IMPROVING EFFICIENCY USING A FULLY LIQUID COMBINATION VACCINE: EVIDENCE FROM A TIME-MOTION STUDY IN INDIA

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ABSTRACT

BACKGROUND AND AIMS

Immunization is essential to achieve the Millennium Development Goal of reducing child mortality. Fully liquid combination vaccines have been developed to rationalize vaccine delivery and to simplify supply and administration of vaccines. A study was carried out to understand the implications of a fully liquid pentavalent DTwP-HepB-Hib vaccine in terms of resource requirements, efficiency, and impact on vaccination programs.

METHODS

A time-motion study was conducted at the Institute of Child Health (ICH) in Calcutta, India. The study compared a single fully liquid DTwP-HepB-Hib vaccine *vs* a lyophilized vaccine with two vials requiring reconstitution. Three hundred and twelve children were vaccinated over 6 weeks in 2006. An economic analysis was done to estimate potential time and cost savings.

RESULTS

Study results indicated significant time savings for vaccine preparation and total vaccine consultation for the fully liquid vaccine of 52% and 23% ($P<0.05$) compared with the lyophilized vaccine. At current vaccine load time savings at ICH would be between 15 and 25 working days per year. Package volume is less for a fully liquid vaccine, leading to potential cost savings for storage and distribution. Extrapolated to India, these savings could be up to US$55.5 million per year. Delivery time savings could be around 107,000 working days per year.

CONCLUSIONS

The fully liquid DTwP-HepB-Hib combination vaccine offers important time gains for vaccine delivery and savings for storage and distribution costs compared with a vaccine requiring reconstitution. Fully liquid combination vaccines might contribute to better resource management and ultimately improve efficiency of immunization programs.

FUNDING

Novartis Vaccines and Berna Biotech.

BACKGROUND

- The WHO Expanded Program on Immunization (EPI) is one of the most effective public health initiatives worldwide.
- To achieve the Millennium Development Goal of reducing child mortality, the expanded use of childhood vaccines will be necessary.
- Providing the poorest countries of the world with appropriate vaccines to meet the WHO objectives of eradicating vaccine-preventable diseases remains a challenge.
- Combination vaccines enable the introduction of new vaccines into immunization programs without additional visits to the healthcare provider.
- Fully liquid vaccines could rationalize delivery by simplifying administration and supply:
  - reduce the potential for handling errors and facilitate training
  - simplify transport and storage, and reach children in remote areas.
- A fully liquid pentavalent diphtheria-tetanus-whole cell pertussis-hepatitis B-*Haemophilus influenzae* type b (DTwP-HepB-Hib) combined vaccine was developed to improve vaccine delivery and safety.
- Study objective: to understand time and logistical implications of delivering a fully liquid vaccine *vs* a lyophilized vaccine requiring reconstitution in an actual program setting in terms of resource requirements, efficiency, and impact on vaccination programs.

METHODS

- Principal investigator and study management: Swiss Tropical Institute, mandated by Novartis Vaccines.
- Observational, comparative time-motion study at the Institute of Child Health (ICH) in Calcutta, India.
- Ethical approval by the Ethics Committee of Basel, Switzerland and the ICH, Calcutta, India.
- Comparison of administration and logistic implications for a single vial and fully liquid DTwP-HepB-Hib vaccine and a lyophilized vaccine with two vials requiring reconstitution (Figure 1).

FIGURE 1. PREPARATION STEPS REQUIRED FOR FULLY LIQUID *VS* LYOPHILIZED VACCINE

- Selection criteria for participants: standard clinical considerations.
- Public campaign (TV, radio, newspapers, flyers, and community mobilization) to increase vaccination clinic attendance.
- Free complete vaccination schedule for DTwP, HepB, Hib, and polio for parents/guardians of eligible children.
- Observation, timing and recording of every vaccination step: obtain, prepare, administer, dispose, document vaccine delivery, overall visit duration.
- Standardized questionnaires for key vaccination staff (EPI manager, stock manager, nurses, and doctors).
- Economic analysis to estimate potential time and cost savings, assuming use of fully liquid DTwP-HepB-Hib combination vaccine only.

RESULTS

- Three hundred and twelve children were vaccinated with the fully liquid vaccine (n=159) or the lyophilized vaccine (n=153) over 6 weeks in 2006.

TIME SAVINGS

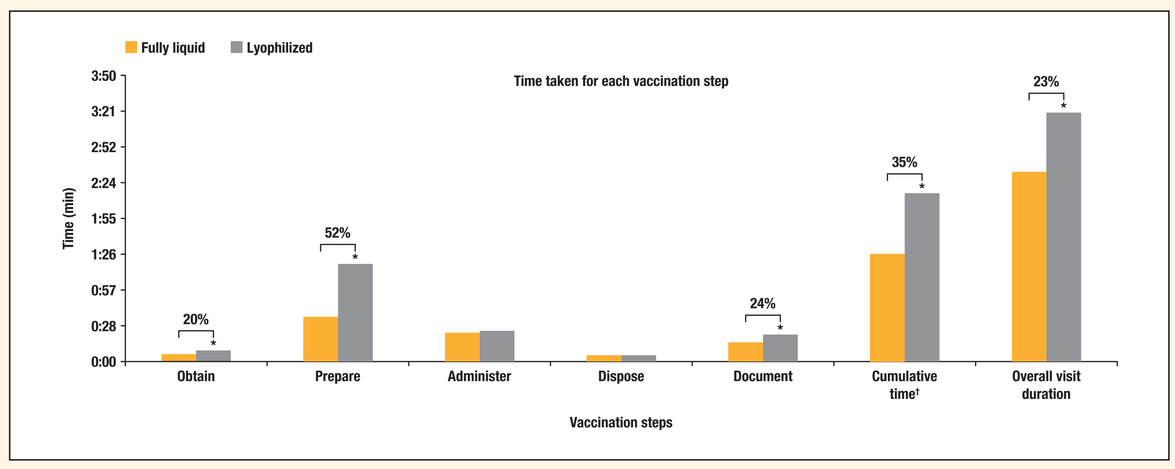
- Important time savings for the fully liquid vaccine compared with the lyophilized vaccine (Table 1, Figures 2 and 3):
  - for vaccine preparation and documentation and overall visit duration, time savings for the fully liquid vaccine were 52%, 24%, and 23%, respectively
  - statistically significant results ($P<0.05$) for obtaining, preparing, and documenting of vaccination, as well as for cumulative and overall visit time.

