ATB - jak dlouho podávat v intenzivní péči

Vladimír Šrámek
ARK, FNUSA v Brně

Colors of Sepsis
26.1.2023, Ostrava

nepodat ATB (když váhám)?

OBECNÝ NÁZOR: podat ATB >> nepodat ATB

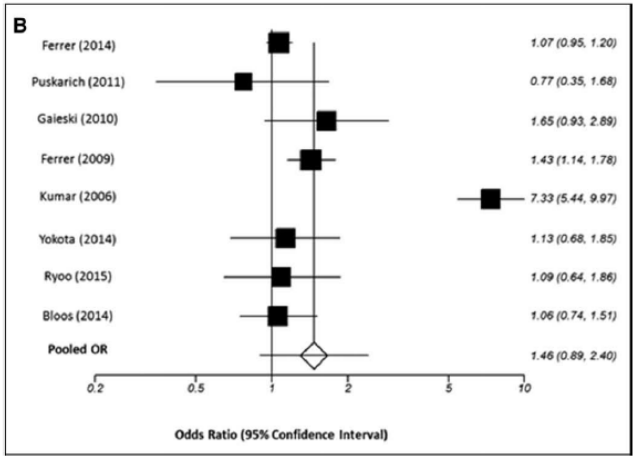
NARRATIVE REVIEW

Antimicrobial-associated harm in critical care: a narrative review

Nishkantha Arulkumaran[1], Matthew Routledge[2,3], Sanmarié Schlebusch[4,5], Jeffrey Lipman[4,6,7] and Andrew Conway Morris[8,9*]

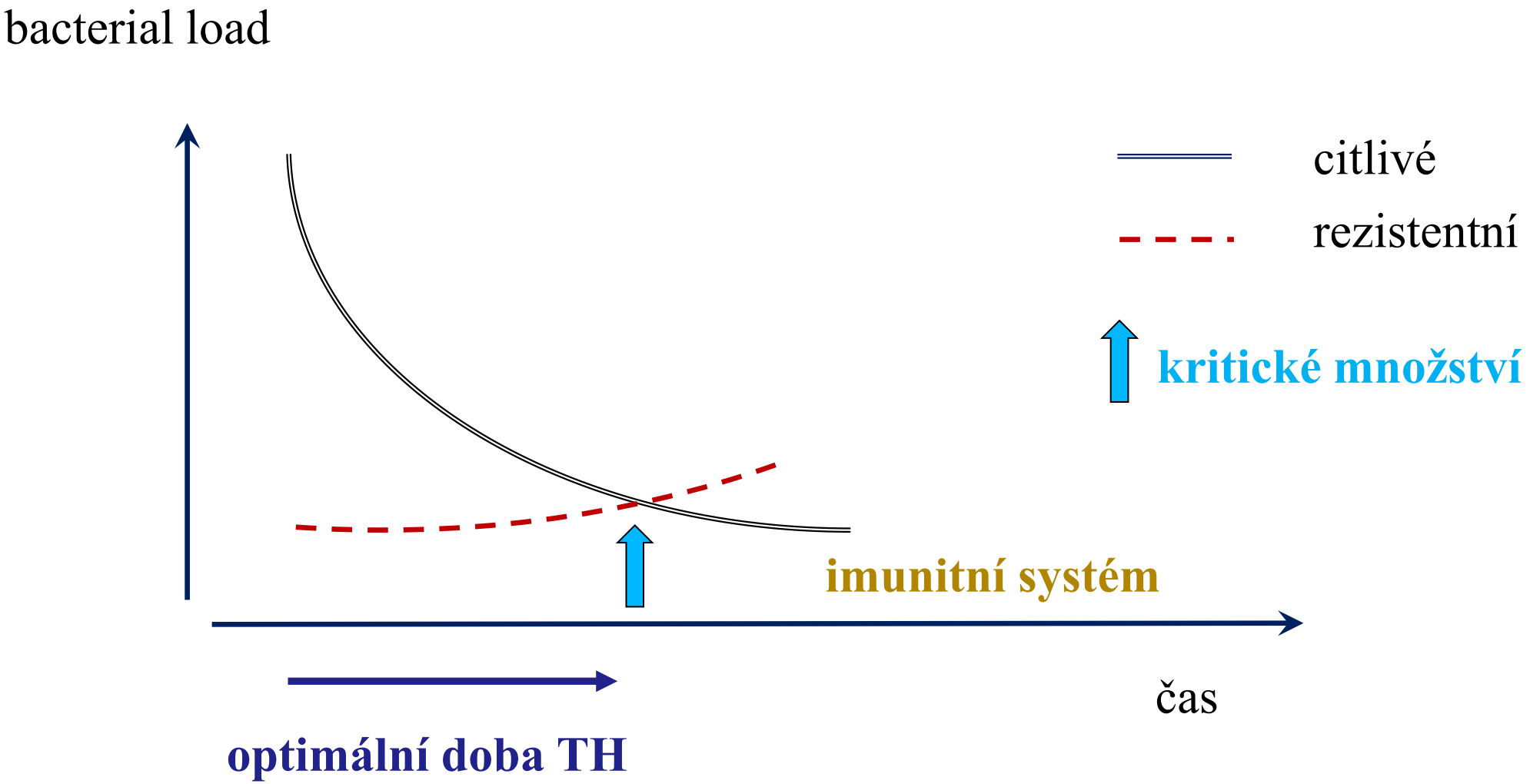
Intensive Care Med (2020) 46:225–235
https://doi.org/10.1007/s00134-020-05929-3

