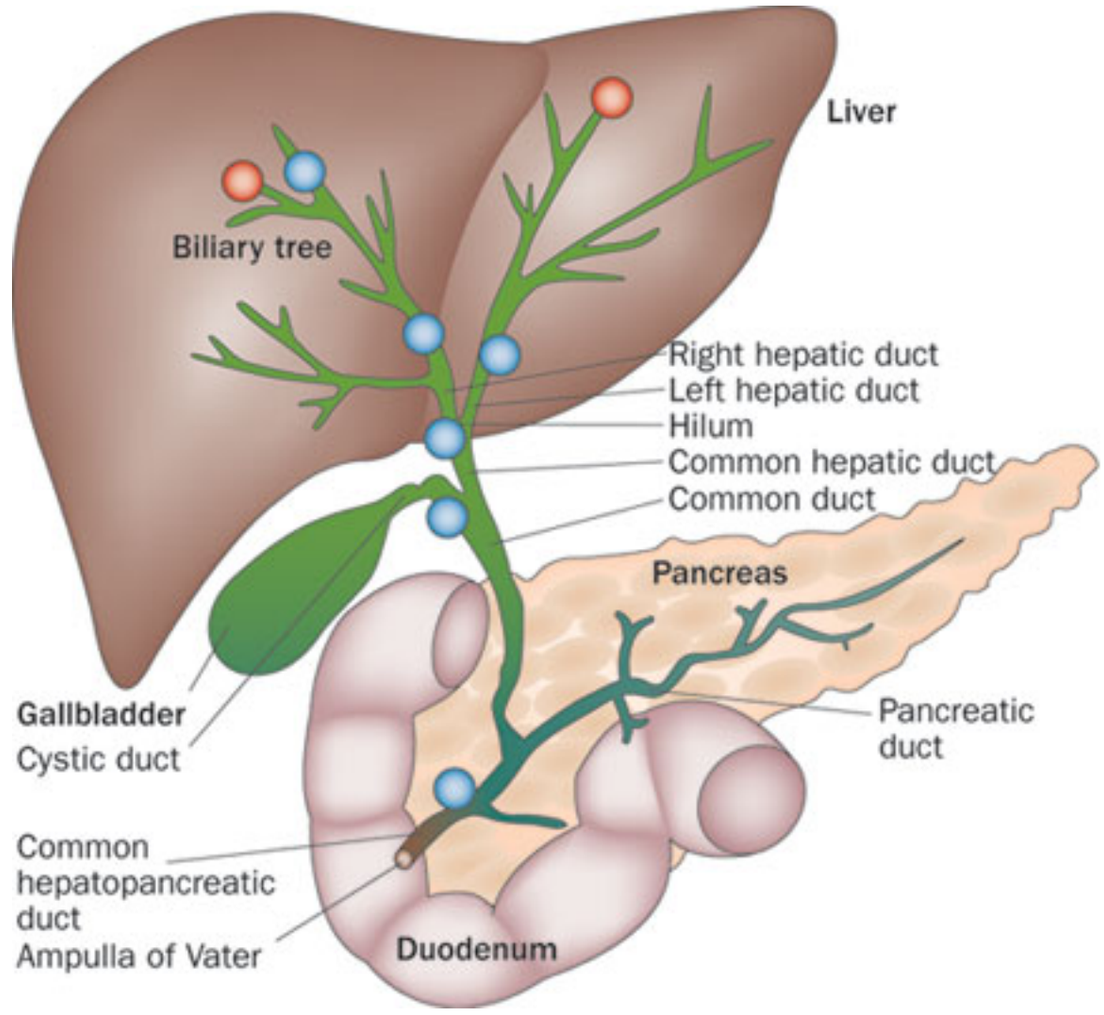
Scoring system	Parameters used		Severe illness criteria	Reference
PBS	Fever (oral temperature)		>4	[7]
	≤35°C or ≥40°C	2		
	35.1–36.0°C or 39.0–39.9°C	1		
	36.1–38.9°C	0		
	Hypotension	2		
	Acute hypotensive event with drop in systolic blood pressure >30 mmHg and diastolic blood pressure >20 mmHg or Requirement for intravenous vasopressor agents or Systolic blood pressure <90 mmHg			
	Mechanical ventilation	2		
	Cardiac arrest	4		
	Mental status			
	Alert	0		
	Disoriented	1		
	Stuporous	2		
	Comatose	4		

Discussione

- One question of interest is the MIC of the isolates and the BLBLI dosage. Stochastic models have shown a 99% probability of attaining the pharmacokinetic/pharmacodynamic target (time above the MIC, .50%) against ESBL producers by using 4500 mg/6 h when the MIC of the isolate is ≤ 8 mg/L, compared with a probability of only 57% when the MIC is 16 mg/L
- A higher pharmacokinetic/pharmacodynamic target has been shown with PTZ using more frequent dosing (3375 mg/4 h) or extended infusions
- There are no similar studies for AMC, although our data would suggest that 1200 mg/8 h, with each dose administered over a 1-hour period, is adequate for most patients.
- In deciding whether BLBLI can be used as empirical monotherapy, the susceptibility of local isolates to these compounds should be taken into account.

Discussione

3. Cosa succede nelle vie biliari ?



Discussione

Pharmacology

Chemotherapy

Chemotherapy 2002;48:280–297
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Biliary Excretion of Antimicrobial Drugs

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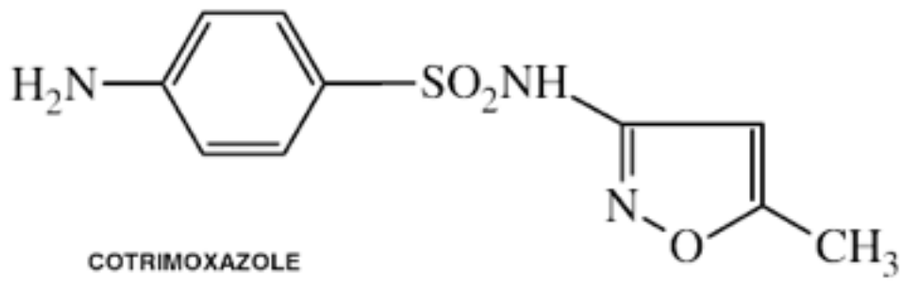
Antibiotici arrivano alle vie biliari attraverso:

- escrezione biliare (ampicillina, pipera+tazo, tigeciclina, fluorchinoloni, cefalosp...)
- via ematica

Discussione

Cotrimoxazolo

- Raggiunge concentrazioni biliari 2-4 volte superiori, rispetto a quelle del plasma, quando assunto per os
- Scarsi dati sull'attività sugli anaerobi (Bacteroides spp)
- Dati di efficacia sul trattamento delle colangiti ricorrenti



COTRIMOXAZOLE

Van den Hazel SJ, Speelman P, Tytgat GN, et al. Successful treatment of recurrent cholangitis with antibiotic maintenance therapy. Eur J Clin Microbiol Infect Dis 1994; 13: 662-5

Goldman LD, Steer ML, Silen W. Recurrent cholangitis after biliary surgery. Am J Surg 1983; 145: 450-4


thank you
danke
謝謝
gracias
merci
obrigado
dziękuję
teşekkür ederim
go raibh maith agat
ngiyabonga
рахмат
спасибо
Баярлалаа
faafetai lava
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dank je
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terima kasih
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