

Evaluation of antimicrobial-loaded calcium sulfate composites for the management of resistant Gram-negative diabetic foot osteomyelitis

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Background and objective: One of the most serious complications of diabetes is diabetic foot osteomyelitis (DFO) which can lead to limb amputation, reduced quality of life, and early mortality (International Diabetes Federation, 2020). Antimicrobial resistance (AMR) is a leading cause of death globally and is an increasing problem within DFO. We investigated the antimicrobial and pharmaceutical properties of antimicrobial-loaded calcium sulfate composites for the targeted treatment of DFO.

Methods: Calcium sulphate (Stimulan® Rapid Cure) beads containing gentamicin, ciprofloxacin, amoxicillin or colistin were tested against *Staphylococcus aureus* (NCTC6571), *Pseudomonas aeruginosa* (NCTC6750 and an extensively drug-resistant clinical isolate from DFO) and *Escherichia coli* (NCTC8196) over time using an adapted EUCAST disk-diffusion methodology. MIC testing and standard disk-diffusion testing were undertaken to determine susceptibility. Synergy testing, drug-release studies, dose uniformity and hygroscopicity testing were undertaken to further characterise these composites.

Results: Amoxicillin and ciprofloxacin released continuously, and zones of inhibition (ZOI) remained consistent, over a six week period. Whereas gentamicin and colistin underwent burst-release, with ongoing release and ZOI decreasing over time. Calcium sulfate had no antimicrobial effect and no synergy was observed between any of the antimicrobials. Amoxicillin and ciprofloxacin had a more uniform dose (4% and 7% variation, respectively) whereas for gentamicin and colistin were not uniform (48.0% and 133.6% variation, respectively). A decrease in mass of beads was seen in hygroscopicity testing, suggesting release of moisture from the composites.

Conclusions: Antibiotic-loaded calcium sulfate beads release drug and inhibit bacterial growth over time, suggesting utility in the management of difficult to treat DFO. Future work should focus on different mixing methods for making calcium sulfate beads to determine effects on dose uniformity.

Keywords: Calcium sulfate; Diabetic foot; Osteomyelitis; Zone of Inhibition; Antimicrobial resistance

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Evaluation of harmful and potentially harmful excipients for newborns found in medications used in Children's Clinical University Hospital (Department Of Neonatology) in 2019

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Background: Not all excipients are biologically inert and, in some patients (especially neonates), may cause adverse effects. Although excipients are essential components of a medicinal product that are needed in the manufacturing process, there are growing concerns about their safety.

Study aim: To study the safety of industrially produced medicines used for neonates in the Neonatology Clinic of the Latvian Children's Clinical University Hospital from the point of view of excipients.

Methods: Data on medications used in the Neonatology Clinic was obtained from the hospital's drug accounting software. Using the summaries of product characteristics, the excipients of each medicine were determined, grouping them into 3 parts: harmful excipients, potentially harmful excipients, and other excipients. Data collection was performed using Microsoft Office Excel 2019 and descriptive statistical methods (natural numbers and percentage distribution), which were presented in the form of graphs. In addition, alternatives to the potentially harmful medicines were evaluated.

Results: Of the purchased medicines, 133 contained at least one undesirable excipient, and in 99 medicines they were not present. Propylene glycol was the most common harmful excipient, used in 20 medicines. Similarly, benzalkonium chloride was used in 18 and ethanol in 16 of the medicines. Among the potentially harmful excipients, the most common were titanium dioxide and disodium edetate, which were used in 21 and 20 of the drugs, respectively. 22 medicines contained at least 4 undesirable excipients, of which only 3 can be replaced by other medicines available in Latvia which have a lower number of undesirable excipients.

Conclusions: Most of the industrially manufactured medicines used by the Neonatology Clinic in 2019 are not appropriate for newborns. The next step would be to analyze the doses of the excipients taken by newborns and other possible solutions.

Key words: harmful excipients, potentially harmful excipients, neonates, toxicity.

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Identification of drug-related problems in elderly patients during hospital care

Background and Objectives: Elderly patients are highly exposed to polypharmacy due to multiple comorbidities, having an increased risk of drug-related problems (DRPs). The aim of the study was to assess the prevalence and type of DRPs arising during patients hospital stay.

