The risk of symptomatic venous thromboembolism in hospitalised patients with active cancer

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Introduction

Up to 75% of fatal pulmonary emboli in general hospitals occur in non-surgical patients immobilised by medical illness. Audits demonstrate that thromboprophylaxis is used in less than one-third of suitable patients. People with active cancer appear to be at significantly higher risk of symptomatic venous thromboembolism (VTE) than those without in epidemiological studies.

Aim

To determine the risk of symptomatic VTE, occurring during hospitalisation and within 90 days of discharge, in acutely ill patients with active cancer admitted to the Royal Hobart Hospital (RHH).

Methods

A retrospective cohort study was conducted. Medical records from patients admitted to the RHH oncology units from 1/1/04 to 31/12/06 were assessed for symptomatic VTE. Patients were identified for inclusion if they had active cancer, were hospitalised for at least four consecutive days, and aged over 18 years.

Results

237 patients were included. 81.4% were eligible to receive thromboprophylaxis according to hospital guidelines. Of these patients, 30.6% received prophylaxis during their hospital stay. The patients who developed VTE had a mean of 5.6 risk factors for VTE. The incidence of symptomatic VTE during the index admission and within 90 days of hospital discharge was 4.2%. Patients with previous history of VTE had a significantly higher risk of a recurrent event ($P < 0.01$). Of those who developed VTE, 40.0% (4 of 10) received prophylaxis during their index admission.

Discussion

Acutely ill in-patients with active cancer were at high risk of symptomatic VTE during and immediately following hospitalisation. Thromboprophylaxis was underused in this population. People with active cancer suffering from an acute medical illness represent a target for quality improvement activities aimed at reducing the risk of VTE in hospitalised patients. However, in some cases, current strategies to reduce the risk of VTE may be inadequate in this population.

Synthesis and biological examination of charged liposaccharides as oral penetration enhancers

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Introduction

A large number of potent drugs, including hydrophilic and peptide-based molecules, are currently unavailable orally due to a lack of absorption in the GI tract. Permeation of the intestinal epithelium requires drug candidates to possess a certain degree of lipophilicity and/or functional groups for recognition by transmembrane transporters (e.g. carbohydrates). Furthermore, enzymatic degradation in the gut and the blood stream is a major issue for many potential drug candidates.

Often, the poor oral availability of these molecules lies in the presence of polar, ionisable residues exhibiting charges at physiological pH.

Methods

Our approach was to design and synthesise a library of counter-ionic molecules which would not only balance the charges born by the tested drug but also enhance its enzymatic stability and membrane permeability by acting as carriers.

Constructs were formed by coupling a carbohydrate moiety to a charged lipoamino acid residue (-amino acid with alkyl side chain, for increased lipophilicity); they were then associated to their counter-ionic drug by lyophilisation.

Results

A series of positively charged liposaccharide constructs were evaluated *in vitro* and *in vivo* using piperacillin as a model anionic drug. Conjugates were tested for plasma stability, toxicity (haemolysis), intestinal permeability (Caco-2) and antimicrobial effect (MIC). Results showed that the compounds still retain antimicrobial activity and