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DTP with or after measles vaccination is associated with increased in-hospital mortality in Guinea-Bissau

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Abstract

Background: The sequence of routine immunisations may be important for childhood mortality. Three doses of diphtheria–tetanus–pertussis vaccine (DTP) should be given at 6, 10, and 14 weeks and measles vaccine (MV) at 9 months of age. The sequence is not always respected. We examined in-hospital mortality of children having received DTP with or after measles vaccine.
Setting: The only paediatric ward in Bissau, Guinea-Bissau.
Participants: Children hospitalised during two periods in 1990–1996 and 2001–2002 who had received MV prior to hospitalisation.
Main outcome measure: The all-cause case fatality at the hospital for children aged 6–17 months.
Result: The case fatality was increased for children who had received DTP with or after measles vaccine compared with children who had received measles vaccine as the most recent vaccine, the ratio being 2.53 (1.37–4.67) and 1.77 (0.92–3.41) in the two periods, respectively. The combined estimate was 2.10 (1.34–3.28). These results were not explained by differences in nutritional status, number of doses of DTP or discharge policy.
Conclusion: Administration of DTP with, or after MV, may reduce the beneficial effect of MV.

Keywords: DTP; Hospital mortality; Measles vaccine; Non-targeted effects of vaccination; Simultaneous administration

1. Introduction

It is recommended that three doses of diphtheria–tetanus–pertussis (DTP) be given at 6, 10, and 14 weeks of age well before measles vaccine (MV) administered at 9 months of age. There are numerous reasons that vaccinations might be delayed in low-income countries; the child was sick, the mother had no money to pay for the vaccination card, the mother and child travelled, vaccine or syringes were not available, or the nurse took part in training or campaign activities. As a consequence many children receive DTP simultaneously with MV or even after MV.

Previous studies have suggested that the sequence of vaccinations may be important. The markedly increased female mortality after high-titre measles vaccine (HTMV) was probably not due to HTMV *per se* but to DTP and inactivated polio vaccine (IPV) administered after MV [1]. African and Asian community studies have also reported that the mortality was increased for children who had received DTP and MV simultaneously [2–5]. We examined whether DTP administered with or after measles vaccination had an impact on paediatric hospital mortality.

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2. Subjects and methods

The Department of Paediatrics at the National Hospital Simão Mendes in the capital of Guinea-Bissau is the only paediatric ward in the country. We have previously examined the impact of vaccinations in two studies from this ward [6,7]. We used these two studies to assess the impact of having received DTP with or after MV compared with children who had received MV after DTP as recommended. There have been two trials of two-dose measles vaccination in the study area in which some children received MV at 6 months of age [8,9]. Since most children in Bissau receive a booster dose of DTP and OPV at 18 months of age, we included only children aged 6–17 months in the analysis.

2.1. Study 1

Between 1990 and 1996, a project assistant reviewed the admission book of the paediatric ward daily for all children coming from the study area of the Bandim Health Project (BHP). Information on vaccination status was available from the routine 3-monthly child surveillance system in the study area. Between 1994 and 1996, we also collected information on immunisation at admission [6]. As presented previously [6], a total of 474 hospitalised children aged 6–17 months had a measles vaccination documented. Since all children in this study came from the project area, it was possible to examine mortality after discharge from the hospital. In the present analysis, we also assessed mortality within 30 days of discharge from the ward.

2.2. Study 2

From May 2001 to April 2002, all children admitted at the hospital had their vaccination card examined by a nurse visiting all beds at the ward daily [7]. Children from the whole city were included in this study. Since the children came from all over Bissau, we could not identify those who died after discharge.

3. Results

In the first study, children having received DTP with or after MV constituted 13% (63/474) of the patients aged 6–17 months who had received MV. The children who received DTP with or after MV had a case fatality ratio (CFR) of 2.53 (1.37–4.67) compared with children having received MV as the last vaccination (Table 1). The CFR was essentially the same for children having received DTP simultaneously with MV (CFR = 2.87 (1.29–6.23)) or after MV (CFR = 2.27 (1.02–5.07)). In the month preceding hospitalisation, the arm-circumference measured in the community did not differ for measles vaccinated and measles-unvaccinated children [6], and among measles vaccinated children it did not differ according to the sequence of vaccinations (data not shown). Control for number of doses of DTP made no difference (CFR = 2.58 (1.21–5.48)). Mortality was similar for children who had received one to two doses of DTP and those who had received the three recommended doses of DTP (CFR (one to two doses/three doses) = 1.11 (0.46–2.70)). Control for year of hospitalisation and season had no impact on the difference between out-of-sequence and recommended vaccinations. When deaths occurring at home within 1 month of discharge were included in the analysis, the CFR was 2.48 (1.45–4.21).

In the second study covering children from the whole of Bissau city (Table 1), 33% (101/305) of the children had received DTP and MV out of sequence. The children with DTP with or after MV tended also to have higher mortality than children having received MV as the last vaccine, the CFR being 1.77 (0.92–3.41). The CFR was 1.54 (0.70–3.41) for children receiving DTP and MV simultaneously and 2.15 (0.95–4.84) for DTP after MV. Weight-for-age measured at admission was similar for children who had received MV after DTP and those having received DTP with or after MV (data not shown). The case fatality was not related to number of doses of DTP before admission (CFR (one to two doses/three doses) = 1.30 (0.59–2.85)). We could not identify who died after hospitalisation since the children came from all of Bissau. Absconding children have a con-

Table 1
Hospital case fatality and case fatality ratios (CFR) according to age and the sequence of DTP and measles vaccines

Age group	Case fatality (deaths/children hospitalised)					
	Study 1: Bandim and Belem, 1990–1996 (6)			Study 2: Bissau City, 2001–2002 (7)		
	DTP ≥ MV[a]	DTP < MV[b]	CFR (95%CI)	DTP ≥ MV[a]	DTP < MV[b]	CFR (95%CI)
6–11 months	20% (4/20)	8% (12/157)	2.62 (0.93–7.34)	12% (4/33)	8% (6/74)	1.49 (0.45–4.95)
12–17 months	19% (8/43)	7% (19/254)	2.49 (1.16–5.32)	16% (11/68)	8% (11/130)	1.91 (0.87–4.18)
Total	19% (12/63)	8% (31/411)	2.53 (1.37–4.67)	15% (15/101)	8% (17/204)	1.77 (0.92–3.41)
Including deaths within 1 month of discharge						
Total	24% (15/62[c])	10% (39/399[c])	2.48 (1.45–4.21)			

Bissau 1990–96 and 2001–2002.
[a] DTP simultaneously with or after MV.
[b] DTP before MV.
[c] Numbers at risk is slightly lower in this analysis because some of the children were hospitalised several times within the same month.