Reducing renal function deterioration by means of increasing medication adherence, improving immunosuppressive drug exposure and supporting a healthy lifestyle - an implementation study.

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We plan to develop and introduce a personalized multi component care program aimed at prevention or postponement of progressive deterioration of kidney functioning. Recently, a medical dashboard (a *Shared Care Record* to which all kidney patients...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON50600

Source
ToetsingOnline

Brief title
RRFD

Condition

- Renal disorders (excl nephropathies)

Synonym
graft function, Kidney transplantation

Research involving

Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Astellas Pharma,Bedrijf

Intervention

Keyword: adherence, dried blood spot technology, lifestyle, renal graft survival

Outcome measures

Primary outcome

The primary study parameter is reduction in renal function deterioration. Renal function will be determined using iohexol measurement. Iohexol will be injected in the vene of the patient according to the routine clinical protocol, subsequently blood drawing will take place at (3 or 4) preset time points. Concentrations will be measured using HPLC technique at the laboratory. Using the blood concentrations in a pre-developed limited sampling model, an area under the concentration time curve will be determined. Subsequently the GFR is calculated. This procedure is performed at study start and study end. The GFR decline will then be calculated based on these two measurement for all patients.

Secondary outcome

Compliance:

Improved compliance (frequency of missing a dose (>4 hours after pre-set time), monitored using electronic medication blisters. Original Advagraf blisters will be repacked and provided with a layer consisting of an electronic circuit including microchip. This chip monitors the amount and time of Advagraf

capsules being extracted from the blister. Compliance will be defined as the percentage of correct dose intakes.

In addition, the Basel Assessment of Adherence to Immunosuppressive Medications Scale (BAASIS, De Geest, 2005) will be completed at 3 points in time (baseline, 12 and 24 months).

DBS / AUC*s:

- Variation in AUC
- Frequency of adjusting the dose
- Feasibility DBS (patient experience / Logistics)
- Addendum 17-06-2019: next to the regular DBS Hemaxis kit, patients will also receive the DBS Mitra Neoteryx kit at the endpoint of the RRFD study in order to calculate the AUC for tacrolimus. The DBS Mitra Neoteryx seems easier to handle, more specifically for patients with reduced vision ability.

Clinical:

- Other biomarkers renal function / kidney damage
- Proteinuria (via alb/creat or protein/creat ratio)
- Blood pressure measurements / number anti-hypertensive drugs => blood pressure measurements (at home/hospital) / Dynamap: 3 times 15 min in chair)
- BMI (Weight hospital) / Waist-hip ratio

Immunological:

- DSA (blood withdrawal)

- Immunological biomarkers (yet to define)

Diabetes / cardiovascular:

- Glucose tolerance test

- HbA1c => incidence / regulation diabetes (blood withdrawal)

- (cholesterol / HDL / LDL/Triglycerides)

- Pulse Wave Velocity => cardiovascular

- Cardiovascular events (cerebral / cardiac / peripheral)

Lifestyle:

- Nutritional pattern: sodium, saturated fat, purine-rich, fructose (via questionnaires, 24 hours-urine (sodium, urea) and nutrition module medical dashboard (only intervention group)

- activities (through questionnaire) and motion detector (optional).

Psychological:

- Satisfaction (Renal Treatment Satisfaction Questionnaire)

- Transplant related psychological parameters (worry about loss of transplant, feeling of guilt regarding donor, Transplant Effects Questionnaire)

- Generic assessment scale for chronic condition self-management (PiH, Partners in Health Scale: Petkov et al., 2010

- Personal beliefs about kidney disease and medicine intake (IPQ-short form: Broadbent et al., 2006; Beliefs about Medicines Questionnaire: Horne et al.,

1999(18))

- Short questionnaire on current health status (EQ5D);

- Quality of life (SF-12)

- Life style behaviours (i.e., sodium intake, smoking habits, alcohol intake,

level of physical exercise)

- A set of new Likert scale questions and open questions about patients*

specific concerns and desires, and self-efficacy regarding self-management and

at home monitoring.

- A small set of new Likert scale to assess expectations and actual experiences

regarding the intervention programme.

Process-evaluation

- Experience healthcare professionals and patients) at study end

- Logging => Number of self-measurements (Blood pressure, weight)

- Feasibility DBS implementation at home

- Number of medication interventions regarding immunosuppressive medication

- Percentage of AUC*s outside of the target range?