odpor proti
1hr SSC guidelines bundle



- toxicita pro mitochondrie
- toxicita bb. imunitního systému
- „adverse drug reactions“
- selekce rezistentních bakterií
- porušení mikrobiomu

čeho chci dosáhnout podáním ATB



jak dosáhnout kritického množství patologických bakterií v co nejkratším čase?

ATB, které je na původce účinné

- předpokládaný/prokázaný původce
- lokální rezistence mikrobů (MIC)

Respektování Pk/Pd podávaného ATB

- biodostupnost (GIT)
- mechanismus účinku (doba nad MIC, AUC nad MIC, peak concentration)
- distribuční objem nemocného
- změny eliminace v kritickém stavu (aGFR)
- průnik ATB (lokální koncentrace ATB)

délka podávání ATB (pro terapeutické účely)

DNY

1 — nekomplikované IMC, gonorrhea

2-5 — akutní tracheobronchitis, *peritonitis, meningitis*

<7>...(10)…14 dní

CAP, VAP, BSI, sepse (ICU)

non-inferiority studies

týdny — IE, osteomyelitis

Jak dlouho?

- Obecně kratší doba, než je tradováno
- VAP

Comparison of 8 vs 15 Days of Antibiotic Therapy for Ventilator-Associated Pneumonia in Adults

A Randomized Trial

Jean Chastre, MD
Michel Wolff, MD
Jean-Yves Fagon, MD

Context The optimal duration of antimicrobial treatment for ventilator-associated pneumonia (VAP) is unknown. Shortening the length of treatment may help to contain the emergence of multiresistant bacteria in the intensive care unit (ICU).

Intensive Care Med
https://doi.org/10.1007/s00134-022-06690-5

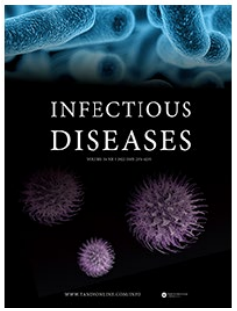
ORIGINAL

Comparison of 8 versus 15 days of antibiotic therapy for *Pseudomonas aeruginosa* ventilator-associated pneumonia in adults: a randomized, controlled, open-label trial

Adrien Bouglé[1*], Sophie Tuffet[2], Laura Federici[3], Marc Leone[4], Antoine Monsel[5], Thomas Dessalle[1], Julien Amour[1], Claire Dahyot-Fizelier[6], François Barbier[7], Charles-Edouard Luyt[8], Olivier Langeron[5], Bernard Cholley[10], Julien Pottecher[11], Tarik Hissem[12], Jean-Yves Lefrant[13], Benoit Veber[14], Matthieu Legrand[15], Alexandre Demoule[9], Pierre Kalfon[16], Jean-Michel Constantin[17], Alexandra Rousseau[2], Tabassome Simon[2] and Arnaud Foucrier[18] on behalf of the iDIAPASON Trial Investigators

