Modern urban myths and legends in chemotherapy

Thursday 10 March 2005
Royal College of Physicians,
London

CPD Accredited
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Programme

09.30 - 09.55  REGISTRATION & COFFEE

09.55 - 10.00  Welcome & introduction
Alasdair MacGowan, Bristol

10.00 - 10.25  Combination therapy for Staphylococcus aureus infection
Kate Gould, Newcastle upon Tyne

10.25 - 10.50  Therapeutic drug monitoring of glycopeptide antibiotics
Alasdair MacGowan, Bristol

10.50 - 11.15  Prolonged parenteral therapy for prosthetic bone and joint infections
Bridget Atkins, Oxford

11.15 - 11.35  COFFEE

11.35 - 12.00  Susceptibility testing of Stenotrophomonas maltophilia as a guide to therapy
Robin Howe, Cardiff

12.00 - 12.30  BSAC ANNUAL GENERAL MEETING

12.30 - 13.30  LUNCH

13.30 - 13.45  BSAC Trainee Award
Urinary Tract Infection (UTI): Over-diagnosed and Over-treated
Hislam Ziglam, Dundee

13.45 - 15.30  Personal views session:
“When I would use…..”
- Daptomycin  Ian Morrissey, London
- Linezolid  Dilip Nathwani, Dundee
- Ertepenem  Graeme Jones, Southampton
- Caspofungin  Rosemary Barnes, Cardiff
- Voriconazole  David Denning, Manchester
- Moxiflloxacin  David Honeybourne, Birmingham

15.30 - 15.45  Closing remarks
Point prevalence study of in-patient anti-infective prescribing
Lal P, Gray J, Graham C
Department of Microbiology, Birmingham Children's Hospital, Birmingham, UK

OBJECTIVE: Prudent antimicrobial use has been proven to be a significant factor in limiting development of antimicrobial resistance. This study was undertaken to evaluate the prevalence and appropriateness of in-patient anti-infective prescribing at BCH. METHOD: A prospective study was performed for the patients receiving antibiotics from 15.11.04–15.12.04 at the BCH during which all wards were visited twice and information on antibiotic prescribing gathered from the patient notes and the treatment charts. The appropriateness of antibiotic prescription was ascertained, taking into account the reason(s) for commencing antimicrobial therapy, relevant microbiological results, the choice of antimicrobial agent (therapy not indicated, agent appropriate for suspected/proven infection, agent inappropriate for the suspected/proven infection in that spectrum of activity inadequate/excessively broad, restricted antibiotic used without microbiology approval). RESULTS: A total of 378 cases were included in the study out of which 108 cases had antibiotic prescriptions. The majority of prescriptions were prophylactic (52%), 33% were based on clinical suspicion, 6% were based on microbiology report alone and 9% of the prescriptions were based on both clinical suspicion and microbiological report. There were 200 anti-infective prescriptions for these patients comprising of 83% antibiotics, 13% antifungals, and 4% antivirals. There were 84%(169) appropriate prescriptions in accordance with the BCH antimicrobial therapy and National guidelines and 16%(31) were inappropriate. Amongst the inappropriate prescriptions in 8%(16) the agent prescribed provided excessive broad-spectrum cover (vancomycin, meropenem), in 5%(9) the agent provided inadequate cover and in 3%(6) anti-infective therapy was not indicated. CONCLUSIONS: The prevalence of in-patients on anti-infective prescription was 28.5%. This is lower than that reported in similar studies earlier. Yet in 16% the anti-infective prescription was inappropriate, in most of these cases the anti-microbial were either excessively broad spectrum 8% or not indicated 3%. The information derived from this study may be used as a reference for further study and research for optimising antibiotic usage.

An Audit of Antibiotic Prophylaxis Prescribing In General Surgery
Mohandas K, Ray E*, Cooke RPD
Departments of Medical Microbiology and Pharmacy*, University Hospital Aintree, Liverpool

Introduction
Antibiotic prophylaxis at the time of surgery can reduce the risk of surgical site infection. Guidelines for antibiotic prophylaxis in general surgery should be evidence-based and adhered to, if inappropriate prescribing practices and antibiotic resistance are to be avoided. The aim of this audit was to assess the compliance by medical staff, of an established local hospital antibiotic policy and the adequacy of antibiotic policy in relation to national standards.1,2

Methods
A retrospective case note review was undertaken. All patients who underwent an elective or emergency general surgical procedure in May 2002 and June 2004 were identified. Antibiotics prescribed either pre, intra or post-operatively were recorded and compared to the hospital antibiotic policy.

Results
302 patients and 253 types of operative procedures were identified. One hundred and eleven (37%) patients underwent a surgical procedure for which there was a specific formulary recommendation. From this group, only 12 (11%) patients received an appropriate antibiotic based on formulary advice. There was also wide variation in pre and post-operative dosing regimes, timing and duration of antibiotic prophylaxis.

