Assessing Importance of Dietary Data in Anticoagulation Treatment

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Oral Anticoagulation Treatment (OAT)

• People with increased risk of thrombosis
  o Mechanical heart valve replacement
  o Deep Venous Thrombosis (DVT)
  o Atrial fibrillation
  o Pulmonary embolism

• Current patient figures
  o DK 100.000 patients\(^1\) (2% of population)
  o Expected to rise

Management of daily oral intake of vitamin K antagonists (warfarin)

Monitoring of INR - *International Normalized Ratio*

Beneficial balance between clotting and tendency to bleed

Affected by dietary vitamin K^2^ 

Slow-acting physiological system

• Conventional treatment
  o Physician managed
• Partly managed by patient
  o Patient self-testing
  o Patient self-management

• Patients have to comprehend:
Self-management and self-testing of OAT

• **Benefits**
  - Cost-effectiveness
  - Clinical effectiveness
  - Reduce frequency of ambulatory visits
  - Increase quality of life for OAT patients

• **Risks**
  - Potential lethal drug
  - Biological variability affecting INR
Summary of challenges

- Medication errors can cause death
- INR values are affected by biological variability as dietary vitamin K

Utilizing vitamin K information when prediction INR values
Methods

- Metabolic modelling
- Collection of data from five patients in “normal, everyday setting”
- Data parameters:
  - INR
  - Warfarin
  - Vitamin K
  - Others
Data collection protocol

• Cooperation with highly specialized ambulatory (Medicinsk Ambulatorium, Brædstrup Sygehus)
• Daily scheme to be filled for one month
• Mail correspondence once a week

<table>
<thead>
<tr>
<th>No. of days</th>
<th>INR</th>
<th>TTR</th>
<th>Warfarin</th>
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<tbody>
<tr>
<td>Mean</td>
<td>27,2</td>
<td>2,5</td>
<td>83,7%</td>
</tr>
</tbody>
</table>

Indications for OAT: Heart valve replacement, DVT, or atria fibrillation. Abbreviations: TTR = Time in Therapeutic Range.
• Already existing model$^3$ expanded
• Break down into compartments
  o Warfarin
  o Coagulation factors
  o Vitamin K
• Predict future INR values

Warfarin modelling

- Warfarin modelled as single compartment
  \[ W(t) = W(0) \cdot e^{-k \cdot t} \]

- Effect of warfarin on coagulation factors
  \[ \frac{dF}{dt} = w \cdot F_{syn} - F_{deg} \quad w = 1 - \tanh(W(t) \cdot warfsens) \]
Coagulation factors
• Modelled effect of vitamin K intake upon INR values

4. Schugers LG., Blood, 2004
**Model summary**

### Mathematical overview of model

1. \( \text{INR}(t) = 1 + (\sum [a_i((100-F_i)/100)^{S_i}] - \text{VitK}) \)

2. \( \frac{dF_i}{dt} = w \cdot F_{\text{syn}} - F_{\text{deg}} \)

3. \( w = 1 - \tanh(W(t) \cdot \text{warf-sens}) \)

4. \( W(t) = W(0) \cdot e^{-(k) \cdot t} \)
Model predictions
Model prediction results

![Graph showing INR Root Mean Square error over days with and without vitamin K information. The graph compares two lines: one for predictions without vitamin K information and another for predictions with vitamin K information. The y-axis shows the INR Root Mean Square error ranging from 0 to 0.6, and the x-axis represents days from 0 to 7. The graph illustrates the improvement in prediction accuracy when vitamin K information is included.]
Model prediction results

\[
\text{Error}_{\text{(without VK)}}^2 = \text{Error}_{\text{(with VK)}}^2 + VK_{info}^2
\]

\[
VK_{info} = \sqrt{\text{Error}_{\text{(without VK)}}^2 - \text{Error}_{\text{(with VK)}}^2}
\]
Model prediction results

![Graph showing model prediction results with different data conditions.](image)
Results for vitamin K rich data
Discussion

• Pros
  o Decision support for management of OAT patients
  o Help to avoid oscillating INR values
  o Opportunity to raise patient’s awareness

• Cons
  o Burden of data collection
  o False or incomplete data pose a potential risk
Thank you for listening

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