Old antibitiotics, new solutions :
old narrow spectrum bétalactamine and cotrimoxazole with PK/PD optimization as a treatment for gram négative bactéria in ICU.

M.Rouyer and S.Diamantis
GHSIF, Hôpital Melun, France

Introduction

- Use of Broad-spectrum antibiotics with anti-anaérobic activities

  -> Increase of antimicrobial resistance

- In Intensive Care Unit, High antibiotics volumes, High ecological pressure

- Limitation of ecological impact is necessary

- Use narrow spectrum molecules with PK/PD optimization is an alternative to Carbapenems, third and fourth generation Cephalosporin or fluoroquinolones.

Rationalizing antimicrobial therapy in the ICU: a narrative review. Jean-François Timsit and all.

Notion of ecological impact

- Spectrum species sensitivity : the lesser, the better
- Activities against anaerobics bacteria : a Shield to protect
- Association with antibioresistance in-vitro : with misuse of every antibiotics.
- Association with antibioresistance in vivo : carbapenem and fluoroquinolones are the worst.

Evaluating and predicting the ecologic impact of antibiotics.A. Andremont and al.

Proof of concept : Antibiostiwardship can reduce antibioresistance

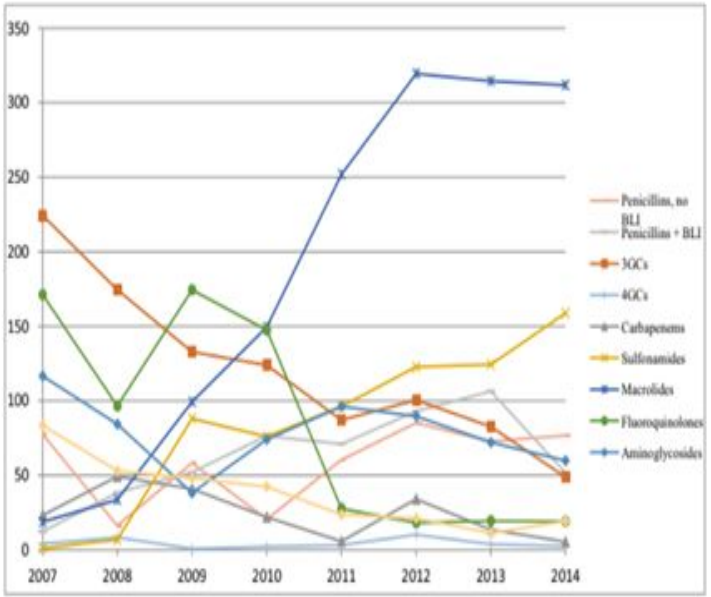

Fig. 1. Evolution of total consumption of different classes of antibiotics as a function of the year. The results are expressed in defined daily doses (DDD) per 1000 patient-days. Standard DDD are presented for all antibiotics, except for penicillins for which DDD divided by 6 are presented. BLI, β-lactamase inhibitor.

Antimicrobial stewardship: local guidelines.

Systematic microbiological sampling prior to initiation of empirical antibiotherapy.
Selection of empirical antibiotherapy according to local bacterial epidemiology and patient's colonisation status.
Tracking of microbiological samples by the medical team of the ICU.
Fast reporting of positive results, including the pattern of resistance of the pathogen, to the medical team by the microbiologist.
Determination of the MIC to antibiotics, if needed.
Carbapenems used in empirical treatment only when the patient had septic shock plus either proof of urinary tract carriage of ESBL-producing micro-organisms in the last 6 months or a history of urinary tract infection with ESBL producing micro-organisms in the last 6 months.
Fluoroquinolones restricted to documented infections only, mainly osteoarticular infections.
Empirical treatment of pulmonary infections in the case of septic shock included a macrolide and a β-lactam with a β-lactamase inhibitor, or piperacillin/tazobactam if *Pseudomonas aeruginosa* was suspected.
Third-generation cephalosporins were restricted as empirical treatment for urinary tract infections in men.
Adapted treatment favoured penicillins, sulfonamides and macrolides over other possibilities.
De-escalation whenever the clinical condition of the patient and microbiological results allowed it.
Duration of antibiotherapy was shortened, following similar rules as later described by Brettonières et al. [12]

ICU, intensive care unit; MIC, minimum inhibitory concentration; ESBL, extended-spectrum β-lactamase.

