

ANTİMİKROBİYAL
YÖNETİM SİMPOZYUMU

ANTIMICROBIAL STEWARDSHIP

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AMY Kılavuzları

ABD

ALMANYA

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Başkent Üniversitesi Tıp Fakültesi

Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji

Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America

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GUIDELINE



Strategies to enhance rational use of antibiotics in hospital: a guideline by the German Society for Infectious Diseases

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ABD'de...

- **2007**, IDSA, Antimicrobial stewardship guideline
- **2014**, CDC, Core elements of hospital antimicrobial stewardship programs
- **2015**, Beyaz Saray, National Action Plan for Combating Antibiotic Resistant Bacteria

- **2016**

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➤ **28 öneri mevcut,
4'ü güçlü öneri**

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Hangi yöntem?

Kısıtlama mı?

Prospektif değerlendirme ve geri bildirim mi (**ikna mı**)?

I. Does the Use of Preauthorization and/or Prospective Audit and Feedback Interventions by ASPs Improve Antibiotic Utilization and Patient Outcomes?

Recommendation

1. We recommend preauthorization and/or prospective audit and feedback over no such interventions (*strong recommendation, moderate-quality evidence*).

➤ İkisi de hiçbir şey yapmamaktan iyidir

Avantajlar... Dezavantajlar...

Table 1. Comparison of Preauthorization and Prospective Audit and Feedback Strategies for Antibiotic Stewardship

Preauthorization	Prospective Audit and Feedback
Advantages	
• Reduces initiation of unnecessary/ inappropriate antibiotics • Optimizes empiric choices and influences downstream use • Prompts review of clinical data/ prior cultures at the time of initiation of therapy • Decreases antibiotic costs, including those due to high-cost agents • Provides mechanism for rapid response to antibiotic shortages • Direct control over antibiotic use	• Can increase visibility of antimicrobial stewardship program and build collegial relationships • More clinical data available for recommendations, enhancing uptake by prescribers • Greater flexibility in timing of recommendations • Can be done on less than daily basis if resources are limited • Provides educational benefit to clinicians • Prescriber autonomy maintained • Can address de-escalation of antibiotics and duration of therapy
Disadvantages	
• Impacts use of restricted agents only • Addresses empiric use to a much greater degree than downstream use • Loss of prescriber autonomy • May delay therapy • Effectiveness depends on skill of approver • Real-time resource intensive • Potential for manipulation of system (eg, presenting request in a biased manner to gain approval) • May simply shift to other antibiotic agents and select for different antibiotic-resistance patterns	• Compliance voluntary • Typically labor-intensive • Success depends on delivery method of feedback to prescribers • Prescribers may be reluctant to change therapy if patient is doing well • Identification of interventions may require information technology support and/or purchase of computerized surveillance systems • May take longer to achieve reductions in targeted antibiotic use

Avantajlar

Kısıtlama yöntemi

- Gereksiz/uygunsuz atb başlanması azalır; daha çabuk sonuç alınır
- Empirik seçenekleri optimize edebilir
- Tedaviye başlarken kültür sonuçlarını değerlendirmeye yönlendirir
- Atb maliyeti azalır
- Atb kontrolü doğrudan sağlanmış olur

İkna yöntemi

- AMY prg açısından iyi; iş birliği yapılmasını sağlar
- İlacı başlayacak kişilere klinik veriler sunularak öneride bulunulur
- Önerilerin yerine getirilmesi konusunda esneklik sunar
- Günlük olarak yapılmak zorunda değildir
- Klinisyenlerin eğitimine katkıda bulunur
- İlacı başlayan kişiye otonomi sağlar

Dezavantajlar

Kısıtlama yöntemi

- Sadece kısıtlanan ilaçlar için uygulanabilir
- İlacı başlayan kişinin otonomisi olmaz
- Tedavi gecikebilir
- Mevut kaynaklara bağlı
- Onay için klinik bulgular yanlı ifade edilebilir
- Diğer atb grupları daha çok kullanılır

İkna yöntemi

- Uyum isteğe bağlı
- Emek yoğun
- İlaç yazanlara geri bildirimde bulunmayı gerektirir
- Hasta iyi ise klinisyen tedaviyi değiştirmek istemeyebilir
- Sürveyans..vb için bilgi teknolojilerinin yoğun kullanılması gerekir
- Daha uzun sürede sonuç alınır

Klinik tablolarla özgü algoritmalar

IV. Should ASPs Implement Interventions to Improve Antibiotic Use and Clinical Outcomes That Target Patients With Specific Infectious Diseases Syndromes?