FNUSA ICRC
FAKULTNÍ NEMOCNICE U SV. ANNY V BRNĚ
MEZINÁRODNÍ CENTRUM KLINICKÉHO VÝZKUMU

MUNI MED



Short- versus prolonged-course antibiotic therapy for sepsis or infectious diseases in critically ill adults: a systematic review and meta-analysis

Kenji Kubo, Yutaka Kondo, Jumpei Yoshimura, Kazuya Kikutani & Nobuaki Shime

INFECTIOUS DISEASES,
2022; VOL. 54,
NO. 3, 213–223

Conclusions: Shorter, fixed-duration antibiotic therapy for clinically heterogeneous sepsis or severe infections was not associated with poorer outcomes, but the overall quality of evidence was poor.

cut-off < 7 dní >

Blood_Stream_Infections

Antibiotic treatment duration for patients with bloodstream infection: a systematic review and meta-analysis

Yuting Li (liyuting-86@163.com)
The First Hospital of Jilin University

Conclusions: Short course of antibiotic treatment is not associated with either an increased risk of mortality or an increased odds of relapse compared with longer antibiotic treatment course for BSI. Furthermore, short course of antibiotic therapy is non-inferior to long course in terms of source control. Further large-scale RCTs are still required to confirm these results.

cut-off < 10 dní >

NARRATIVE REVIEW

How to use biomarkers of infection or sepsis at the bedside: guide to clinicians

Intensive Care Med
https://doi.org/10.1007/s00134-022-06956-y

Pedro Póvoa[1,2,3*], Luís Coelho[1,3], Felipe Dal-Pizzol[4,5], Ricard Ferrer[6,7], Angela Huttner[8,9], Andrew Conway Morris[10,11,12], Vandack Nobre[13], Paula Ramirez[14,15], Anahita Rouze[16], Jorge Salluh[17,18], Mervyn Singer[19], Daniel A. Sweeney[20], Antoni Torres[21,22,23,24], Grant Waterer[25] and Andre C. Kalil[26]

Table 2 Main host-response biomarkers used in routine practice in critically ill patients

	C-reactive protein	Procalcitonin
Properties	Acute phase protein (pentraxin)	Hormokine
Normal values	0.08 mg/dL (median)	< 1 ng/mL
Maximum peak	> 50 mg/dL (> 1000 × reference value)	> 100 ng/mL (> 10.000 × reference value)
Source	Liver	Virtually all cells and macrophages
Time to increase after insult	4–6 h	3–4 h
Time to peak concentration	36–50 h	Around 24 h
Half-life	19 h	22–35 h
Possible confounders		
Steroids	No effect	frequent false negatives
Immunosuppression	No effect	frequent false negatives
Neutropenia	No effect	frequent false negatives
Renal failure	No effect	⬆⬆
Renal replacement therapy	No effect	⬇⬇
Chronic liver failure	⬇ (70% of the normal)	No effect
Acute liver failure	No CRP increase	No effect
Secondary infection (2nd hit)	⬇ (70% of 1st episode)	⬇⬇⬇ (10% of 1st episode)
Bacterial vs viral infections	Poor	Poor

CAPTAIN study,

Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections (Review)

Cochrane Library

Cochrane Database of Systematic Reviews

Schuetz P, Wirz Y, Sager R, Christ-Crain M, Stolz D, Tamm M, Bouadma L, Luyt CE, Wolff M,

Data 4/2017 – publikace 2019

Key results

We studied 6708 participants from 26 trials in 12 countries. Mortality at 30 days was significantly lower in procalcitonin-guided participants compared to control participants (286 deaths in 3336 procalcitonin-guided participants (8.6%) versus 336 deaths in 3372 controls (10.0%)). There was no significant difference with regard to treatment failures. Results were similar for different clinical settings (primary care, emergency department, intensive care unit) and types of respiratory infection. Regarding antibiotic exposure, participants in the procalcitonin-guided group had a 2.4-day reduction in antibiotic exposure and a reduction in antibiotic-related side effects (16.3% versus 22.1%).

PCT development

FDA

The biomarker Procalcitonin (PCT) is widely used to assess the risk of bacterial infection and progression to severe bacterial sepsis and septic shock in conjunction with other laboratory findings and clinical assessment. Further, the change of PCT over time is used to determine the mortality risk in patients with bacterial sepsis.