Conclusion
Local antibiotic prophylaxis guidelines were not followed. The guidelines also did not cover the range of surgical procedures for which prophylaxis was considered necessary by surgeons. Antibiotic surgical prophylaxis is recognised as one of the areas of greatest variation in practice. Hence, if the Department of Health’s ‘Winning Ways’ document is to be actioned, surgeons need to develop a local consensus on antibiotic prophylaxis which should reflect national standards. Local guidelines in addition should clearly state when antibiotic prophylaxis is not indicated.

References
Susceptibility of Streptococcus pneumoniae to levofloxacin 12 months after introduction as empirical treatment of community acquired pneumonia in hospitalised patients

White SL, Mitchell N and Rao GG
Microbiology Dept, University Hospital Lewisham

The discovery of levofloxacin resistant S.pneumoniae has coincided with increased usage of the drug to treat lower respiratory tract infection (LRTI).

**Aim:** To determine whether isolates of S. pneumoniae continue to be sensitive to levofloxacin a year after its introduction at University Hospital Lewisham as antibiotic of choice for treatment of community acquired pneumonia in patients admitted to the hospital.

**Methods**
S.pneumoniae from specimens sent to the diagnostic microbiology laboratory were collected over a 6 month period (July-December 2004). 45/177 (25%) representative isolates from various sites (blood, sputum etc) were tested for MIC of levofloxacin and moxifloxacin using E-test. All isolates were fully sensitive to both antibiotics.

**Results**
Leovloxacin had a MIC range of 0.064-0.5mg/l and an MIC90 of 0.38mg/l . Moxifloxacin had a MIC range of 0.032-0.125mg/l and an MIC90 of 0.125mg/l.

**Conclusion**
We conclude that in year following introduction of levofloxacin for empirical treatment of CAP, there has been no emergence of resistance. As previously observed, moxifloxacin has an MIC 2-4 fold lower than that of levofloxacin against S.pneumoniae.

Treatment of Experimental Escherichia coli Infection with Recombinant Bacteriophage-Derived Capsule Depolymerase

Taylor PW, Mushtaq N, & Luzio JP
School of Pharmacy, University of London & Cambridge Institute for Medical Research

Objective: *Escherichia coli* is one of the major causes of neuroinvasive neonatal infection and a large majority of isolates synthesize the K1 polysaccharide, a “-2,8-linked homopolymer of sialic acid. We examined the contention that selective removal of the protective K1 capsule in infected neonatal rat pups would allow host defences to remove the attenuated pathogen and provide a novel strategy for treatment of severe systemic infections.

**Methods:** We identified, characterized, cloned, sequenced and expressed in high yield a “-2,8-linkage-specific endosialidase (endoE), carried by a K1-specific coliphage. Bacteraemia was established in neonatal Wistar rat pups by feeding cultures of the virulent K1 strain A192PP; rapid colonisation of the gastrointestinal tract preceded a lethal bacteraemia. Doses of endoE were administered intraperitoneally.

**Results:** Blood infection was markedly age-dependent. Two-day-old rats were extremely susceptible to infection but the incidence of infection in five-day-old pups was significantly lower, mirroring the disease pattern in humans. Appropriate intraperitoneal administration of recombinant endoE prevented bacteraemia and death in this model: a single dose of 0.25-20 g protein given 24 h after administration of the infecting dose produced a complete curative effect whereas doses in this range given 72 h after infection were less effective. EndoE-mediated removal of K1 capsular polysaccharide led to increased ingestion by peritoneal macrophages and sensitisation to the bactericidal action of complement.

**Conclusions:** These studies demonstrate the potential therapeutic efficacy of agents that influence host – pathogen interactions by modifying the bacterial phenotype rather than through conventional bacteriostatic or bactericidal effects. Enzyme-mediated stripping of the K1 capsule, a polymer with very low immunogenicity, sensitises the neuropathogen to both cellular and humoral components of the hosts’ defences and this appears sufficient to facilitate the elimination of the phenotypically attenuated organism.

Funded through BSAC Grants GA230 and GA382.
Risk factors for ESBL producing Klebsiella pneumoniae, E.coli and Enterobacter aerogenes in patients admitted to hospital

Soleimanian S and Rao GG
University Hospital Lewisham, London

Introduction: Extended spectrum beta-lactamase producing coliforms are becoming an important cause of infections in hospitals throughout UK. Knowledge regarding risk factors for developing these infections in UK hospitals is relatively sparse.

Aim: To identify possible risk factors associated with infections caused by ESBL producing coliforms.

Methods:
Design- Prospective cohort study for 12 months (Jan-Dec 2004).
Subjects- In-patients with proven infection with ESBL producing coliforms (K. pneumoniae, E.coli and E. aerogenes)
Data collection- Case notes and laboratory records review to collect information regarding:
Demographic details, site of infection, h/o catheterisation, antibiotic treatment, and antibiotic sensitivities.