Recommendation

4. We suggest ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes (*weak recommendation, low-quality evidence*).

Örneğin

- Toplum kökenli pnömoni
- Hastane kökenli pnömoni
- Selülit
- Asemptomatik bakteriüri...vb

Hangi ölçütler?

Table 3. Possible Metrics for Evaluation of Interventions to Improve Antibiotic Use and Clinical Outcomes in Patients With Specific Infectious Diseases Syndromes

Process Measures	Outcome Measures
Excess days of therapy (ie, unnecessary days of therapy avoided based on accepted targets and benchmarks) ^a	Hospital length of stay 30-day mortality Unplanned hospital readmission within 30 d
Duration of therapy	Proportion of patients diagnosed with hospital-acquired <i>Clostridium difficile</i> infection or other adverse event(s) related to antibiotic treatment ^a
Proportion of patients compliant with facility-based guideline or treatment algorithm ^a	Proportion of patients with clinical failure (eg, need to broaden therapy, recurrence of infection)
Proportion of patients with revision of antibiotics based on microbiology data	
Proportion of patients converted to oral therapy	

Süreç ölçütleri

- Fazladan tedavi süresi
- Tedavi süresi
- Kurumdaki tedavi algoritmasına uyum oranları
- Lab.sonuçlarına göre ilaç modifikasyon oranları
- Oral tedaviye geçen hasta oranları

Sonuç ölçütleri

- Hastanede kalış süresi
- 30 günlük mortalite
- *C.difficile* enf..vb
- Tedavi yetersizliği, rekürrens..vb

C.difficile sorunu

V. Should ASPs Implement Interventions Designed to Reduce the Use of Antibiotics Associated With a High Risk of CDI?

Recommendation

5. We recommend antibiotic stewardship interventions designed to reduce the use of antibiotics associated with a high risk of CDI compared with no such intervention (*strong recommendation, moderate-quality evidence*).

Comment: The goal of reducing CDI is a high priority for all ASPs and should be taken into consideration when crafting stewardship interventions.

- *C.difficile* için yüksek riskli antibiyotiklerden uzak durulmalı
- Enfeksiyon kontrol önlemlerine uyum önemli

IV antibiyotikler için PK monitorizasyon

IX. In Hospitalized Patients Requiring Intravenous (IV) Antibiotics, Does a Dedicated Pharmacokinetic (PK) Monitoring and Adjustment Program Lead to Improved Clinical Outcomes and Reduced Costs?

Recommendations

9. We recommend that hospitals implement PK monitoring and adjustment programs for aminoglycosides (*strong recommendation, moderate-quality evidence*).
10. We suggest that hospitals implement PK monitoring and adjustment programs for vancomycin (*weak recommendation, low-quality evidence*).

Aminoglikozitler ve vankomisin için düzey takibi önemli

Oral tedavi

XI. Should ASPs Implement Interventions to Increase Use of Oral Antibiotics as a Strategy to Improve Outcomes or Decrease Costs?

Recommendation

12. We recommend ASPs implement programs to increase both appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics (*strong recommendation, moderate-quality evidence*).

Oral tedavi

- Başlangıç tedavisi olarak
- Ardışık tedavide PE'den sonra

Avantajları

- İlaç maliyeti daha düşük
- Yatış süresi daha kısa

Tedavi süreleri

XIII. Should ASPs Implement Interventions to Reduce Antibiotic Therapy to the Shortest Effective Duration?

Recommendation

14. We recommend that ASPs implement guidelines and strategies to reduce antibiotic therapy to the shortest effective duration (*strong recommendation, moderate-quality evidence*).

Tedavi süreleri etkin olan en kısa süreye kısaltılmalıdır

Tedavi sürelerini karşılaştıran çalışmalardan örnekler

Table 2. Meta-analyses and Examples of Randomized Clinical Studies Comparing Shorter Versus Longer Duration of Antibiotics

