SAFETY AND IMMUNOGENICITY OF HAEMOPHILUS INFLUENZAE TYPE B CONJUGATE VACCINE IN COPD

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ABSTRACT

BACKGROUND

To evaluate the safety and immunogenicity of Haemophilus influenzae type B conjugate vaccine in COPD.

MATERIALS AND METHODS

48 stable COPD cases from the admission in to the Pulmonary Medicine Department of Govt. General & Chest Hospital, Hyderabad were given 0.5 mL of conjugated Hib vaccine.

RESULTS

The seroconversion rates: 40 (90.9%) and 44 (100%) at visit-1 (pre-vaccinated) and visit-3 (post-vaccinated) respectively. Seroprotection rates: 18 (40.9%) and 43 (97.7%) at visit-1 (pre-vaccinated) and visit-3 (Post vaccinated) respectively. GMT values: 0.7 micrograms/mL and 2.9 micrograms/mL at visit-1 and visit-3 respectively. More than 4-fold increase in GMT values by visit-3 was observed, P value- 0.00002. 22 (50%) subjects showed 4-fold increase in antibody titre from pre-vaccination to post-vaccination. Four mild adverse events reported. Out of 44 subjects, 4 (9.09%) reported pain and redness at site of vaccination.

CONCLUSION

Hib vaccine is safe and immunologically effective in COPD at the dosage tested by producing 4-fold increases in anti-PrP antibody titres in comparison with baseline titres.

KEYWORDS

Conjugated Vaccine, Seroprotection, Seroconversion.

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BACKGROUND

Haemophilus influenzae is a common Gram-negative human-restricted bacterial pathogen that frequently colonises the nasopharynx in healthy individuals and can cause local infections such as otitis media, sinusitis, pneumonia, or exacerbations of chronic obstructive pulmonary disease (COPD). Exacerbation of COPD will increase the burden on morbidity and mortality and it will have economic burden for the patients especially in developing countries such as India. Exacerbated COPD is usually associated with increased airway and systemic inflammation that causes the physiological changes which leads to the development of hyperinflation. The exacerbated COPD is usually triggered by virus and bacterial infection of lower respiratory tract, in response some patients develop exacerbated COPD. Drugs like long acting beta 2 agonist and long acting steroids or their combination may be effective in control of exacerbated COPD. Pulmonary rehabilitation, self-management and house ventilator support have got their own importance in the management of exacerbated COPD, but it requires further controlled trials.

The results of exacerbated COPD depends upon the optimum use of the combination of both pharmacological and non-pharmacological drugs and it will increase the health status and decrease the hospital admission and mortality of COPD.

In the recent past, epidemiology and clinical manifestations of H. influenzae infection underwent major changes. The use of vaccines almost eradicated the H. influenzae infection in developed countries where vaccines are used routinely. Higher rates of infection were observed in pre-vaccinated era and in developing countries like India where vaccination is not used regularly. These vaccines have got both genetic and acquired components in protecting immune response.

When the bacteria breach the epithelial barriers, they are able to cause invasive disease, including meningitis, sepsis, and epiglottitis.^{1,2} Most invasive infections are caused by encapsulated strains, in particular H. influenzae type B (Hib), characterised by a polyribosylribitol phosphate (PrP) capsule, which is an important virulence factor. In immune individuals, circulating anti-PrP antibodies effectively protect against the disease by activating the classical complement pathway, as well as opsonising bacteria for phagocytosis.³ In the present study, safety and efficacy of Hib vaccine has been studied.

AIM OF THE STUDY

Evaluating the immunogenicity and safety of Haemophilus influenzae type-B conjugate vaccine (Hib) in stable COPD patients.

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MATERIALS AND METHODS

Setting

650-bed tertiary referral hospital.

Study Design

Randomised, open label, prospective clinical study.

Subjects

48 stable COPD patients attending the outpatient department during the period of May to September 2015

- No. of subjects enrolled-48.
- No. of subjects who completed study-44.
- No. of subjects who discontinued study-4.

Inclusion Criteria

Written Consent

1. Stable COPD patients (mild-to-moderate) of either sex between 30-64 yrs. at the time of consent.
2. Spirometry values- FEV1% predicted 30-80%, FEV1/FVC<70% predicted without bronchodilator.
3. Non-pregnant and non-lactating females.
4. Not participating in any clinical trials.
5. Normal body temperature.
6. Not on immunosuppressive therapy.
7. No serious (life threatening) comorbid conditions.

