Knowledge-Based Tacrolimus Therapy for Kidney Transplant Patients

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29. August 2012
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Identify adaptation rules for Tacrolimus therapy from a clinical data set
Forecast

- Identify adaptation rules for Tacrolimus therapy from a clinical data set
- Applying a regression tree to create homogeneous groups of data
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Applying a regression tree to create homogeneous groups of data

Generate models for these groups that can predict the level of the drug concentration
Forecast

- Identify adaptation rules for Tacrolimus therapy from a clinical data set
- Applying a regression tree to create homogeneous groups of data
- Generate models for these groups that can predict the level of the drug concentration
- Develop a clinical decision support system for Tacrolimus therapy planning
Chronic kidney disease treatment:

**kidney transplantation - Immunosuppressive therapy**

Narrow range between kidney transplant rejection and the side effects of over-immuno-suppression

Calcineurin inhibitor:

**Tacrolimus**

Close therapeutic drug monitoring necessary.
Data

- 1995 - 2008
- 492 patients
- 13053 examinations
- Immunosuppressive therapy data and
- laboratory data
Confounding Effect

Confounding

Following Medication Level

Confounding Effect

n= 1877
n= 10816
n= 948

Medication Adoptions

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Validation

Group 6 - Model Validation

Adapt down
Stay
Adapt upward

Following Medication Level

Trained set  Test set

1.1  n = 137  2.1  n = 42
1.0  n = 2419  2.0  n = 554
1.1  n = 123  2.1  n = 31

Medication Adjustments
Application

Tacrolimus (Prograf)-Level Prediction

- Coverage probability of the prediction interval:
  - 70%
  - 75%
  - 85%
  - 90%
  - 95%

- Medication data:
  - Previous level [ng/ml]: 17.0
  - Previous Prograf [day]: 2
  - Increase dose [mg]: 5

Other immunosuppressants (proliferation inhibitors):
- None

Results

- Distribution of medication: adaptation from historical data
  - Reduce medication [%]: 0.837
  - Leave medication [%]: 0.682
  - Increase medication [%]: 0.081

- Prediction interval of the expected values at each level in the selected medication in the chosen decision coverage probability:
  - Reduce medication [ng/ml]: 4.011 - 11.949 - 16.725
  - Leave medication [ng/ml]: 6.110 - 11.949 - 17.865
  - Increase medication [ng/ml]: 8.571 - 10.199 - 13.823

Explanation

- Slightly reduced tacrolimus level and no more than 2mg Prograf per day previously predicted.

Request
Summary

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- Confounding effect in the data
- Regression tree to get homogeneous groups
- Within this groups the confounding effect is gone
- First approach of more accurate forecasting models
- Development and integration of an application in the clinical routine system (i.s.h.med) of the Vienna General Hospital
Thank You!