Reference	Clinical Condition/Population	Treatment Duration, d	Clinical Outcome ^a
Meta-analyses			
Dimopoulos et al, 2008 [123]	Adults and children with CAP	3–7 vs 5–10	Clinical success, relapse, mortality, adverse events
Pugh et al, 2011 [124]	Adults with VAP	7–8 vs 10–15	Antibiotic-free days ^b , recurrence ^b
Dimopoulos et al, 2013 [125]	Adults with VAP	7–8 vs 10–15	Relapse, mortality, antibiotic-free days ^c
Randomized clinical trials			
Chastre et al, 2003 [127]	Adults with VAP	8 vs 15	Mortality, recurrent infections ^d
El Moussaoui et al, 2006 [128]	Adults with CAP	3 vs 5	Clinical and radiological success
Greenberg et al, 2014 [129]	Children with CAP	5 vs 10	Treatment failure ^e
Hepburn et al, 2004 [130]	Adults with cellulitis	5 vs 10	Clinical success
Sandberg et al, 2012 [131]	Adult females with acute pyelonephritis	7 vs 14	Clinical efficacy, adverse events
Talan et al, 2000 [132]	Women with acute uncomplicated pyelonephritis	7 vs 14	Bacteriologic and clinical cure ^f
Runyon et al, 1991 [133]	Adults with spontaneous bacterial peritonitis	5 vs 10	Mortality, bacteriologic cure, recurrence
Saini et al, 2011 [134]	Neonatal septicemia	2–4 vs 7 (with sterile culture)	Treatment failure
Sawyer et al, 2015 [135]	Adults with intra-abdominal infection	4 vs ≤10	Composite of surgical site infection, recurrent intra-abdominal infection, or death
Bernard et al, 2015 [136]	Adults with vertebral osteomyelitis	42 vs 84	Cure at 1 y by independent committee and secondary outcomes

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Tabakalı (Stratified) Antibiyogram

XIV. Should ASPs Work With the Microbiology Laboratory to Develop Stratified Antibigrams, Compared With Nonstratified Antibigrams?

Recommendation

15. We suggest development of stratified antibigrams over solely relying on nonstratified antibigrams to assist ASPs in developing guidelines for empiric therapy (*weak recommendation, low-quality evidence*).

Yaşa, hastalığa, birime, örnek türüne... göre antibiyogramlar geliştirilebilir

Antibiyotik rotasyonu

VIII. Should ASPs Implement Strategies That Promote Cycling or Mixing in Antibiotic Selection to Reduce Antibiotic Resistance?

Recommendation

8. We suggest against the use of antibiotic cycling as a stewardship strategy (*weak recommendation, low-quality evidence*).

Direnci azaltmak üzere antibiyotiklerin siklik kullanımı
ÖNERİLMEMEKTEDİR

Antibiyotik kullanım ölçütü olarak DDD mi? DOT mu?

XX. Which Overall Measures Best Reflect the Impact of ASPs and Their Interventions?

Recommendation

21. We suggest monitoring antibiotic use as measured by days of therapy (DOTs) in preference to defined daily dose (DDD) (*weak recommendation, low-quality evidence*).

DDD: Daily Defined Dose

- **DSÖ** tarafından öneriliyor
- Birim bazında yapılabildiği için DOT'tan daha kolay
- Yaygın kullanıldığı için karşılaştırma yapılabiliyor
- Çocuk dozları için uygun değil

DOT: Days of Therapy

- Doz düzenlemelerinden etkilenmediği için hem pediatrik hem erişkin hastalarda kullanılabilir
- **CDC**, DOT olarak rapor ediyor
- Verinin hasta bazında elde edilmesi gerekiyor; her yerde yapılamayabilir

'End of life antibiotic treatment'

XXVII. Should ASPs Implement Interventions to Reduce Antibiotic Therapy in Terminally Ill Patients?

Recommendation

28. In terminally ill patients, we suggest ASPs provide support to clinical care providers in decisions related to antibiotic treatment (*good practice recommendation*).

- Terminal dönem malignite hastalarında
- İleri derecede demansı olan yaşlı hastalarda
yaşamın uzaması beklentisi olmadığına göre
antibiyotikler ile ilgili nasıl bir yol izlenmeli?

Hızlı tanı:

Prokalsitonin, viral antijen testleri, mantarlar için biyobelirteçler, moleküler yöntemler

XVI. Should ASPs Advocate for Use of Rapid Viral Testing for Respiratory Pathogens to Reduce the Use of Inappropriate Antibiotics?

Recommendation

17. We suggest the use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics (*weak recommendation, low-quality evidence*).

Comment: Although rapid viral testing has the potential to reduce inappropriate use of antibiotics, results have been inconsistent. Few studies have been performed to assess whether active ASP intervention would improve those results.

XVII. Should ASPs Advocate for Rapid Diagnostic Testing on Blood Specimens to Optimize Antibiotic Therapy and Improve Clinical Outcomes?