In patients with suspected or confirmed lower respiratory tract infections (LRTI), including community-acquired pneumonia (CAP), acute bronchitis and acute exacerbations of COPD (AECOPD), PCT is an aid in decision making on antibiotic therapy for inpatients or patients presenting in the emergency department (ED).

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CRP development

CRP ratio at Day4 > 0.6 – poor outcome for CAP,VAP, BSI and sepsis

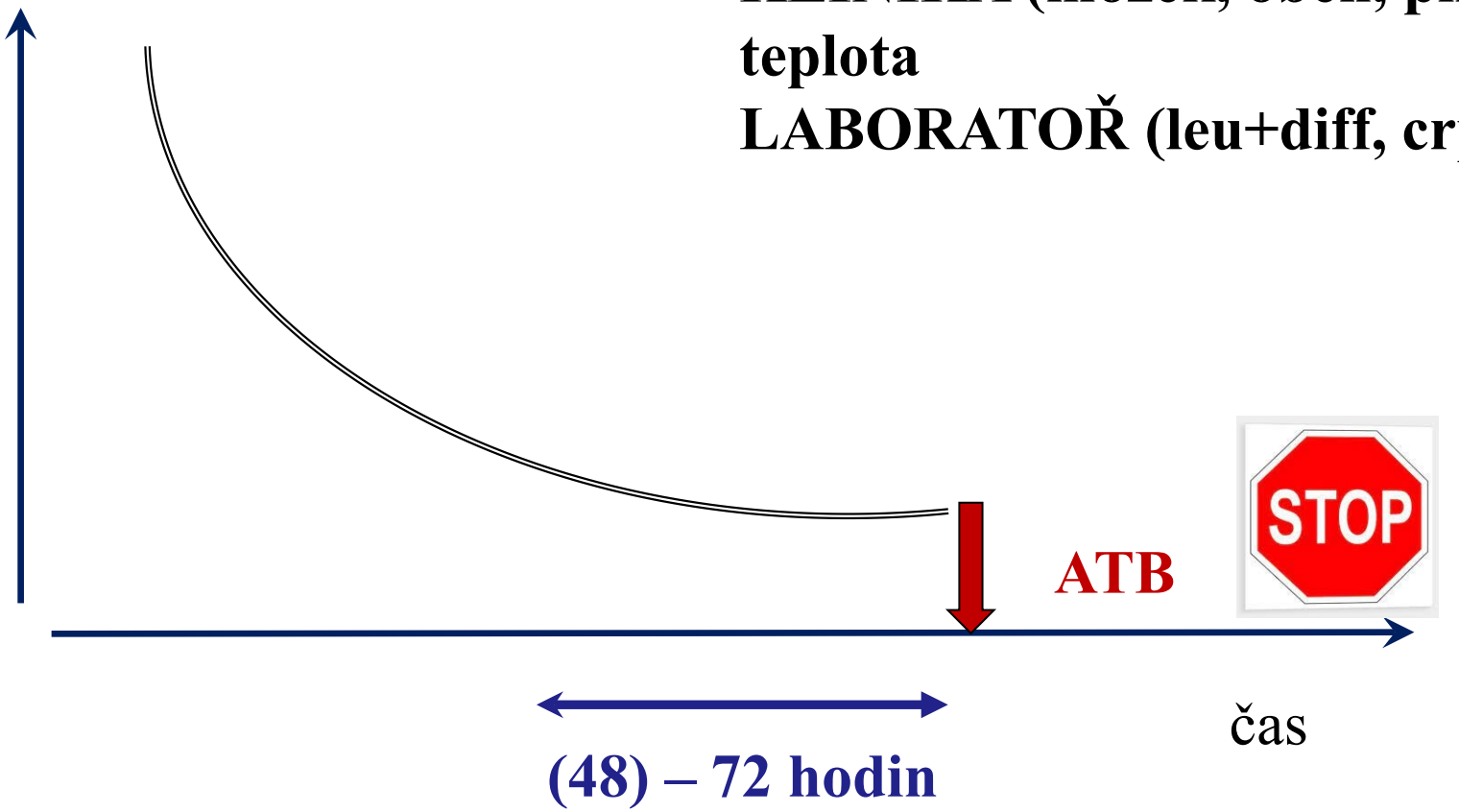
CRP development (CRP ratio) for VAP, CAP, BSI:

