Cytomegalovirus (CMV) Vaccines: Reinfection and Antigenic Variation

ClinicalTrials.gov Identifier (NCT Number)
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Section 4 - Protocol Synopsis (Study 230183)

4.1. Study Design

4.1.a. Detailed Description

The proposed cognitive-behavioral intervention protocol to modify the risk of exposure and acquisition of HCMV in pregnant women will include a two components. The pilot study will consist of 100 women enrolled from the population of women enrolled in the observational study that will determine the sources of HCMV infection in pregnant women. 100 women will be asked to participate in this substudy to determine uptake of educational materials. We will target women with young children in the household and households with more than 5 inhabitants as these two characteristics have been shown to be associated with virus excretion in pregnant women in this population, and by inference, exposure and acquisition of HCMV during pregnancy in this maternal population.

Women will be counseled at enrollment utilizing both a brief counseling session that will provide basic information about HCMV and congenital HCMV (cCMV) infections, and an individualized behavioral skills session. A take home packet describing the; (i) cCMV infections, (ii) routes of virus acquisition/spread and measures to limit virus spread, and (iii) guidance in behavior modifications to reduce risk of exposures and infection with HCMV will be provided. The behavioral intervention group will also watch a short video detailing basic information about HCMV, the natural history of HCMV infections (sources and routes of transmission), and consequences of maternal infection during pregnancy to the outcomes of pregnancy. Within this video will be explicit and specific descriptions of exposures, such as kissing young children on the mouth, handling objects that have been or could have been in the mouths of young children, and the importance of hygiene after exposure to urine during diaper changing. After viewing the video, a nurse (or health educator) specifically trained to reinforce the information in the video will provide a brief behavioral skills session, and distribute a take home packet containing an information pamphlet. Study participants will receive weekly brief text messages for the initial 12 weeks to deliver reminders of recommended behaviors to limit risks of exposures. Enrollees will be seen during their following prenatal visits and asked to complete a questionnaire that will include a self-assessment of adherence to recommended risk reduction behaviors, understanding of routes of HCMV transmission, and importantly, the burden of introducing recommended risk reduction practices into their daily routines. In addition, we will poll these women on the most effective components of the cognitive-behavioral intervention pilot. A group of 200 women receiving routine, standard of care during pregnancy will be asked to complete the same questionnaire as given to the cognitive-behavioral intervention group in the 3rd trimester of their pregnancy and will serve as controls Data derived from these questionnaires will represent the outcome of this pilot study and will permit us to modify the strategy that will be deployed in a future, larger intervention trial that can test the impact of cognitive-behavioral interventions on the prevalence of congenital cmv infections in this highly CMV seroimmune population.

As part of enrollment in this study, all women will provide permission to screen their newborn infants or any specimens from miscarriages or fetal loss for HCMV infection. Samples of prenatal blood specimens collected as part of routine care will be stored for future use and enrollment saliva swab, vaginal swab, and urine will be obtained and stored for studies of viral load and baseline viral genomic diversity.

4.1.b. Primary Purpose: Other

We are attempting to reduce the risk of exposure and acquisition of HCMV in seroimmune women and to reduce the risk of reinfection and delivery of an infant with congenital HCMV infection.

4.1.c. Interventions

Type	Name	Description
Diagnostic Test	Women Enrolled	Diagnostic Testing will be performed. Results of individual test results will determine the degree of intervention offered.
Diagnostic Test	Newborns of Female Study Participants	Newborns will be tested after birth as soon as possible for CMV positivity.

4.1.d. Study Phase: N/A

Is this an NIH-defined Phase III Clinical Trial? ❍ Yes ● No

4.1.e. Intervention Model: Single Group

4.1.f. Masking ❍ Yes ● No

❑Participant ❑Care Provider ❑Investigator ❑Outcomes Assessor

4.1.g. Allocation: Non-randomized

4.2. Outcome Measures

Type	Name	Time Frame	Brief Description
Primary	efficient uptake of behavioral recommendations and modifications of simple hygiene behaviors	baseline through 10 months	Participants are educated on personal hygiene behaviors which have previously been shown to decrease exposure and acquisition of HCMV. Study visits will included survey for these questions.

4.3. Statistical Design and Power: 4.3_Statistical_Design_and_Power.pdf

4.4. Subject Participation Duration: approx 22 weeks, depending on their enrollment date and delivery date

4.5. Will the study use an FDA-regulated intervention? ❍ Yes ● No

4.5.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.6. Is this an applicable clinical trial under FDAAA? (SEE SECTION 6.6)

4.7. Dissemination Plan: Dissemination_Plan2-19-2018.pdf

Statistical Design and Power

The primary outcome for the proposed study is increased protective behaviors resulting in a decrease in congenital CMV (cCMV) infection. Based on previous data, the cCMV infection rate in the population is 0.6-1.0%. The outcome for the study was designated as the increased awareness and knowledge of CMV risks for CMV acquisition. Although no data existed on women's CMV awareness in Brazil, CMV awareness in Brazilian women was believed to be similar to US women where less than 15% of women have heard of CMV and even fewer are aware of behaviors that might decrease their risk of acquiring CMV infection. Our previous study in the US using this behavioral intervention found that correct knowledge in the intervention group increased from a mean CMV knowledge score of 7.7 (SD, 3.2) to 11.3 (SD, 2.2) on a 16- point scale. Based on the previous data, a sample size of 200 (100 in each group) was viewed to be adequate to determine a 3-point mean difference in pre and post correct CMV knowledge in the study cohort.

All statistical analyses will be included in all participants in the study. Although data on some participants may be missing, all relevant data available from each participant will be used in the analyses. The primary statistical analysis will consist of a simple comparison of binomial proportions. The relative risk and confidence interval will be reported. If the two groups show a difference in cCMV infection rates, knowledge, protective behaviors or risk behaviors, then interactions will be evaluated and subgroup analyses will be conducted to determine whether the effect is found throughout the subgroups of participants. The following factors were considered for subgroup analysis: race and ethnicity, maternal age, and maternal CMV infection. Since many of the data are dichotomous variables, standard statistical methods for rates and proportions was applied. The Wilcoxon rank sum test will be used to compare continuous variables, and survival analysis methodology may be used to compare time-to event variables. Means, standard deviations, and percentages will be collected on the number of intervention sessions attended, the mean length of the intervention session, and implementation fidelity. Descriptive statistics will be calculated for the participant satisfaction about intervention and level of care they received. Intent-to-treat approach will be used for the overall benefits of the intervention. For lost to follow-up, i.e., missing data, we will take into account the type of missing data and use appropriate methods.
For ignorable missing data, we will use multiple imputation method through the SAS MI procedure. For non- ignorable missing data, we will consider selection models and pattern-mixture models. If many participants are lost to follow-up, a sensitivity analysis will be performed including participants lost to follow-up with different assumptions regarding their outcome, to determine whether the results are robust.