Impact of a multimodal strategy combining a new standard of care and restriction of carbapenems, fluoroquinolones and cephalosporins on antibiotic consumption and resistance of Pseudomonas aeruginosa in a French intensive care unit. S.DIAMATIS and al

PK/PD antibiotics optimisations : 10 commandements

- Better efficacy with less mortality : [C]> 5 MIC (piperacillin+tazobactam)
- Less antibioresistance : [C]>MBC (carbapenem)
- Depend of the diagnosis of comorbidities, diseases,organs and bacterias
- Time dependance antibiotics = continuous infusion
- Continuous infusion always begin with a Bolus
- In ICU, frequent Hyper clairance need High doses
- Acute Kidney Injury = first 24h of full dose, and then doses adapted to GFR
- Doses adapted to BMI and albuminemia
- Use bactericidic’s antibiotics firstly, bacteriostatic secondarly
- In cases of doubt, make a dosage and MIC

The "Old" and the "New" Antibiotics for MDR Gram-Negative Pathogens: For Whom, When, and How.Ilias Karaiskos

Antimicrobial stewardship programs in adult intensive care units in Latin America: Implementation, assessments, and impact on outcomes Rodolfo E Quirós

Old antibiotics

- Cotrimoxazole
- Cefoxitin
- Temocillin
- Aztreonam
- Piperacillin with tazobactam
- Aminosid
- Amoxicillin with clavulanic acid

Preparing and administering injectable antibiotics: How to avoid playing God. Longuet P

Old antibiotics : cotrimoxazole

- Bacteriostatic > bactericidal
- Inoculum effect
- Time dependant effect
- Dilution in G5% or in Nacl 0.9% : 1/20
- Stability 4h at 25°C
- DOSES max in adults :
  - Sulfamethoxazole 1200 mg + trimethoprim 240mg x4/ day
  - IV in 4 hours
- Volumetric pump

Trimetoprim-sulfametoxazole in ventilator-associated pneumonia: a cohort study .Alessio Strazzulla

Old antibiotics : cefoxitin

- Bactericidal
- No Inoculum effect
- Time dependant effect
- Dilution in Nacl 0.9% : 1g in 10ml
- Stability 24h at 25°C
- DOSES max in adults :
  - 12g/day
  - IV in 24 hours
- Volumetric pump

Old antibiotics : temocillin

- Bactericidal
- Inoculum effect
- Time dependant effect
- Dilution in Nacl 0.9% : 80mg/ml
- Stability 24h at 25°C
- DOSES max in adults :
  - 8 g/day
  - IV in 24 hours
- Volumetric pump

Old antibiotics : aztreonam

- Bactericidal
- Inoculum effect
- Time dependant effect
- Dilution in Nacl 0.9% : 100mg/ml
- Stability 24h at 25°C
- DOSES max in adults :
  - 12g/ day
  - IV in 24 hours
- Volumetric pump

Old antibiotics : Piperacilline 4g + Tazobactam 500mg

- Bactericidal
- Inoculum effect
- Time dependant effect
- Dilution in Nacl 0.9% or G5% : 4g in 50ml
- Stability 24h at 25°C
- DOSES max in adults :
  - 24 g/day
  - IV in 24 hours
- Volumetric pump

Old antibiotics : aminosid

- Bactericidal
- Post antibiotic effect
- Concentration dependant effect
- Dilution in Nacl 0.9% or G5% : 20mg/ml
- Stability 24h at 25°C
- DOSES max in adults :
  - 30mg/kg/day
  - IV in 30 min
- Syringe pump

- Old antibiotics : Amoxicillin 1g + clavulanic acid 200mg

- Bactericidal
- Inoculum effect
- Time dependant effect
- Dilution in Nacl 0.9% : 20mg/2ml
- Stability 4h at 25°C
- DOSES max in adults :
  - 8 g/day
  - IV in 4 hours x4/day
- Volumetric pump

Prescribed daily dose	Minimum dilution volume	Dilution and administration volumétric pump
3g	150ml	1g in 50ml sur 4h x3/j
6g	300ml	2g dans 100ml sur 4h00 x3/j
8g	450m	2g dans 100ml sur 4h00 x4/j

Stability studies of amoxicillin/clavulanic acid combinaison in polyolefin infusion bags. Kambia N,

Conclusion

Old antibiotics with PK/PD optimisation is an efficient, low cost, and high ecological solution to the major problem of bacterial infections and antibiotic resistances.