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The WHO ACTION-II (Antenatal CorticosTeroids for Improving Outcomes in preterm Newborns) Trial

Current Project Brief

Objectives and Background

A multi-country, multi-centre, two-arm, parallel, double-blind, placebo-controlled, randomized trial of antenatal corticosteroids for women at risk of imminent birth in the late preterm period in hospitals in low-resource countries to improve newborn outcomes

Background and Objectives

An estimated 14·9 million neonates were born preterm in 2010, accounting for 11·1% of live births worldwide, the majority occurring in the late preterm period (34 to <37 weeks). Complications of preterm birth (PTB) are the leading causes of under-5 mortality, and preterm neonates are at increased risk of a range of short- and long-term respiratory, infectious and neurological morbidities. While these risks are substantially higher in infants born at earlier gestations, late preterm infants still experience a significantly higher rate of morbidity and mortality compared to term infants.

Antenatal corticosteroids (ACS) have long been regarded as a cornerstone intervention in preventing neonatal deaths and severe morbidities due to preterm birth. However, there are several important limitations that restrict generalizability of this evidence on ACS use to facilities in low- and middle-income countries (LMICs). There is little efficacy evidence to support or refute the use of ACS in the late preterm period. Furthermore, serious concerns regarding whether ACS are safe and/or effective in low-resource settings have been raised by findings of the recent Antenatal Corticosteroids Trial (ACT).

In 2016, the publication of the Antenatal Late Preterm Steroid (ALPS) trial reported that there is probably benefit to using ACS in the late preterm period to reduce newborn morbidity (particularly respiratory morbidity) with no evidence of harm. However, this trial was conducted in tertiary care facilities in the USA, where there is a high level of care available for preterm infants and their mothers.

There is currently a lack of clarity on clinical benefits of ACS use in the late preterm period, and uncertainty about the potential for harm. While the ALPS trial suggests benefit for late preterm newborns, the generalizability of these reported benefits to lower-resource settings is unclear. The possibility of additional benefit for mortality reduction in settings with high mortality amongst preterm newborns has also not been explored.

The aim of this trial is thus to determine whether antenatal corticosteroids are safe and efficacious for women and newborns in resource-limited settings, when given to women with a live fetus/es at risk of imminent preterm birth from 34 weeks 0 days to 36 weeks 0 days gestation in facilities for the prevention of neonatal mortality, and maternal and newborn severe morbidity outcomes.

Objectives:

1. To compare the effect of dexamethasone to placebo on stillbirth and neonatal death
2. To compare the effect of dexamethasone to placebo on severe neonatal respiratory distress
3. To compare the effect of dexamethasone to placebo on possible maternal bacterial infections

Geographic location	Bangladesh, India, Kenya, Nigeria, Pakistan
Main deliverables	Safety and efficacy of dexamethasone when given to women at imminent risk of late preterm birth, at 34 weeks 0 days to 36 weeks 0 days
Partners	• International Center for Maternal and Newborn Health, Johns Hopkins Bloomberg School of Public Health, USA • Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh • KLE University's Jawaharlal Nehru Medical College, Belgaum, Karnataka, India • Kenyatta National Hospital, Hospital Road,Upper Hill, Nairobi, Kenya • University of Nairobi, Nairobi, Kenya • University of Ibadan, Nigeria • Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria • Aga Khan University, Pakistan • Department of Reproductive Health and Research, WHO • Department of Maternal, Newborn, Child and Adolescent Health, WHO
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