ANTIEMETICS FOR PREVENTION OF NAUSEA AND VOMITING CAUSED BY HIGHLY EMETOGENIC CHEMOTHERAPY: A COCHRANE SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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INTRODUCTION

Combining NK1- and 5-HT3-inhibitors plus dexamethasone is effective in preventing CINV in patients receiving highly emetogenic chemotherapy (HEC)

AIM OF THE STUDY

to compare different agent-combinations to rank treatments according to efficacy and safety

METHODOLOGY

- Protocol of this review was previously published in Cochrane Library¹
 - Literature search: Systematic literature search in MEDLINE, CENTRAL, EMBASE, study registries, and conference proceedings (search date 04/2019)
 - Inclusion criteria: RCTs including adult cancer patients receiving HEC
 - Outcomes of interest:
 - complete response (CR) in acute (AP), delayed (DP), and overall phase (OP)
 - complete control of nausea in AP, DP, OP
 - adverse events (AE), on-study mortality (OSM)
 - quality of life (QoL)
 - Quality assessment: Assessed with Cochrane Risk of Bias Tool
 - Data analysis:
 - Random-effects network meta-analysis (NMA) using frequentist graph-theoretical approach
 - Treatment effects: risk ratios (RR) with 95% confidence intervals (CI); RR >1 indicates an advantage for the intervention, if not indicated otherwise
 - P-scores for treatment ranking: ranging from 0 to 1; higher P-score indicates a greater chance of being the best treatment
 - Studies were selected, extracted, and evaluated in duplicate.
- This project was funded by the Federal Ministry of Education and Research, grant number: 01KG1510

RESULTS

- INCLUDED STUDIES:
- 50 studies comprising 23,476 patients and 19 treatment regimens (figure 1)
 - Overall risk of bias: generally low to unclear across studies

- EFFICACY:
- CR:
- Combinations including NK1- and 5-HT3 inhibitors appear to be more effective during AP vs. combinations including only a 5-HT3 inhibitor
 - Aprepitant + palonosetron showed highest efficacy vs. granisetron in DP (RR 1.42 [95% CI: 1.22-1.65]) and OP (RR: 1.51 [95% CI: 1.32-1.74]), cf. figure 2 for all comparisons during DP
- No nausea:
- In AP, ezlopitant + granisetron appears to be most effective (P-Score: 0.94)
 - In DP palonosetron (RR: 1.37 [95% CI: 1.11-1.70]), aprepitant + ondansetron (RR: 1.35 [95% CI: 1.06, 1.71]), and rolapitant + granisetron (RR: 1.26 [1.07, 1.47]) showed a higher efficacy vs. granisetron, respectively
 - In OP, evidence suggests fosaprepitant + palonosetron to be most effective (P-Score: 0.96)

Figure 1: network illustration of the evidence; lines: represents direct comparisons; line widths: number of patients; nodes: treatment

- SAFETY:
- AEs: aprepitant + granisetron showed a slightly lower risk vs. granisetron (RR: 1.10 [95% CI: 1.06-1.14]), cf. figure 3 for all comparisons
 - SAEs, Febrile neutropenia, OSM: evidence suggests no differences between combinations
 - Neutropenia: aprepitant + ondansetron showed a lower risk vs. ondansetron (RR: 2.56 [95% CI: 1.08- 6.07]) and casopitant + ondansetron (RR: 2.84 [95% CI: 1.19- 6.78]), respectively

- QoL:
- Evidence suggests fewer impairments of QoL for rolapitant + ondansetron vs. ondansetron (RR: 1.46 [95% CI: 1.01- 2.10])
 - Evidence suggests no other advantages between combinations

Figure 2: Exemplary NMA forest plot for the outcome CR in DP.

Figure 3: Exemplary NMA forest plot for the outcome AEs.

SUMMARY AND CONCLUSIONS

- This is the first NMA comparing antiemetics for patients receiving HEC
- Aprepitant + palonosetron showed highest CR during DP
- Results may best be confirmed by additional direct comparisons of combinations including NK1- and 5-HT3-inhibitors plus dexamethasone
- Further trials should focus on consistent reporting of safety outcomes and should use a standardized instrument to evaluate QoL to ensure comparability of treatment-combinations

REFERENCES

1: Skoetz N, Haque M, Weigl A, Kuhr K, Monsef I, Becker I, Jordan K. Antiemetics for adults for prevention of nausea and vomiting caused by moderately or highly emetogenic chemotherapy: a network meta-analysis. Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD012775. DOI: 10.1002/14651858.CD012775.