Recommendation

18. We suggest rapid diagnostic testing in addition to conventional culture and routine reporting on blood specimens if combined with active ASP support and interpretation (*weak recommendation, moderate-quality evidence*).

XVIII. In Adults in Intensive Care Units (ICUs) With Suspected Infection, Should ASPs Advocate Procalcitonin (PCT) Testing as an Intervention to Decrease Antibiotic Use?

Recommendation

19. In adults in ICUs with suspected infection, we suggest the use of serial PCT measurements as an ASP intervention to decrease antibiotic use (*weak recommendation, moderate-quality evidence*).

XIX. In Patients With Hematologic Malignancy, Should ASPs Advocate for Incorporation of Nonculture-Based Fungal Markers in Interventions to Optimize Antifungal Use?

Recommendation

20. In patients with hematologic malignancy at risk of contracting invasive fungal disease (IFD), we suggest incorporating nonculture-based fungal markers in ASP interventions to optimize antifungal use (*weak recommendation, low-quality evidence*).

Otomatik order (Stop orders)

VI. Do Strategies to Encourage Prescriber-Led Review of Appropriateness of Antibiotic Regimens, in the Absence of Direct Input From an Antibiotic Stewardship Team, Improve Antibiotic Prescribing?
Recommendation

6. We suggest the use of strategies (eg, antibiotic time-outs, stop orders) to encourage prescribers to perform routine review of antibiotic regimens to improve antibiotic prescribing (*weak recommendation, low-quality evidence*).

IDSA- Güçlü öneriler

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Avrupa'da...

- 2001, Avrupa Komisyonu
- 2010, Avrupa Birliği, Direnç s rveyansı ve antibiyotik t ketiminin izlenmesi

Grup/Kurul/Takım kimlerden oluşmalı?

1 Requirements

1.1 Availability of a team of ABS experts

The team should consist of at least one infectious diseases physician (or clinician with infectious diseases training) and an experienced clinical pharmacist/hospital pharmacist, as well as a specialist in microbiology, virology and infection epidemiology being responsible for laboratory diagnostic and microbiological consultation; furthermore, the physician

Various ABS programmes describe an FTE of 0.5 per 250 beds as being the minimum staff resources necessary to cost-effectively conduct an ABS programme.

- 250 yatak için 0.5 FTE
- FTE: Full time equivalent
- **Enf. Hast. uzmanı**
- **Klinik eczacı**
- Mirobiyoloji uzmanı
- Epidemiyolog
- Enf. Kontrol doktoru

Sürveyans- Antibiyotik tüketimi takibi

1.2 Availability of surveillance data on pathogens, resistance, and antimicrobial consumption

Conducting an additional material analysis (e.g. number of blood culture sets per patient or 1000 patient-days, number of urine cultures per patient, number of catheter-associated urine cultures, etc.) also with regard to

Use density should be presented by antibiotic class and not only by individual agent.

Reporting consumption data and antiinfective costs ranked by individual agent or class (e.g. top 5 or 10) is also reasonable.

Point prevalence surveys are a simple tool to examine process quality.

- **Alınan kültür sayısı** izlenmeli: örneğin 1000 hasta gününde alınan kan, idrar kültürü...vb

- Direnç verileri –en azından- **yıllık** bazda ulaşılabilir olmalı
- Bölüm, etken, örnek türüne..vb göre raporlandırılmalı
- **Sürveyans** örnekleri ayrı rapor edilmeli
- Sürveyans sistemi önemli
- Tüketilen ant miktarları **grup bazında** da izlenmeli

Klinik tablo bazında tüketilen antibiyotik takibi

Table 4 Examples for performing targeted proactive audits of antiinfective use

- Perioperative antibiotic prophylaxis in selected surgical fields
- Targeted therapy of bacteremic patients hospital-wide
- Community-acquired pneumonia in the emergency department
- Sequential therapy on general wards with antibiotics of high bioavailability

- En çok tüketilen 5 veya 10 antibiyotik listesi rapor edilebilir
- 3 aylık, 6 aylık, yıllık..vb olabilir

Nokta prevelans ile

- Cerrahi profilaksi için kullanılan atb'ler
- Bakteriyemilerde kullanılan atb'ler
- Acil serviste pnömoni için önerilen atb'ler
- Ardışık olarak oral tedaviye geçme oranı izlenebilir

