Clinical validation of a dried blood spot (DBS) method for the analysis of rifampicin (RIBOD study).

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PrimairyTo clinically validate a finger prick DBS method compared to conventional venous sampling for the analysis of rifampicin.Secondairy* Feasibility of the novel finger prick DBS method in the target population will be assessed. This includes...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON42070

Source
ToetsingOnline

Brief title
RIBOD

Condition

- Bacterial infectious disorders

Synonym
analysis of drugs used for tuberculosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: DBS (dried blood spot), Rifampicin, TDM (therapeutic drug monitoring), Validation

Outcome measures

Primary outcome

The primary objective of this study is the clinical validation of a DBS method for rifampicin in the target population. The related endpoint is the evaluation of the the association between the concentration obtained by venous sampling and the concentration obtained by means of DBS sampling. The predictive performance of the DBS method as a measure for the venous concentration will be evaluated.

Secondary outcome

- To assess the feasibility of finger prick DBS in the target population. The related endpoint is the response to a questionnaire. Results will be used to prepare implementation of the novel method for home-based monitoring as well as to prepare a HTA analysis.

- To design an inventory of cost types related to DBS sampling and conventional sampling. The cost types will function as a basis for future HTA analysis of this novel sampling method compared to conventional venous sampling.

Study description

Background summary

Both TB and NTM have a huge impact on world health. About 1/3 of the world population is latently infected with TB. The highest burden of TB exists in

limited-resource countries, mostly in sub-Saharan Africa and Asia. NTM is impacting world health more over the last two decades. Despite this high burden and long experience with rifampicin, the optimal dose of rifampicin to eradicate TB is still subject of ongoing investigation. The current standard dose is 600 mg daily, though no clear evidence based on pharmacokinetic/pharmacodynamic relationships exist. So future studies will be performed on the optimal dosis, hereby investigating the pharmacokinetics of TB.
Therapeutic drug monitoring (TDM) offers the possibility to individualize and improve a patient*s pharmacological treatment, based on the measurement of drug concentrations in biological samples. In clinical practice, TDM comprises the measurement of one or more drug concentrations associated with the administration of the dose of a certain drug. Dependent on the drug exposure measured, the dose of the drug may be increased or decreased. This is expected to result in a change in exposure, which in turn may yield more efficacy or less toxicity. In this way, the aim of TDM is to improve exposure aiming at maximizing efficacy and minimizing toxicity for an individual patient. TDM is often peformed in patients treated with rifampicin.
Conventionally, TDM is performed with blood or plasma obtained by venous blood sampling. This method is associated with several challenges such as i) the need for the patient to travel to the hospital or health center; ii) special conditions for sample transport to guarantee stability of the analyte and to decrease the biohazard risk; iii) sampling times not always representing the preferable peak or trough concentrations; iv) the method being invasive and v) delay of the outcome of the analyses with regard to the outpatient visit.
The Dried Blood Spot (DBS) may offer a solution for all these challenges. To perform the DBS technique, only a small amount of blood is needed and this sample can easily be obtained via a finger prick is put on a piece of filter paper, can be taken at home and is sent to the laboratory by post mail. Patients or their caregivers can perform the sampling at the appropriate time in the concentration curve, e.g. at the time of the trough concentration, while avoiding an extra visit to the hospital or health center. When arriving at the hospital for a meet-up with the physician, adaptation of the dose based on the already available drug concentration is directly possible and a delay introduced by conventional sampling procedures is thereby avoided

In addition to TDM of rifampicin, also PK research with this drug is thought to benefit from DBS. DBS is thought to offer benefits especially for the performance of PK studies in remote areas and limited-resource countries with a tropical climate. The cold chain required for conventional blood sampling is generally not required with DBS. Moreover, as PK studies and dose-finding regimes should be carried out in each target population, most of research is to take place in Asia and Africa.

In an earlier study (PROTECT) from the hospital pharmacy of the Radboudumc, a similar approach was used and approved by the local ethics committee (Commissie

Mensgebonden Onderzoek, CMO regio Arnhem-Nijmegen).

Study objective

Primairy
To clinically validate a finger prick DBS method compared to conventional venous sampling for the analysis of rifampicin.

Secondairy
* Feasibility of the novel finger prick DBS method in the target population will be assessed. This includes scoring of relevant characteristics (attributes) of blood drawing methods for TDM, evaluation of the experience and attitude of the patients regarding finger prick DBS sampling and evaluation of the understanding of the written instructions provided for performing the finger prick at home. The data obtained in this validation study will be used for the implementation of the DBS in therapeutic drug monitoring (TDM) being a less invasive procedure, for DBS as a method of blood drawing in futuer PK studies and as a base for a discrete choice-experiment as part of the HTA.
* To design an inventory of types of costs that will be incurred in the process of DBS-based and conventional TDM as a preparation step for later health economic analysis.

Study design

This is an observational single-centre study in which DBS sampling is compared with conventional sampling for concentration measurment of rifampicin. The concentration of rifampicin will be determined in dried blood spots obtained by a finger prick and in plasma obtained by simultaneous venous sampling in a tube of blood. Statistical analysis will be deployed to assess the association of the concentrations obtained with both methods of blood drawing. Also, the predictive performance of the DBS method will be assessed (for details on the statistical analysis we kindly refer to chapter 8 of the protocol).

Study burden and risks

As in this study no change in therapy is performed it possesses a minimal risk. The risks associated with a finger prick are pain at the puncture site and risk of bleeding. We will actively assess those factors during the study. The risks associated with venous blood sampling are similar (e.g., risk of infection, risk of hematomas and pain and/or discomfort at the puncture site). Venous blood will be drawn as much as possible from a central venous catheter (CVC or PAC), that will be placed in the vene. Only experienced personnel will perform the study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Patients aged 18 or over
* Treated at the Radboud University Centre for Chronic Diseases Dekkerswald
* Treated with rifampicin
* The drug concentration being in steady state

Exclusion criteria

none

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO

Date:	15-04-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL52029.091.15