Methods: A retrospective observational study was conducted on Geriatric ward. Seventy-six patients aged ≥ 65 years, consecutively admitted from February-May 2017 were enrolled in this study. Data were obtained from medical records. Drug-related problems were classified according to the criteria of the American Society of Health-System Pharmacists 1,2. Statistics was performed using IBM SPSS software ver. 25.

Results: The study included 43% (33/76) male and 57% (43/76) female patients, mean age 80 ± 6 years. At least one DRP was present in 93% (71/76) of patients. The highest prevalence was observed for potential drug-drug or drug-disease interactions that are clinically significant 93% (71/76), followed by medications with no indication 91% (69/76), condition for which no drug is prescribed 88% (67/76), medications prescribed inappropriately for a particular condition 70% (53/76), inappropriate medication dose or schedule 17% (13/76), therapeutic duplication 12% (9/76), and prescribing of medications to which the patient is allergic 1% (1/76). Median number of DRPs per patient was 10, mainly resulting from potential drug-drug or drug-disease interactions (median 4).

Conclusions: DRPs occur frequently among elderly patients during hospital care. An important task for hospital pharmacist is to identify, resolve, and prevent the occurrence of DRPs in this patient group. The hospital setting play a pivotal role in therapy optimization, due to facilitated cooperation of health professionals with different specialities.

Keywords: drug-related problems; prevalence; geriatrics; hospital setting; polypharmacy

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Clinical evaluation of Druglog® apparatus for the control of parenteral preparations in operative room and high dependency unit.

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Background and objectives: Medication errors (ME) might affect patient's prognosis in operative room (OR) and high dependency unit (HDU). Despite drug labelling or barcode reader use, checking the prepared drug before administration could secure medicinal care. With UV absorption technology, a new apparatus, Druglog® can identify and quantify drugs in two seconds. The objective was to assess the Druglog®'s robustness to intercept ME.

Methods: According to french society of pharmaceutical science and technology recommendations, 28 drugs were calibrated at concentrations commonly used in anaesthesia. During three months, in OR and HDU, a 1mL sample of random prepared drugs was analysed. In case of non-conformity, it was prepared and analysed once again. A multi-professional meeting assesses the criticality of intercepted DE according to the french society of clinical pharmacy table.

Results: 22 drugs were calibrated with 5 to 15 calibration points. Lack of UV absorption, crossed identifications and non-granted accuracy profile caused calibration failures, probably because of the high inter-variability between manufacturers' batches. Relative errors vary from 0.5 to 7.9%. With 232 samples (3/4 in OR), 6.9% (n=16) ME were intercepted. Druglog® was not able to analyse mix of drugs (n=7). 81% of ME had a low criticality, mainly in the OR thanks to the anaesthetist acute survey.

Conclusion: Druglog® is compatible with clinical use and can intercept ME. However, some calibration rules have to be followed to ensure reliable results in clinical use, and without medico-economic study, we can't predict his impact in unit's organisation. Moreover, neonatology might be more relevant, where multiple dilutions are required.

Keywords: Medication error - Pharmaceutical technology – Pharmaceutical preparation – Anaesthesia – Medication system, hospital

Control of chemotherapy-induced nausea and vomiting in patients with gastrointestinal tumours

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Objectives: During cancer treatment, many patients experience chemotherapy-induced nausea and vomiting (CINV), which leads to a lower quality of life and poorer adherence to the subsequent chemotherapy cycles. The aim of the study was to assess antiemetic therapy prescribing and CINV control in the acute phase (24 hours post-chemotherapy) and the delayed phase (days 2–4 post-chemotherapy). Factors influencing CINV control were also determined.

Methods: Information on antiemetic premedication was gathered from patient medical records. Data regarding antiemetic therapy post-discharge and CINV control were in both phases obtained using patient questionnaires. Antiemetic therapy prescribing was compared with internal CINV prevention and control guidelines. Predictive factors for CINV control were evaluated using binary logistic regression.

Results: There were 62 patients enrolled in the study, out of which 50 (80.6%) received adequate antiemetic premedication. In the acute phase, 46 (74.2%) patients reported well-controlled CINV, whereas 16 (25.8%) reported uncontrolled CINV. None of the patients was prescribed post-discharge antiemetic therapy as per guidelines. In the delayed phase, CINV was more frequent as 39 (62.9%) patients reported well-controlled CINV, whereas uncontrolled CINV was reported in 23 (37.1%) patients. The predictive factors for overall CINV control were prescription of corticosteroids (OR=9.025, p=0.019) and patient age (OR=0.851, p=0.002). The delayed CINV control was dependent on age (OR=0.885, p=0.030) and acute

CINV control (OR=17.377, p=0.001).

