Right Dose, Right Now: Model Validation

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Sepsis is a major and growing problem. In the Netherlands alone, around 15.000 patients are diagnosed with severe sepsis each year. Despite major scientific efforts, including many failed clinical trials mainly focusing on inflammatory mediators and...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON21977

Bron
Nationaal Trial Register

Aandoening

Pharmacometrics

Prediction

Sepsis

Infectious disease

Personalized medicine

Antibiotics

Antibiotica

Farmacometrie

Infectieziekten

Predictiemodellen

Ondersteuning

Primaire sponsor: VU University Medical Center
Overige ondersteuning: ZonMw

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

• Agreement between predicted and observed relevant pharmacometric parameters using Bland-Altman analysis
• Percentage of correct first predictions of each pharmacometric model.
• Extent to which all relevant pharmacometric goals are being met.

Toelichting onderzoek

Achtergrond van het onderzoek

Sepsis is a major and growing problem. In the Netherlands alone, around 15.000 patients are diagnosed with severe sepsis each year. Despite major scientific efforts, including many failed clinical trials mainly focusing on inflammatory mediators and the introduction of care bundles, the mortality rate for severe sepsis still remains unacceptably high at around 30%. This is alarming, especially since the incidence of sepsis continues to increase and now exceeds that of colon cancer, breast cancer and AIDS combined.

Antibiotics are essential for treating sepsis. Their early and appropriate use has repetitively been shown to reduce mortality rates. However, achieving adequate antibiotic exposure in critically ill patients is a major challenge due to markedly different pharmacokinetic (PK) profiles in the critically ill. Nevertheless, doctors still rely on standard antibiotic dosing schemes, that were developed based on data from healthy volunteers and non-critically ill patients. Depending on patient characteristics, clinical course and therapy, this strategy may result in underdosing and/or drug-related toxicity during the course of intensive care treatment.

Therefore, we developed AutoKinetics (AutoK) software. AutoK aims to make use of patient data that is available from the electronic patient records, for example about fluid balance and renal function. Using this data, AutoK is able to give fast and precise dosing advice, using published pharmacokinetic models of any drug. AutoK runs on the computer at the bedside. Thus, advice is readily available, even before treatment is started, and is continuously

updated as disease and therapy evolve: true personalized dosing.

We believe that AutoK can improve antibiotic dosing, morbidity and mortality for severe sepsis.

Eventually, we will test AutoK in multicenter clinical trial (Right dose, Right now: randomized clinical trial). We will randomize patients with severe sepsis (n=42 per group, per antibiotic), for antibiotic dosing through AutoK or standard therapy.

This study concerns the validation of pharmacometric models using prospectively collected data which is not being collected in the context of regular patient care and / or quality controls and using routinely collected data which has been and is being collected in regular patient care and/or quality control.

The aim of this study is to select the most accurate pharmacometric models.

Doel van het onderzoek

Sepsis is a major and growing problem. In the Netherlands alone, around 15.000 patients are diagnosed with severe sepsis each year. Despite major scientific efforts, including many failed clinical trials mainly focusing on inflammatory mediators and the introduction of care bundles, the mortality rate for severe sepsis still remains unacceptably high at around 30%. This is alarming, especially since the incidence of sepsis continues to increase and now exceeds that of colon cancer, breast cancer and AIDS combined.

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This study concerns the validation of existing pharmacometric models which are publicly available from the international literature, using prospectively collected data which is not being collected in the context of regular patient care and / or quality controls and using routinely collected data which has been and is being collected in regular patient care and/or quality control. The core part of this research will consist of validating pharmacometric models of the following antibiotics: Vancomycine, Meropenem, Ceftriaxon, Cefotaxim, Ciprofloxacine, Ceftazidim and in addition, depending on analysis availability, the following antimycotics: anidulafungin, voriconazol and fluconazol. However, we intend to validate pharmacometric models of all relevant antibiotics and antimycotic agents that are being used at the ICU.

The aim of this study is to select the most accurate pharmacometric models.

Onderzoeksopzet

-

Onderzoeksproduct en/of interventie

For the prospective part of the study we will take an average of six blood samples per patient, per antibiotic/antimycotic.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

For the prospective part of this study, the inclusion criteria are:

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- Age ≥ 18 years

- The patient is receiving antibiotics and/or antimycotic agents to treat an infectious disease.

For the retrospective part of this study the inclusion criteria are:

- The patient has been treated on the Intensive Care unit of the VUmc or OLVG Oost and the patient data has been stored in an electronic patient file (in OLVG from 1999 and VUmc from 2003)

- There is at least 1 relevant pharmacometric outcome measure available (e.g. vancomycine plasma concentration)

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

none

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	16-06-2017
Aantal proefpersonen:	500
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	25-08-2017
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6502
NTR-old	NTR6690
Ander register	METc VUmc : ABR:NL60826.029.17

Resultaten