Exclusion Criteria

1. H/O Asthma, allergic rhinitis, atopy.
2. On screening, increase in FEV1 more than or equal to 12% of the pre-dose value after inhalation of salbutamol 400 micrograms.
3. Subjects with any contagious disease.
4. Any history of allergic disease likely to be precipitated by any component of the vaccine.

Composition and Dosage

Each single dose of 0.5 mL contains lyophilised preparation of H. influenzae type-B capsular polysaccharide (PrP)-10 micrograms (Conjugated to 20 micrograms of inactivated tetanus toxoid). 0.5 mL single dose deep IM over deltoid.

Criteria for Evaluation

Proportion of subjects- seroconverted (>0.15 micrograms/mL), seroprotected (>1 microgram/mL) and attained 4-fold raise in anti-PrP antibody titre level at 28th day.

Proportion of subjects showing untoward medical occurrences, all episodes of abnormal finding (including laboratory values) & subjective and objective symptoms of disease during the study.

Study Protocol

Clinical features and physical examination Investigations.

CBP, RBS, LFT, CUE, RFT.

Sputum for AFB, CXR PA view, PFT and anti-PrP antibody assay (ELISA).

RESULTS

The seroconversion rates - 40(90.9%) and 44(100%) at visit-1 (pre-vaccinated) and visit-3(post-vaccinated) respectively.

Seroconversion

Seroprotection rates-18(40.9%) and 43(97.7%) at visit-1 (pre-vaccinated) and visit-3 (post-vaccinated) respectively. The P value <0.0001.

Seroprotection

GMT values 0.7 micrograms/mL and 2.9 micrograms/mL at visit-1 and visit-3 respectively. More than 4-fold increase in GMT values by visit-3 was observed, P value- 0.00002.

22 (50%) subjects showed 4-fold increase in antibody titre from pre-vaccination to post-vaccination.

Four mild adverse events reported. Out of 44 subjects, 4 (9.09%) reported pain and redness at site of vaccination.

No serious adverse events reported during study period.

DISCUSSION

In 97% of healthy unvaccinated adults, circulating IgG antibodies against Hib capsular polysaccharide were above the level ensuring longterm protection against invasive Hib disease, i.e. 0.15 µg/mL (3); Moreover, 56% of healthy individuals had antibody levels of ≥1 µg/mL, a correlate of protection in the vaccinated population⁴, which is similar to the present study. These data suggest that the general adult population is well protected against invasive Hib disease, which is indeed extremely rare in healthy adults.⁵ Because none of the subjects had been vaccinated against Hib, natural anti-Hib antibodies may have been induced by exposure to some common environmental bacteria that carry antigens cross-reacting with PrP such as Escherichia coli K 100.⁶

In compliance with earlier studies, we considered serum IgG anti-PrP levels the major indicator of protection against Hib invasive disease.⁷ A similar discordance between anti-capsular IgG levels and their functional activity had previously been documented in response to vaccination against Hib and Neisseria meningitidis serogroup C.^{8,9}

In the present study, we did not see a correlation between anti-PrP IgG levels and serum bactericidal activity.

Our study correlates with the recent data on emerging invasive Hib disease in unimmunised adults, provide a rationale for extended indications for immunisation of vulnerable groups of adults against Hib.^{10,11}

It was found that the major cause of exacerbated COPD is the infection which contributes 50%. Heart failure contributes nearly 20% - 25% of exacerbated COPD. Approximately, 30% of exacerbated COPD will not have proved aetiology. Environmental pollution like sulphur dioxide (SO₂), ozone (O₃) and nitrogen dioxide (NO₂) are also contributing in producing exacerbated COPD, outdoor and indoor pollution also impact in developing exacerbated COPD. In India, especially in rural areas, the burning of animal dung also is a common factor for exacerbated COPD. Firewood for cooking purpose in certain parts of country and use of pesticides in agriculture are also contributing for the exacerbated COPD.

CONCLUSIONS

There was significant evidence in the aetiology and pathogenesis of Exacerbated COPD. It was concluded that the airway inflammation is the main reason for the Exacerbated COPD which leads to Exacerbated COPD. It was found that the main causes for the Exacerbated COPD are bacterial, viral and environmental factors. The mortality increases with each episode of Exacerbated COPD, hence importance should be given to treatment and prevention of exacerbated COPD. But still further control trials are needed to manage Exacerbated COPD to the expected level.

Hib vaccine is both safe and immunologically effective in COPD at the dosage tested by producing 4-fold increases in anti-PrP antibody titres in comparison with baseline titres.

Further authentic and long term trials are required to confirm our results and the effectiveness of Hib vaccine in COPD patients.

Frequency of administration and combination with other vaccines (Pneumovax) has to be evaluated.

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