Conclusions: The majority of the patients were prescribed adequate antiemetic therapy for the acute phase but not for the delayed phase, which may have resulted in more patients experiencing delayed CINV.

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Compliance with the Health Information and Quality Authority of Ireland National Standard for Patient Discharge Summary Information: a retrospective study in secondary care

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Background: Unexplained changes to medication are common at hospital discharge and underscore the need to standardise patient discharge clinical documentation. In 2013, the Health Information and Quality Authority in Ireland published a Standard on the structure and content of discharge summaries. The intention was to ensure that all necessary information was complete and communicated to the next care provider.

Objectives: This study investigated one Hospital's compliance with the Standard, and appraised two methods of electronic discharge communication (Symphony or Tallaght Education and Audit Management System (TEAMS)).

Method: A retrospective survey of 198 randomly selected discharge summaries was conducted at the study hospital, a 600 bed academic teaching hospital located in Dublin, Ireland.

Results: Of the 198 evaluated summaries, mean total compliance was 77%±4.2 (95% CI 76.3 to 77.5). Most (84.7%, n=173) summaries were completed using one of the systems (TEAMS). Absence of communication about alteration of preadmission medication was frequent (107 out of 130 patients (82.3%, CI 76.2 to 89.2)). Higher compliance rates were observed however, when information was interfaced or where there were dedicated fields to be completed.

Conclusions: Efforts to improve compliance with the National Standard for Patient Discharge Summary Information should focus on reporting changes made to medication during hospitalisation.

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Pharmacist intervention in pain management following heart surgery

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Objectives: Pain is a common symptom in cardiac surgery patients. This study aimed to investigate the influence of pharmacist intervention to ease postoperative pain in cardiac surgery patients.

Methodology: Patients undergoing heart surgery were randomised to control or intervention. The intervention group was given systematic verbal information and, at discharge, a pharmaceutical care plan. Pain score and diary assessment were compared up to 6 weeks after the surgery.

Results: 100 patients participated. Mean Pain Score was lower in the intervention group from week 1 to 6 ($p < 0.05$). Compliance with analgesic was higher in the intervention group.

Conclusions: The intervention improved compliance and decreased pain score, illustrating the positive effect the pharmacist had on these patients.

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Molecular characterisation of CTX-M-type extended-spectrum β -lactamases of *Escherichia coli* isolated from a Portuguese University Hospital

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Study objectives: The aim of this work was to study the prevalence of CTX-M-producing *Escherichia coli* isolates collected from the Hospital of the University of Coimbra (HUC) and to characterise these isolates both phenotypic and genotypically.

Methods: Between November and December 2007, 220 non-duplicate *E. coli* isolates were recovered at HUC. The extended-spectrum β -lactamases (ESBL)-producers were identified by the automatic VITEK 2 system and advanced expert system (bioMérieux, Marcy l'Étoile, France), further confirmed by the disk diffusion synergy test. The blaCTX-M genes were detected by PCR, and the amplicons were sequenced. Genetic relatedness was assessed by ERIC-PCR. A CTXM-15-producing *E. coli* isolate collected in 2004 at the same hospital was included in the study.

Results: Twenty-one isolates were identified as ESBL-producers resistant to all penicillins, first generation cephalosporins, cefotaxime and/or ceftazidime, but susceptible to imipenem.

The majority of the isolates were collected from urines. Sequence analysis identified the CTX-M-15 enzyme in all isolates. All the isolates were clonally related. DNA fingerprinting was identical with the CTX-M-15-producing strain collected in 2004.

Conclusion: Our results showed the spread of hospital-acquired urinary tract infections caused by CTX-M-15-producing *E. coli*, and the prevalence of these infections in women. Also, the emergence of CTX-M-15 in this institution is related to the spread of a clone over time. We concluded the need to upgrade the control infection measures in this hospital, as this study confirmed the presence of an endemic *E. coli* clone disseminated in different wards, a clone already identified in 2004, and according to our results, maintained at this hospital until 2007.

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Last update: 29 March 2023

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