Assessing the importance of gender and age-related influences of CYP enzyme activity; the next step into personalized medicine

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Background

- The cytochrome P450 (CYP450) system is a group of enzymes found in the liver, crucial for the breakdown and elimination of drugs from the body.
- Drug response is highly variable, 40-70% of patients experience ineffectiveness or adverse drug reactions (ADRs) [1]
- Psychiatric medications are frequently metabolized by CYP450 enzymes, and variations in enzyme activity can significantly impact their effectiveness and safety, and this can aid in selecting personalized medication [2].

Methods

- A systematic search has been performed in Medline, Embase, PsycINFO, clinicaltrials.gov and The Cochrane Library to look for peer reviewed articles reporting on the human in-vivo original data on the influence of age or gender on the activity of five CYP enzymes with the help of the Ovid app interface.

Results

- A first search yielded close to n = 2200 articles. After narrowing search terms, n = 593 articles were left. With 5 more articles found in the Cochrane library.
- These articles were screened with the help of screening app Rayyan, n = 487 articles were excluded, and n = 111 articles were sought for retrieval.
- Full-text articles are currently being assessed for eligibility

Preliminary findings

Some findings when looking at past reviews and current literature:

- Not all studies assessing P450 activity managed to genotype their subjects, opening their results up for a big confounding effect
- A first search yielded some results, indicating that:
  - Some articles suggest a marginal difference in CYP2C19 and CYP1A2 activity between genders [4, 5], while others CYPs seem to be unaffected [6].
  - There is an effect of age on CYP3A4 and CYP2C19 activity [5].
  - CYP2D6 activity seems to be largely unaffected by age or gender [7].

Identification of studies via databases and registers

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<th>Records identified from:</th>
<th>Records removed before screening:</th>
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<td>Duplicate records removed (n = 0)</td>
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<td>Cochrane Library (n = 5)</td>
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<th>Records screened (n = 598)</th>
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<tr>
<td>Reports sought for retrieval (n = 111)</td>
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<tr>
<td>Full-texts being assessed for eligibility (n = 110)</td>
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<tr>
<td>Studies included in review (n = 7)</td>
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Figure 2. PRISMA flowchart

Figure 1. Visualisation of variability in cytochrome P450 enzymes and its effects on drug safety

Genetic Variations

Drug-Drug interactions

Gender

Age

Etc.

Lower CYP activity

Higher CYP activity

Higher blood concentration

Lower blood concentration

More ADR’s

Less effectiveness

References


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