TABLE 1. TIME SAVINGS BETWEEN VACCINES

Step	Lyophilized		Fully liquid		Time difference (seconds)	Time savings	P value
	n	Mean†	n	Mean†			
Obtain	153	00:06:38	159	00:05:10	00:01:28	20.07%	P<0.05
Prepare vaccine	153	01:15:24	159	00:36:00	00:39:24	52.15%	P<0.05
Administer	153	00:23:36	159	00:23:20	00:00:16	0.69%	n/s
Dispose	153	00:05:45	159	00:05:40	00:00:05	0.92%	n/s
Document	153	00:20:25	159	00:15:35	00:04:90	24.20%	P<0.05
Cumulative time	153	02:11:08	159	01:25:05	00:46:03	35.12%	P<0.05
Overall visit duration	153	03:17:00	159	02:32:00	00:45:00	22.84%	P<0.05

†Time classification (min: sec: hundredth of sec)

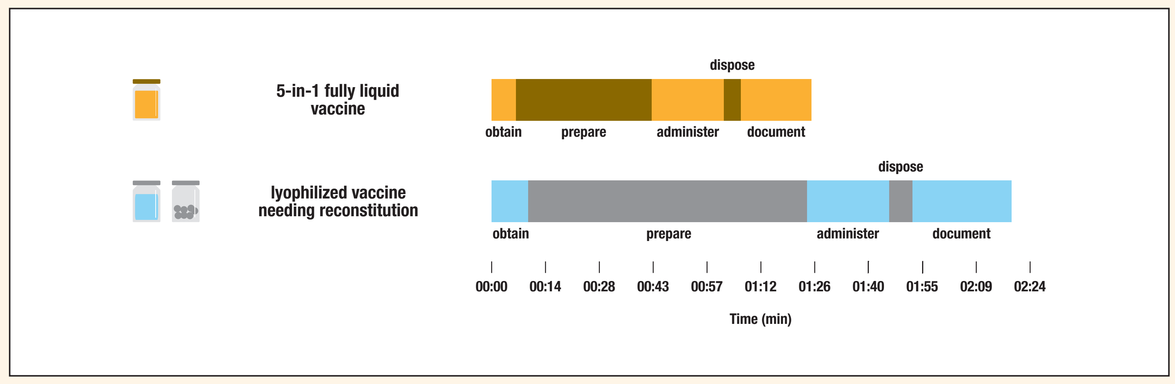
FIGURE 2. TIME DIFFERENCE BETWEEN VACCINES BY VACCINATION STEP AND OVERALL VISIT DURATION



*$P<0.05$ *vs* lyophilized vaccine; percentage values indicate time saved

†Total time taken to obtain, prepare, administer, dispose, and document

FIGURE 3. MEAN CUMULATIVE TIMES



POTENTIAL ECONOMIC BENEFITS

- Delivery time savings at facility level with fully liquid vaccine, estimation for ICH:
  - 15 to 25 working days/year
  - *Assumptions: current vaccination workload at the ICH of 30-50 children/day, 5 days/week, 48 weeks/year.*
- Delivery time savings with fully liquid vaccine at national level, extrapolated to India:
  - Around 107,000 working days/year
  - *Assumptions: 27.5 million live births/year, 6.8% mortality rate, 6 hours/working day, DTP3 coverage 64%.*
- Cost savings over whole supply chain with fully liquid vaccine at national level, extrapolated to India:
  - Cost savings with the fully liquid vaccine up to US$55.5 million per year
  - *Assumptions: packed volume 79% less, DTP3 coverage 64%, wastage rate 10%.*

QUESTIONNAIRE

Staff perceptions

- Vaccine handling was described as easier and more convenient, and two-thirds less space was required for the fully liquid vaccine:
  - Convenience: *'Fully liquid vaccine easier to handle and prepare…'*
  - Syringe aspiration: *'Some dissolution and withdrawing problems with lyophilized vaccine…'*
  - Time: *'Savings with fully liquid vaccine…'*
  - Space: *'Less storage and preparation space needed for fully liquid vaccine…'*

CONCLUSIONS

- **The fully liquid DTwP-HepB-Hib combination vaccine offers important time gains for vaccine delivery, and considerable savings for storage and distribution costs compared with a vaccine requiring reconstitution.**
- **Fully liquid combination vaccine might contribute to:**
  - **rationalization and simplification of vaccine logistics and delivery**
  - **strengthening immunization programs**
  - **better resource management**
  - **economic savings in countries with limited resources**
  - **potential human resource savings in countries with healthcare worker shortage**
  - **improving efficiency of immunization programs.**

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