- fast response ….. D4/D1 < 0.4
- slow response …. D4/D1 0.4-0.8
- non-response….D4 > 0.8
- biphasic response … initial decrease < 0.8 but then increase

jsme klinici – aplikujme klinický přístup
DEEFERVESCENCE

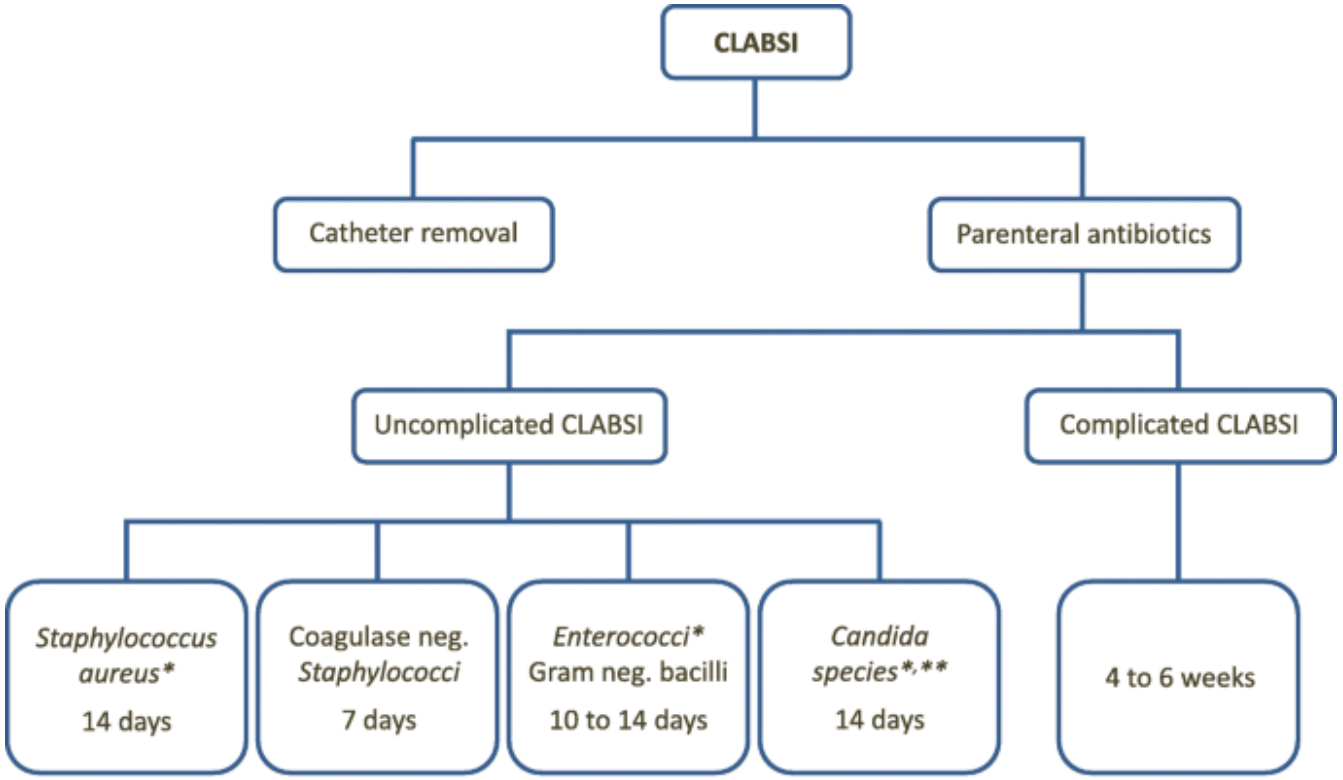
průběh onemocnění

KLINIKA (mozek, oběh, plíce)
teplota
LABORATOŘ (leu+diff, crp, PCT)



katetrové infekce
CRBSI nebo CLABSI

IDSA 2009
CDC 1/2023
Up-to-date



* Transesophageal echography recommended
** Ophtalmologic examination recommended

