Lipopolysaccharide (LPS) Specific Avidity of IgA and IgG antibodies in children given the Vivotif Vaccine and Typhoid patients in Bangladesh

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10th International Conference on Typhoid & Other Salmonelloses
Kampala, Uganda
April 5, 2017
Typhoid vaccine

Two licensed vaccines are commercially available

1. **Parenteral Vi polysaccharide vaccine**
   - Given single dose subcutaneously
   - Recommended for use in person aged over 2 years

2. **Ty21a Live Oral Vaccine (Vivotif)**
   - Requires 3 doses orally
   - Not approved for use in children aged below 5 years
In order to better understand the immune response to the available and new vaccines we are evaluating the following methods:

- Bactericidal assay
- Opsonophagocytosis assay
- T cell responses
- **Antibody Avidity**

In patients with confirmed typhoid fever and in children vaccinated with the Ty21a live oral vaccine
Comparison of bactericidal antibody responses among typhoid fever patients

![Graph showing bactericidal antibody responses among different age groups](image-url)
Opsonophagocytosis in vaccinees and typhoid fever patients.
What is Avidity?

**Affinity**
- strength of interaction between a single epitope and a single paratope

**Avidity**
- a measure of the overall strength of an antibody-antigen complex
Avidity ELISA: The General Perspective

- **Pathogen**
- **Time**
- **Antibody Concentration**

Higher Affinity; Higher Avidity

Lower Affinity; Lower Avidity

Maturation

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During ELISA, treatment with chaotropic agents (like urea or NaSCN) can selectively dissociate the low-avidity antibodies generated early in the course of infection. Such assays can be used as a tool to differentiate between acute and chronic infection.
Avidity measurements in natural infections

- Distinguishing between a newly acquired (primary) and a preexisting (prolonged) infection in:
  - Cytomegalovirus (CMV) infection
  - Rubella Virus Infection
  - Human Immunodeficiency Virus (HIV)
  - *Neospora caninum* infection
  - *Toxoplasma gondii* infection
  - Dengue Virus Infection
  - Cholera and ETEC diarrheal patients

- To elucidate the efficacy of vaccination
The Avidity Index is the percentage of antibodies that remains bound at the antigen coat after the treatment with NaSCN.

\[
A.\ I. = \frac{\text{Optical density of the wells treated with chaotrope agent}}{\text{Optical density of the wells without treatment}} \times 100
\]
Study Participants and specimens

Plasma from the S. Typhi bacteremic patients of three age groups *(young children: 1-5 years; older children: 6-17 years; and adults: 18-59 years)* at day of enrolment (day 1) and then day 7 (day 2) and 21 days later (day 3)

Plasma from the Vivotif vaccinees *(2-5 years)* immediately before the first immunization (day 1) and then 7 (day 2) and 21 days (day3) after the third vaccination
Result

Plasma antibody responses in vaccinees

![Graphs showing plasma antibody titer changes in vaccinees over time for IgA and IgG antibodies.]
Plasma antibody responses in patients

Plasma anti-LPS IgA (ELISA unit)

Plasma anti-LPS IgG (ELISA unit)
LPS-IgA avidity indices in vaccinees

Plasma anti-LPS IgA Avidity Index (%)

- Day 1
- Day 2
- Day 3

P = 0.0001

P = 0.0001
LPS-IgG avidity indices in vaccinees

Plasma anti-LPS IgG Avidity Index (%)

Day 1 Day 2 Day 3

P=0.0058

P=0.0001
LPS-IgA avidity indices in S. Typhi bacteremic patients
LPS-IgG avidity indices in S. Typhi bacteremic patients
Conclusion

The patients mounted LPS-IgA and IgG antibodies with high avidity.

The vaccinees had significant higher antibody avidity after vaccination.

The avidity ELISA can be helpful to evaluate immunogenicity of the upcoming conjugate vaccines.

We plan to analyze other immunological parameters to better understand the functional role of these antibodies.
Acknowledgement

Funding

Sida

icdr,b

NIAID/NIH

GCE Grantee: OPP1015309