Results:
Isolates were identified as K. pneumoniae 40 (55.6%), E.coli 27( 37.5%) and E. aerogenes 5 (6.9%). 72 patients were infected with ESBL producing coliforms. – 60 (83%) of the patients were >65 years old. 42 (58.3%) and 30 (41.7%) were females and males respectively. 12 (16.7%) patients were resident of nursing homes. 45 Patients (62.5%) were admitted to medical, 11 (15.3%) to orthopaedic, 9 to surgical (12.5%) and 7 (9.7%) to vascular wards. The infection sites were urine 57 (79.2%), wound swabs 7 (9.7%), sputum 6 (8.3%), blood 1 (1.4%) and CVP tip 1 (1.4%). 43 patients (79.2%) had history of urinary catheterization. In 43 (74.2%) catheterised patients, catheter was in place for >7 days. 64 of patients (88.9%) received previous antibiotic therapy. Cefuroxime 35 (54.7%) was the commonest antibiotic. All the ESBL producing isolates were resistant to cephalosporins and ciprofloxacin. 24 (33.3%) were sensitive to gentamicin. All were sensitive to meropenem.

Conclusions:
Infections with ESBL producing coliforms are most common in elderly patients. Patients with prolonged urinary catheterisation and those receiving previous antibiotic therapy especially with cephalosporins appear to be at greatest risk.

The Role of Solid-Phase Chemistry in the Discovery of Novel Chemotherapeutic Leads

Anne Routledge1*, Barbara Santry1, Ruth Fake1, Gustav Boije af Gennas1, Kevin Kerr2 and Val-Edwards Jones3
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Carbohydrate-protein interactions play a major role in biological processes such as cell-cell recognition and signaling. Many bacteria utilize carbohydrate-protein interactions to initiate pathogenesis via carbohydrate specific adhesin recognition of host cell glycoconjugates. Synthetic glycoconjugate mimics have been synthesised in an attempt to identify potent ligands of bacterial adhesins but only a limited number of compounds have been synthesised and screened in each study. These compounds do provide some limited information on the three dimensional structural requirements of bacterial adhesins but rapid access to a large number of synthesised glycoconjugates could ultimately lead to the development of novel therapeutics that interfere with bacterial adhesion and thus prevent/inhibit pathogenesis.

Herein we report our work (supported by BSAC GA344) towards developing a rapid combinatorial approach to generate glycoconjugate libraries where each member has a distinct three-dimensional shape and glycoside valency. These libraries are designed to probe the topology of bacterial adhesins to give information on the structural requirements for any potential anti-adhesive chemotherapeutic.

The library synthesis is performed on solid-phase using a building block approach to allow the rapid generation of library members in a minimum number of synthetic steps. The resultant scaffold library can be capped with a specific glycoside. This chemistry is designed to be ammenable to automation. To date we have validated the chemistry with mannose (uropathogenic E. coli) but research is on going and will be expanded to pathogens which are now developing resistance to current treatments (3'-sialyllactose- Helicobacter pylori).
An outbreak of Serratia marcescens on the Neonatal Unit: A Tale Of Two Clones
David M¹, Lambert P², Fraise AP³, Weller TMA⁴
Microbiology Department, Aston University¹, Hospital Infection Research Laboratory² and Microbiology Department ³⁴, Sandwell and West Birmingham NHS Trust

**Background** Serratia marcescens, a well recognised nosocomial pathogen was isolated from several babies on a Neonatal Unit between October 2001 - April 2002. We describe the outbreak and the phenotypic and genotypic characteristics of the organisms involved.

**Methods** Clinical isolates were collected from 18 patients infected or colonised with S.marcescens during the study period. These were compared to one environmental isolate and other temporally unrelated clinical isolates from patients elsewhere in the same hospital. All isolates were typed with pulsed field gel electrophoresis (PFGE) and random amplified polymorphic DNA-polymerase chain reaction (RAPD-PCR). The blactamase was characterised by isoelectric focusing.

**Results**: In the study period 4 babies had severe invasive S. marcescens infections (meningitis and/or septicaemia), of which 2 died. A further 14 babies were colonised with the organisms or had only superficial infections. Extensive environmental and staff screening, revealed no common source. The outbreak ended following enhanced compliance with infection control measures and a change of antibiotic policy. S marcescens continued to be isolated sporadically from various clinical sites for another six months. Isoelectric focusing confirmed the presence of an inducible beta lactamase with a high pl, consistent with the presence of an AmpC beta-lactamase. Both molecular typing methods revealed that two clones were present. The first, which caused invasive clinical infection in 4 babies, was afterwards replaced by a second, non-invasive clone which affected 14 babies. Phenotypically, the two strains also differed in their prodigiosin production, the first one being non-pigmented whereas the second one displayed pink-red pigmentation. The environmental isolate and clinical isolates from other wards were genetically distinct. Although S. marcescens continued to be isolated occasionally, the end of the outbreak was signalled by the replacement of the original strains with sporadic strains with other molecular typing patterns.

**Conclusion**: There was a clear difference in the pathogenicity of the two outbreak clones. The molecular typing methods were useful epidemiologic tools which emphasized the difference between the two outbreak strains. RAPD-PCR, although relatively easy to perform, has limited reproducibility, whereas PFGE is discriminatory and reproducible.
Exhibitors

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