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What are we waiting for a large scale clinical testing of human chorionic gonadotropin for the prevention of preterm births?

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Birth before 37th completed gestational week is considered preterm. Preterm births are the leading cause of perinatal morbidity and mortality. The prematurely born babies require intensive medical care during the first several weeks after birth followed by medical interventions to take care of short and long term health problems and the developmental disabilities. In addition, parents go through considerable amount of emotional turmoil. Preterm labor results in preterm birth in approximately 40-50% of the cases. The incidence of preterm births is about 10% in US and higher in third world countries. Despite an extensive basic science and clinical research advances, the incidence of preterm birth has not only remained the same but also may now be on the increase. The current therapies with calcium antagonists, calcium channel blockers and non-steroidal anti-inflammatory drugs can delay birth for about 24-48 hours when corticosteroids are administered to increase the fetal lung maturity. These therapies are invariably associated with maternal and fetal side effects and sometimes even death. The paradigm shift on human chorionic gonadotropin (hCG) actions revealed that it can act on human myometrium. It contains hCG/luteinizing hormone receptors and their activation results in an inhibition of contractions *in vitro* and *in vivo* in animals and in women. These findings are consistent with the notion that hCG promotes myometrial quiescence which is a prerequisite for pregnancy initiation and continuation. The quiescence declines as pregnancy advances which permits myometrial stimulants to dominate so that they can facilitate normal labor progression. The maintenance of myometrial quiescence by hCG suggests that it could be used for suppression of prematurely activated myometrial contractions that are responsible for preterm birth. In fact, hCG has been shown to be effective in preventing preterm birth in a mouse model. Based on these findings, several studies have tested hCG as a treatment in women with preterm labor and as a prophylactic to prevent preterm birth. In women with preterm labor, hCG has been found to be just as effective as magnesium sulfate ($MgSO_4$), a first line therapy with an important difference. That is while $MgSO_4$ had side effects in 100% of the women, hCG had none. In another study, hCG treatment prolonged the gestation by approximately 38 days, without any side effects. In prophylactic use, hCG has been found to be superior to micronized vaginal progesterone therapy. In spite of these advances, there are no large scale multinational clinical trials with hCG. hCG is not expensive and is safe to use. In third world countries where access to medical care in rural areas is minimal to non-existent, inexpensive therapies that have a minimal or no maternal or fetal side effects are easy to adopt. Should hCG be proven useful, it is possible to develop combination therapies to increase the treatment effectiveness and oral and other (nanoparticles) hCG administration strategies. hCG therapy may not turn out to be a panacea, but it is likely to become an important part of an obstetricians tool box to prevent preterm births.

Biography

C V Rao has obtained his PhD from Washington State University in 1969. He did his Postdoctoral work at Albert Einstein College of Medicine and Cornell University Medical College. He has joined University of Louisville School of Medicine in 1972 as an Assistant Professor and became Full Professor with tenure in 1979. In 2008, he moved to Herbert Wertheim College of Medicine, Florida International University, Miami. He has extensively published in peer reviewed journals, trained more than 60 Post-doctoral and clinical fellows, and students, and gave 200 invited presentations in the US and around the world.

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