Personalizing analgesia during labor

VRIJE UNIVERSITEIT AMSTERDAM & UNIVERSITEIT VAN AMSTERDAM
AMSTERDAM PUBLIC HEALTH RESEARCH INSTITUTE

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Which laboring women needing pain relief benefit from

Remifentanil patient controlled analgesia

Epidural analgesia
Background

- Epidural analgesia (EA) most effective method
- EA is associated with e.g. assisted vaginal birth, fever, hypotension
- Alternative is desirable when EA is not available, not wished or contra-indicated

- Remifentanil-PCA (RPCA): opioid, fast onset of action, metabolized and redistributed quickly by the fetus
- RPCA associated with desaturation, respiratory depression
Remifentanil patient controlled Analgesia Versus Epidural analgesia in Labor

Randomly allocated to RPCA or EA in case of a request for pain relief

1823 women → 1414 with intermediate/high obstetric risk
→ 409 with low obstetric risk

Primary outcome: maternal satisfaction with pain

Secondary outcome: overall satisfaction with pain relief, pain intensity scores during labor, mode of delivery, maternal and neonatal outcomes
Hourly satisfaction score during active labor

Conclusion: women with RPCA were less satisfied with their pain compared to women with EA
Study question

- Is the treatment effect similar in all women?
- Are there any markers that could be helpful in identifying women who benefit from one treatment more than the other?
Objective

To investigate if choice of analgesia during labor can be personalized based on characteristics of pregnant-/laboring women:

1. To evaluate the potential of individual baseline characteristics of women for guiding the decision between RPCA and EA
2. To develop and internally validate a combination of baseline characteristics that identifies women which could benefit more from RPCA or EA during labor
3. To evaluate how good the derived combination score performs
Plan of analysis

1. Define a set of baseline characteristics (markers)
2. Harmonize variables of the two datasets
3. Regression models to predict satisfaction as a function of the treatment, the specific marker and marker-by-treatment-interaction
4. Two separate linear regression models to predict the outcome
5. Determine the benefit function → create a subpopulation treatment effect pattern plot (STEPP) → promising subgroup
6. Evaluate the calibration of the predicted benefit in comparison with the observed benefit and estimate size of the group who benefits from RPCA
Markers at randomization

- Medical indication (low obstetric risk vs. intermediate/high obstetric risk)
- Age at randomization
- Ethnicity
- BMI
- Parity (nulliparous vs. multiparous previous vaginal birth vs. previous caesarean section)
- Fear of childbirth score antepartum
Markers at request pain relief

- Onset of labor (spontaneous vs. induction)
- Augmentation with oxytocine
- Dilatation (cm)
- Gestational age (weeks and days)
- Hours between start active labor and request pain relief
## Planning

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>October 1st, 2017</td>
<td>Starting study</td>
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<tr>
<td>October-November 2017</td>
<td>Selecting the markers and finalizing the study protocol</td>
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<td>November 23rd 2017</td>
<td>An oral presentation for APH-PM meeting</td>
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<tr>
<td>December 2017- February 2018</td>
<td>Completing analysis</td>
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<td>Late January 2018</td>
<td>Sharing first results</td>
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<td>February-March 2018</td>
<td>Corrections and complementary analysis (in case required)</td>
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<td>March 2018 - May 2018</td>
<td>Writing manuscript and making a report of the study</td>
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<td>July 1st, 2018</td>
<td>Final report (deadline)</td>
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Any questions?

› Thank you for your attention
References

1. Tajik P. Markers to guide treatment decisions: Methods and applications in obstetrics and gynecology. *The Department of Clinical Epidemiology, Biostatistics and Bioinformatics, and the Department of Obstetrics and Gynecology*. 2015;PhD:206


8. NVOG (Dutch society of obstetrics and gynecology). Guideline medicamenteuze pijnbehandeling tijdens de bevalling (pain relief during labor). 2008