Children's Anti-inflammatory REliever (CARE) study

An open-label randomised controlled trial of as-needed budesonide-formoterol vs salbutamol reliever therapy in mild childhood asthma

Rationale

One in seven children in NZ have asthma, accounting for more than 10% of all GP consultations for children, 325,000 asthma-related prescriptions and 3000 hospital admissions annually. Many children only use a short-acting beta$_2$-agonist (SABA) reliever inhaler, such as Ventolin, which provides fast symptom relief, but does not treat the underlying inflammation; this increases their risk of an asthma attack.

Two recent studies in adults found that Symbicort taken as needed was more effective than SABAs at controlling asthma. In particular, Symbicort reduced asthma attacks (including severe asthma attacks requiring the use of oral steroids) by more than half. The 2020 NZ adolescent and adult asthma guidelines were changed in response to these findings, recommending that Symbicort be used instead of SABAs. There have been no similar studies in children; if comparable efficacy of this regimen is shown in childhood asthma, then its implementation would transform international guideline recommendations and has the potential to markedly reduce asthma morbidity globally.

Study design

The CARE study is an investigator-initiated, multi-centre, New-Zealand based, open-label randomised control trial, designed by a team of international asthma experts and paediatricians. We plan to enrol 380 children aged five to 15 years with asthma, only using a SABA inhaler (children who are prescribed a maintenance inhaler (e.g. ICS), but have not used it in the last six months, may still be eligible for this study). Participants will be enrolled for 52 weeks and randomised to receive either:

- Salbutamol pMDI (Ventolin, GlaxoSmithKline) via spacer, two puffs as needed
- Budesonide-formoterol pMDI (Symbicort Rapihaler, AstraZeneca) via spacer, two puffs as needed

The primary outcome is the difference in the rates of asthma attacks between the two treatment arms. Participants will attend five visits during the study, at 13-weekly intervals. Three visits will be conducted at a participating research site (or virtually using video conferencing software) and two via telephone. Visit procedures include performing lung function tests (for those taking part in person) and completing asthma questionnaires.

The CARE study is sponsored by the MRINZ, and funded by the Health Research Council of New Zealand (20/389) and Cure Kids, and the study team includes academic paediatricians from Auckland and London. It is approved by the Northern B Health and Disability Ethics Committee (20/NTB/200) and the Standing Committee on Therapeutic Trials (20/SCOTT/98).

Benefits to participants

- Parent(s)/guardian(s) of participants will be reimbursed $50 per in-person or virtual visit attended. The child will receive a $30 gift card at the third visit.
- Participants will receive regular asthma education, training, and contact from an experienced team of asthma researchers.
- Participants enrolled into research studies tend to have better outcomes.
- Medication is provided free of charge throughout the study.
- There is no obligation to take part and participants can withdraw at any time.

Relevance to General Practices and PHOs

- You will be assisting with world-leading research that could help to reduce asthma burden in children as well as the burden on GPs through reduced visits.
- We will provide you with the child's lung function test results at the end of the study, if done.
- Participants will remain under the care of their usual doctor throughout the study, and should be managed as per normal practice. Participants who require treatment with oral corticosteroids will have their treatment stepped up, in line with the study protocol. This may reduce the burden on GP teams.