

Immunogenicity of the Brazilian Recombinant Hepatitis B Vaccine in Adults

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Background

- Safe and immunogenic recombinant vaccines against Hepatitis B available since late 80ies.
- Instituto Butantan, a São Paulo's State public vaccines manufacturer developed its recombinant hepatitis B vaccine, Butang.

Background

Previous phase III trial in adults:

	Age group	Butang	Engerix B
n	20 – 30	280	288
	31 – 40	198	198
% Sero protection	20 – 30	91.8	95.5
	31 – 40	79.8	92.4
GMT	20 – 30	453.5	1369.0
	31 – 40	122.7	686.2

Martins RM et al, Multicenter study on the immunogenicity and safety of two recombinant vaccines against hepatitis B, 2004 Mem Inst Oswaldo Cruz 99:865-71

Background

- Instituto Butantan introduced a change in the HBsAg concentration of the vaccine, from 20 to 25 μ g/ml.
- The present study evaluated Butang's safety and immunogenicity among adults from 31 to 40 years of age, after the antigen concentration change.

Methods

- A randomized, double blind, controlled phase III trial was undertaken.
- Experimental group received three 1 ml doses (0, 30 and 180 days) of Butang and the control group of the reference vaccine, Engerix B ® (GSK Biologicals), in the same dose and schedule.
- Three blood samples were collected for serological tests, the first at recruitment, the second before the third vaccine dose, and the third 30 days later.
- Volunteers, servicemen from the City of São Paulo civilian guard, were randomly assigned to one of the groups.

Methods

- Adverse events were monitored by telephone calls during a 5-day period after each vaccine dose.
- Study's objectives and procedures were presented in meetings with the target population. The ones who presented interest in participation were individually interviewed. Once the willingness to participate was confirmed, the Informed Consent Form was discussed and signed by volunteers and study's staff representatives.

Methods

- HBsAg serologic assays were carried out using the commercially available automatic assay Access® AbHBsII, Beckman Coulter.
- Seroprotection was defined as HBs antibody titers equal or above 10 mUI/ml. Mean, median and GM were calculated.
- Titers were classified as negative (< 10 mUI/ml; weak positive response (between 10 and 100 mUI/ml) and strong positive response (above 100 mUI/ml).

Results

- A total of 564 volunteers were randomized. Baseline characteristics were similar in both groups.
- 419 (74.3%) completed the follow up, 216 in the experimental group and 203 in the control group ($p > 0.05$).
- Analysis per protocol was carried out in the present study.

Results

Safety profile

Frequency of adverse reactions after vaccine dose

Dose	Butang	Engerix
1 st	28.3 %	31.0 %
2 nd	19.4 %	16.4 %
3 rd	17.8 %*	10.5 %

* > 0.05

Results

Safety profile

- The majority of reported adverse reactions were local reactions: local pain, swelling, redness. Frequency of fever was reported by 4 volunteers after 1st dose (3 Butang and 1 Engerix B); 4 after second dose (2/2) and none after the third dose.
- No serious systemic adverse events were registered.

Results

Immunogenicity

	Butang	Engerix B
n	216	203
% sero protection	98.6 (213/216)	95.6 (194/203)
GMT	12557	11673

Of the seroprotected, 95.4% of the experimental (206/216) and 84.7% of the control group presented a strong response (titers above 100 mUI/ml).

Distribution according to Anti-HBs response categories

Anti-HBs response categories	Vaccine	
	Butang	Engerix
Strong (> 100 mUI/ml)	95.4% (206/216)	84.7% (172/203)
Weak (10 – 100 mUI/ml)	2.2% (7/216)	10.8 (22/203)
Negative	1.4% (3/216)	4.4% (9/203)

Discussion

- No serious adverse events after vaccination were observed.
- Both vaccines presented high immunogenicity, with a high proportion of strong serologic response, as well as high antibody titers.
- Results favor the hypothesis of equivalence of the two vaccines, in respect to immunogenicity and reactogenicity.

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Thank you

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