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

Current Project Brief

Objectives and Background

A multi-country, multi-centre, three-arm, parallel group, double-blind, placebo-controlled, randomized trial of two doses of antenatal corticosteroids for women with a high probability of birth in the late preterm period in hospitals in low-resource countries to improve newborn outcomes

Background and Objectives

Every year, an estimated 15 million babies are born preterm, the majority of these births occur in the late preterm period (gestation 34 to <37 weeks). Preterm birth complications are the leading cause of death among children under 5 years of age, responsible for approximately 1 million deaths in 2015. Preterm neonates are at increased risk of a range of short- and long-term respiratory, infectious and neurological morbidities.

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, the optimal dose is unknown with concerns around high steroid peak levels which are likely to mediate unwanted side effects in newborns, while lower more prolonged exposure is responsible for the efficacy and durability of the lung maturation response. 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 as well as the optimal dose in the late preterm period, as well as 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 to assess the benefits and possible harms of two regimens of antenatal corticosteroids, dexamethasone phosphate 4x6mg IM q12h and betamethasone phosphate 4x2mg IM q12h, compared to placebo, when given to pregnant women in the late preterm period (gestation age of 34^{+0} to 36^{+5} weeks) when they are at risk of preterm birth.

Geographic location	Bangladesh, India, Kenya, Nigeria, Pakistan
Main deliverables	Safety and efficacy of dexamethasone (standard dose, 4x6mg 12-hourly) and betamethasone (low dose, 4x2mg 12 hourly) when given to women at imminent risk of late preterm birth, at 34 weeks 0 days to 36 weeks 5 days
Partners	International Center for Maternal and Newborn Health, Johns Hopkins Bloomberg School of Public Health • 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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