Other parameters

- Calcium, phosphate, PTH, vit D => Bone parameters

- Haemoglobin => cardiovascular risk

- Uric acid => risk of gout

Study description

Background summary

Over the last decades, novel immunosuppressive drug regimen have significantly reduced the incidence of acute graft rejection episodes after kidney transplantation. However, long-term graft survival has not improved concomitantly [1]. Optimal survival of the transplanted kidney depends on a number of factors; the donor and transplant procedure characteristics such as living versus deceased donor, cold ischemic time, donor age, HLA matching as well as co-morbidities of the recipient and optimal immunosuppressive therapy [2*5]. Immunosuppressive agents have a small therapeutic window and have often highly variable pharmacokinetics which makes therapeutic drug monitoring (TDM) of immunosuppressive drug concentrations essential for individualizing the dose and thereby preventing serious toxicity or rejection [6*9]. Furthermore suboptimal use of immunosuppressive medication and incompliance plays a central role in the shortened long-term graft survival in renal transplantation [10].
The main causes of late graft loss are death with graft function (dominated by cardiovascular disease) and chronic allograft dysfunction (dominated by a complex interplay between immunological and non-immunological causes). The key of new technological and scientific developments is to enhance personalized treatment regimens in order to meet each patient*s specific health needs.

Study objective

We plan to develop and introduce a personalized multi component care program aimed at prevention or postponement of progressive deterioration of kidney functioning. Recently, a medical dashboard (a *Shared Care Record* to which all kidney patients and their treating physician(s) have access) was implemented in our regular outpatient care, including: 1. laboratory results, 2.results of self-monitoring by the patient regarding blood pressure, body weight and 3. e-coaching to optimize communication between patients and doctors. Using the medical dashboard is expected to increase patients* active participation in their care. In addition to the general medical dashboard, we plan to offer study participants the following:
* Improving (both intentional and non-intentional) compliance of patients by (a) improvement of knowledge and skills of the patient, (b) improving motivation, (c) offering practical tools, and (d) improving communication skills of involved health care practitioners
* Medication review by outpatient pharmacy
* Use of Dried Blood Spot Technology for at-home based eAUC-monitoring (to obtain optimal immunosuppressive drug exposure)
* Option of participation in a life-style program (exercise / nutrition)
* Additional medical dashboard features, being a personal care plan addressing personal goals and concerns regarding compliance and optional e-modules that

support patients in adopting and maintaining a healthy life-style.

Study design

Single center implementation study.

Intervention

There are 3 interventions:
1. Interventions to help improve compliance
2. At home monitoring of immunosuppressive drugs
3. Lifestyle program (optional)

1. Monitoring of immunosuppressive drugs via Dried Blood Spot technique (tacrolimus)
2. Improvement of compliance (stepwise additional effect of different tools):
- App with medication alarm
- Medication review
- Feedback when medication is administered four ours too late (through Electronic blistering).
3. Lifestyle modules (optional) with/without support, focused on nutrition and physical exercise.

Study burden and risks

In addition to regular care (potential burden)
- completing questionnaires at baseline, 12 and 24 months
- pulse wave velocity measurement at baseline and 24 months
- use of Dried Blood Spot technique to sample blood at home to determine drug exposure (AUC) (3 additional measurements compared to regular care)
- one visit to a lifesteyle coach at baseline (remainder is facultative)
- two medication reviews with a hospital pharmacist

Risks
Participation within the trial comes with minimal risks (if present). At home monitoring of tacrolimus blood concentration via fingerprick can result in some discomfort. Venapunctures at the hospital could eventually result in hematoma.

Addendum 17-06-2019: at the endpoint of the RRFD study the only extra intervention will be the use of DBS Mitra Neoteryx kit, in order to calculate the AUC of tacrolimus. As described in section E4: the DBS Mitra Neoteryx kit will be handed out to patients in the RRFD study who agree to participate in the side project of this study, meaning a total of 25 patients (from the original N=100 RRFD study group).

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

- > 1 year after kidney transplantation
- Follow-up visits take place in LUMC
- Creatinine clearance (CKD-EPI > 25 ml/min)
- Immunosuppressive regimen based on tacrolimus
- Sufficient mastery of Dutch
- Access to and capacity to use the internet.
- Availability of a Smart-phone (necessary for blistering)
- Informed consent

Exclusion criteria

- No internet access
- Creatinine clearance (CKD-EPI * 25 ml/min)
- Insufficient knowledge of Dutch language
- Proven allergy for iodine contrast

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-02-2017
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	09-11-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	25-08-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	01-10-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	07-07-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 20914
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL58000.058.16
OMON	NL-OMON20914