Örnek: 3 aylık dilimler halinde en sık kullanılan anyibiyotik grupları

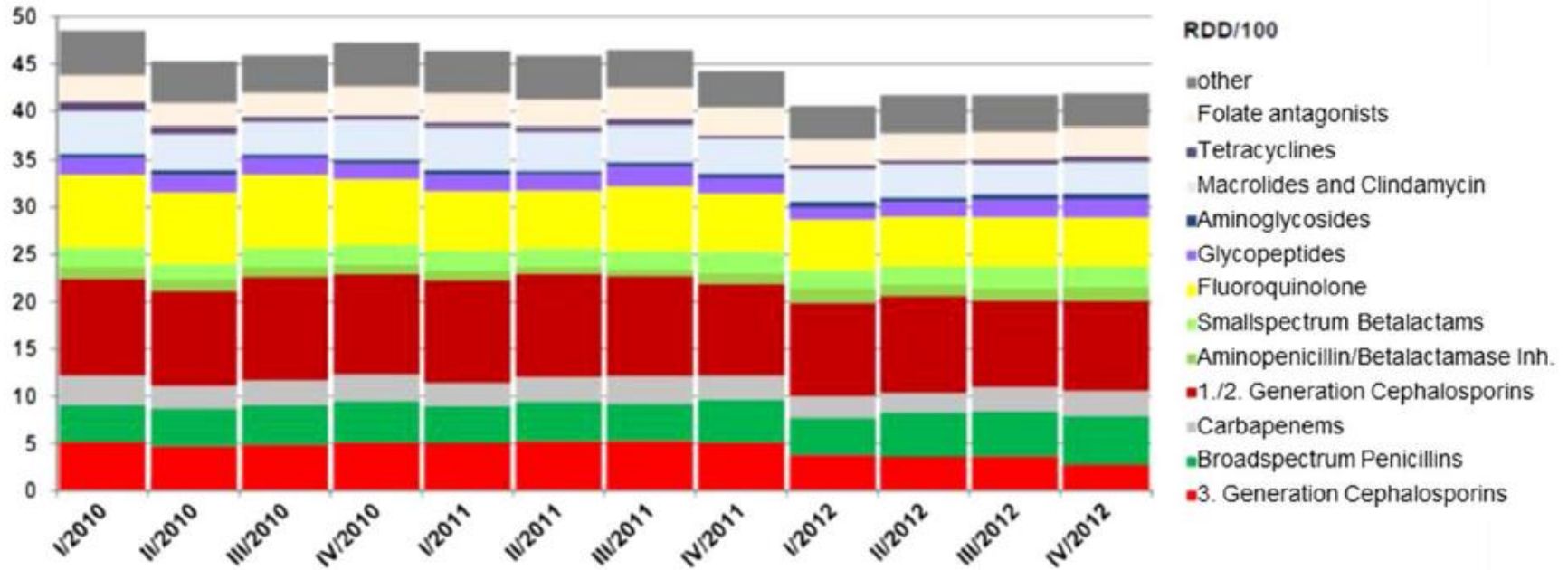


Fig. 1 Graphical presentation of quarterly use density (RDD/100 patient-days) for different antibiotic classes

Hastane formülleri (klinik eczacı tarafından) oluşturulmalı

Formülerde ilaçla ilgili sunulması gereken temel bilgiler:

- Jenerik adı (çoğu zaman ticari adlarıyla birlikte)
- Farmasötik formu
- Yitiliği
- Temel farmakodinamik/farmakokinetik özelliği
- Temel endikasyon(lar)ı
- Kontrendikasyon(lar)ı
- Kullanım şekli
- Talimat ve uyarılar
- Dikkatli olunması gereken durum(lar)ı
- Advers/yan etkiler
- İlaç etkileşimleri

Formülerde ilaçla ilgili sunulması gereken ilave bilgiler:

- Fiyatı
- Geri ödeme durumu
- Reçete kategorisi
- Saklama koşulları
- Raf ömrü
- Hasta bilgisi
- Etiket bilgisi
- Temel ilaç listesinde bulunma durumu
- Üretici firma bilgileri