neg., negative

Tab S1 - Sample set characteristics

	CVC (N = 363)					
Site of insertion	SUB sin	SUB dx	JUG sin	JUG dx	FEM sin	FEM dx
Collected samples	27	53	125	107	16	35
No of lumen*	0/17/10	5/37/13	2/62/60	5/56/49	0/7/9	1/20/14
Patients´data						
Males	19	39	91	72	10	25
Females	8	16	34	35	6	10
Age (mean±SD)	54,6 (18,1)	59,4 (18,5)	63,0 (15,9)	62,8 (15,6)	59,0 (13,8)	57,6 (16,7)
Age (median)	52,5	64	66	67	59,5	61
Length of insertion						
1-5	2	12	21	18	3	4
6-10	21	24	62	55	7	24
11-15	3	13	33	27	6	5
16-20	1	4	9	7	0	2
Catheter blockage	3	4	21	6	1	2
Febrilia	11	19	57	48	4	16
ATB treatment	22	37	95	77	13	28
Antiseptic covering	12	24	41	40	8	14

Tab S2 - Culture results

	CVC					
	SUB sin	SUB dx	JUG sin	JUG dx	FEM sin	FEM dx
Positive samples (% of analyzed)	9 (33,3%)	18 (32,7%)	41 (33,3%)	40 (37,4%)	6 (37,5%)	12 (34,2%)
Monomicrobial infection (% of positive)	6 (66,6%)	13 (72,2%)	26 (63,4%)	26 (65%)	6 (100%)	6 (50%)
Dual-species infection (% of positive)	2 (22,2%)	3 (16,6%)	12 (29,3%)	12 (30%)	0	5 (41,7%)
Three-species infection (% of positive)	1 (11,1%)	2 (11,1%)	3 (7,3%)	2 (5%)	0	1 (8,3%)
Isolates	13	25	59	56	6	19
Unique species	8	10	18	17	4	14

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	Sum	10^4	10^3	10^2	10^1	BF 0 (%)	BF 1(%)	BF 2 (%)	BF 3 (%)	Mono BF	Dual BF	Tri BF
Pseudomonas aeruginosa	3	0	0	2	1	0	1	1	1	0	1	2
Staphylococcus aureus	6	0	0	1	5	0	3	1	2	3	2	1
Klebsiella pneumoniae	4	2	0	1	1	0	1	3	0	3	0	1
Candida albicans	2	1	0	0	1	1	1	0	0	1	1	0
Candida glabrata	1	0	0	0	1	0	1	0	0	1	0	0
Candida lambica	1	0	0	1	0	NA	NA	NA	NA	1	0	0
Cutibacterium acnes	66	0	9	25	32	14	13	23	16	30	26	10
Staphylococcus epidermidis	46	5	7	7	27	3	13	18	12	21	19	6
Staphylococcus haemolyticus	10	1	2	2	5	3	5	0	2	5	5	0
Staphylococcus hominis	12	0	4	2	6	1	3	6	2	5	5	2
Staphylococcus warneri	21	2	1	2	16	11	8	0	2	9	9	3
Sum of strains	212	16	26	53	117	49	57	58	46	97	81	33

2011

International Journal of Antimicrobial Agents 38 (2011) 480–485

Contents lists available at SciVerse ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: http://www.elsevier.com/locate/ijantimicag

Antibiotic treatment duration for bloodstream infections in critically ill patients: a national survey of Canadian infectious diseases and critical care specialists

Nick Daneman[a,b,c,*], Kevin Shore[a], Ruxandra Pinto[c], Rob Fowler[a,c,d]

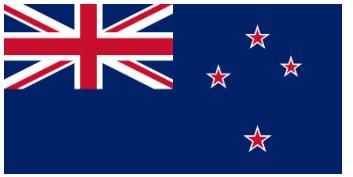
2019

International Journal of Antimicrobial Agents 54 (2019) 184–188

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag



Duration of therapy recommended for bacteraemic illness varies widely amongst clinicians

Mostafa Alwan[a,*], Joshua S. Davis[b,c], Nick Daneman[d], Robert Fowler[d], Yahya Shehabi[a,e], Benjamin Rogers[a,e]

