ANTI-SICKNESS MEDICINES FOR CHILDREN HAVING CHEMOTHERAPY

University of York
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Why do they work well for some children and not others?

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BACKGROUND

Despite the availability of effective anti-sickness medicines, an estimated **70% of children undergoing chemotherapy will experience nausea and vomiting** (sometimes called chemotherapy-induced nausea and vomiting (CINV).

Research into ways to prevent CINV is ongoing, with **clinical trials** testing new medicines by comparing them to those already in use. However, we don't fully understand **why anti-sickness medicines work well for some children but not others.**

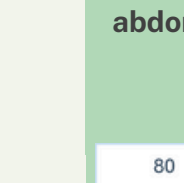
WHAT IS A CLINICAL TRIAL?

Clinical trials are research studies that test new treatments. People are often randomly assigned to receive different treatments, and then their outcomes are compared.

In clinical trials of anti-sickness medicines, outcomes might be feeling or being sick.

METHODS

To explore this more, we combined the findings of clinical trials using a statistical technique called a "**network meta-analysis**", which allows you to compare several medicines at the same time. We focused on anti-sickness medicines that are currently recommended in children **to understand which medicine(s) work best**.



We also included some **adult evidence** to see if this improved our understanding of how well medicines work in children.

Finally, we worked with clinical trial investigators to access their **'raw' data**.
This helped us better explore the **side effects of anti-sickness medicines** and how **children's characteristics and their treatments affect how well the medicines work.**

Throughout, we **worked with children and families,** online and at the Candlelighters centre in Leeds to understand **which outcomes were most important** (so we could focus on these), **what our findings meant to them**, and **how we can best share the findings**.

RESULTS

We found 19 clinical trials of 3523 children.

Patients and families had told us **outcomes**, including **nausea, quality and quantity of sleep, appetite, need for a feeding tube and side effects** (unintended effects) of anti-sickness medicines were **important.**

Clinical trials only consistently reported nausea, vomiting and need for additional (rescue) anti-sickness medication, on the day of chemotherapy (acute CINV) and in the days after (delayed CINV), so these were the outcomes we could focus on.

The following anti-sickness medicines/ combinations of medicines* were compared and are listed **broadly** in terms of how well they prevent nausea and vomiting:

1. Olanzapine + NK1 antagonist (aprepitant/ fosaprepitant) + Ondansetron
2. NK1 antagonists + Ondansetron
3. Palonosetron
4. Ondansetron alone
5. Granisetron
6. Metoclopramide

*These combinations may be given alongside dexamethasone

Including **adult evidence did not improve our understanding** of how well these medicines work in children, and we found differences between children and adults.

We accessed 'raw' data from clinical trials comparing the combinations of the newer anti-sickness medicines of olanzapine and aprepitant.

We found these combinations better prevented nausea and vomiting, but caused more **side effects**, including **constipation, diarrhoea** and **abdominal pain** and **sedation (**Figure 1).

These more effective combinations are currently recommended for children at high risk of CINV, i.e. those on chemotherapy regimens which are very likely to make you sick. However, more research is needed to know whether other children would also benefit from these anti-sickness medicines.

Figure 1. Benefits and side effects of anti-sickness medicine(s)

We also found that **older children may benefit more from these combinations**, whilst characteristics like biological sex did not make a difference.

Not all characteristics of interest were collected, and there was little information on quality of life outcomes.

WHAT DO FINDINGS MEAN TO CHILDREN AND FAMILIES ?

When we shared the results with patients and their families, they told us:

- **Nausea** was often **less well controlled** than vomiting
- **Taking multiple tablets each day** was **difficult** when you felt sick.
- **Anti-sickness medicines** could **make** the **side effects** of other treatments **worse**, particularly constipation.
- Children **modify** the number/ type of **anti-sickness medicines** they take to try **to prevent side effects**.
- **CINV before chemotherapy** and in the **days after** chemotherapy were important.

CONCLUSIONS

How well medicines prevent nausea and vomiting isn't the whole story; whilst taking combinations of anti-sickness medicines might lead to less nausea and vomiting, they could cause **more** (or make worse existing) **side effects**, which are not trivial to patients.

As **older children may benefit more** from taking combinations of anti-sickness medicines, **they may choose this option from their first round of chemotherapy** (depending on which chemotherapy they are receiving).

We are still unsure how well anti-sickness medicines prevent some patient-important outcomes. We will try to encourage those running clinical trials to **focus on the outcomes that matter most** to patients, and consider testing combinations of fewer anti-sickness medicines (including those given intravenously) to see if patients can safely reduce the number of tablets they take each day.

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