Formüler örneği

Table 2 Example of a formulary

Antibiotic (AB)- Group	Appl.	Trade Name	Active agent	Recommended daily dose RDD		DTC
				Normal renal function CrCl > 80 ml/min	Impaired renal function CrCl 80-50 ml/min	
Penicillins	i.v.	Infectocillin	Benzylpenicillin	3 x 10 million IU or 4 x 5 million IU	2 x 10 million IU	€€
	oral	Penicillin V 1 Mega	Phenoxymethyl penicillin	3 x 1 million IE	3 x 1 million IU	€
Aminopenicillins	i.v.	Ampicillin	Ampicillin	3 x 2 g	2 x 2 g	€€
	oral	AmoxiHexal	Amoxicillin	3 x 1 g	3 x 1 g	€
Aminopenicillins + beta-lactamase inhibitors	i.v.	Ampicillin+ Subactam	Ampicillin/ Subactam	3 x 2000/1000 mg	2 x 2000/1000mg	€€
	oral	Amoclav 500 plus	Amoxicillin/ Clavulanic acid	3 x 500/125 mg	3 x 500/125 mg	€
Acylaminopenicillins	i.v.	Piperacillin	Piperacillin	3 x 4 g	2 x 4 g	€€
Acylaminopenicillins + beta-lactamase inhibitors	i.v.	Piperacillin+ Tazobactam	Piperacillin/ Tazobactam	3 x 4g/0,5 g	2 x 4g/0,5 g	€€
Carbapenems	i.v.	Meropenem	Meropenem	3 x 1 g for meningitis: 3 x 2 g	4 x 500 mg	€€€€
Tetracycline	i.v.	DoxyHexal SF	Doxycycline	1 x 200 mg, then 100-200 mg/day	no dose adjustment necessary	€
	oral	DoxyHexal Tabs	Doxycycline			€
Aminoglycosides	i.v.	TobraCell	Tobramycin	1 x 5-6 mg/kg KG	Confer with Senior physician	€€
	i.v.	Gentamicin	Gentamicin	1 x 4,5 mg/kg KG		€€
Nitroimidazoles	i.v.	Metronidazol	Metronidazole	3 x 500 mg	3 x 500 mg	€
	oral	Metronidazol	Metronidazole	3 x 400 mg	3 x 400 mg	€
Oxazolidinons	i.v.	Zyvoxid	Linezolid	2 x 600 mg	2 x 600 mg	€€€€
	oral	Zyvoxid	Linezolid	2 x 600 mg	2 x 600 mg	€€€€
Green: Recommended Antibiotic	As a matter of principle preference should be given to oral drugs, provided that the patient's condition allows					
Yellow: Reserve Antibiotic	The recommended daily dose refers to an adult patient (~ 70 kg)					
Red: Special Antibiotic, Confer with senior physician	DTC: Daily Therapeutic Cost DTC: €: 0 to €2; €€: 2 to €10; €€€: 10 to €25; €€€€: 25 to €50; €€€€€: more than 50 € to €150					
Bold	Available oral antibiotics					

Tedavi optimizasyonu

3.1 Special programmes for treatment optimisation

De-escalation includes conversion from an empirical combination therapy to targeted monotherapy based on knowledge of the microorganism isolated, susceptibility and infectious disease.

De-escalation should be initiated early on (after 48–72 h), which also includes discontinuation of initial therapy if diagnosis is not secured. Observational studies show that this strategy is not adopted in 20–60 % of cases.

De-escalation programmes should point out that depending on the exact diagnosis in some cases instead of de-escalation, escalation may in fact be necessary.

Prolonged infusion of beta-lactams (taking into account physico-chemical stability) is reasonable and recommended particularly in critically ill patients.

TDM can avoid under-/over-dosing and minimise organ toxicity.

Programmes for doses optimisation are cost-effective.

- Her zaman de-eskalasyon olmayabilir; eskalasyon da bir optimizasyondur
- Tedavi 48-72 saatte gözden geçirilmeli
- Uzamış infüzyon..vb uygulamalar değerlendirilmeli
- Serum düzeyi takibi önemli

Bilgi sistemleri teknolojisi gerekli

3.4 Computerised information technology

The local treatment guideline and the antiinfective formulary should be readily electronically accessible from every clinical computer workstation.

For ABS activities or for surveillance and analysis of antimicrobial usage, computer physician order entry (CPOE) systems should be designed in such a way as to allow automated generation of exact lists of the antiinfectives used.

Surgical software should be utilisable in such a manner as to ensure that antibiotic prophylaxis is compliant with guidelines.

Computer-based expert systems cannot replace a physician's clinical judgement.

Elektronik ortamda

- Tedavi rehberlerine
- İlaç formülerine
- Sürveyans sonuçlarına
-

ulaşılabilmeli



ANTİMİKROBİYAL YÖNETİM REHBERİ

Hazırlayan: KLİMİK DERNEĞİ

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Belki de daha erken!