BALANCE study

praxe v postupech kliniků (infektologové + intenzivisté) je velmi rozdílná

CURRENT OPINION

Duration of antibiotic therapy in central venous catheter-related bloodstream infection due to Gram-negative bacilli

María Ruiz-Ruigómez[a] and Jose María Aguado[a,b]

Curr Opin Infect Dis 2021, 34:681–685

Infect Dis Ther (2021) 10:1591–1605
https://doi.org/10.1007/s40121-021-00464-0

ORIGINAL RESEARCH

Short-Course Versus Long-Course Systemic Antibiotic Treatment for Uncomplicated Intravascular Catheter-Related Bloodstream Infections due to Gram-Negative Bacteria, Enterococci or Coagulase-Negative Staphylococci: A Systematic Review

Severin Muff · Alexis Tabah · Yok-Ai Que · Jean-François Timsit · Leonard Mermel · Stephan Harbarth · Niccolò Buetti

GNB-BSI 7
CoNS-BSI 0-3
Enterokoky 7-14
(ne STAU, *Staph. lugdunensis*, Candidy…)

zohlednit klinický (a laboratorní) stav po 3 dnech a to, o jakého nemocného jde (imunokompromitovaný? cizí materiál v těle?...)

Table 3 Summary of recommendations and expert opinions

	First author	Journal	Year	Setting	Recommended treatment duration			When prolonged therapy?
					Gram-negative CRBSI/CLABSI	Coagulase-negative staphylococcal CRBSI/CLABSI	Enterococcal CRBSI/CLABSI	
German guidelines	Böll	*Ann Hematol*	2021	Oncology	*Pseudomonas* and *Stenotrophomonas*: ≥ 2 weeks	5–7 days after defervescence	5–7 days after defervescence	Complications (endocarditis, osteomyelitis)
French recommendations	Timsit	*Ann Intensive Care*	2020	ICU	Enterobacteriaceae, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*: 7 days	7 days	7 days	Remote complications
Expert statement	Buetti	*Semin Respir Crit Care Med*	2019	ICU	Enterobacteriaceae: (5–) 7 days *Pseudomonas aeruginosa*, *Acinetobacter baumannii*: 7 days	(5–) 7 days	(5–) 7 days	Persistent CRBSI, complicated courses (i.e. another vascular line infection, metastatic abscess, septic thrombophlebitis or endocarditis)
Spain recommendations	Chaves	*Med Intensiva*	2018	ICU	≥ 7 days	5–7 days	7–14 days	For CoNS: 10–14 days for patients with intravascular devices, biomedical devices or persistent markers of inflammation after catheter removal
International expert consensus statement	Timsit	*Intensive Care Med*	2018	ICU	7–14 days	5–7 days	7–14 days	Persistent bacteraemia, complications related to bacteraemia (i.e. suppurative thrombophlebitis, endocarditis, osteo myelitis, metastatic infection)
Expert statement	Rupp	*Infect Dis Clin North Am*	2018	All catheters	*Pseudomonas* or MDR GNB: 10–14 days Other GNB: 7–14 days	5–7 days	7–14 days	Complicated CRBSI (i.e. suppurative thrombophlebitis, persistent bacteraemia, osteomyelitis, infective endocarditis)
IDSA guidelines (USA)	Mermel	*Clin Infect Dis*	2009	All catheters	7–14 days	5–7 days or under certain circumstances observation without antibiotics	7–14 days	Complicated CRBSI (i.e. suppurative thrombophlebitis, osteomyelitis, infective endocarditis)

ICU intensive care unit, *CRBSI* catheter-related bloodstream infection, *CLABSI* central line associated bloodstream infection, *USA* United States, *IDSA* Infectious Diseases Society of America, *GNB* Gram-negative bacteria, *MDR* multidrug-resistant.

závěr

- ATB u kriticky nemocných lze většinou podávat kratší dobu než (kdysi) doporučovaných 10 – 14 dní
- Délku podávaných ATB upravujme dle klinické stavu a laboratoře („defervescence“)

INDIVIDUALIZACE

- Zohledněme vyvolávajícího původce (STAU, PSAE, NF-GN bacterie, Candida)
- Zohledněme imunostatus nemocného, umělý materiál v těle nemocného (BSI, CLABSI)