Vaccines Safety in Children and in General Population: A Pharmacovigilance Study on Adverse Events Following Anti-Infective Vaccination in Italy

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Introduction: The concern for adverse events following immunization (AEFI) and anti-vaccination movements that lacked scientific evidence-based supports may reduce vaccine uptake in the general population. Thus, the aims of the present study were to characterize AEFI in general population (all age groups), in terms of frequency, preventability and seriousness, and to define predictors of their seriousness in children.

Material and Methods: A retrospective study was performed on suspected AEFI reports for children and adults who received any form of vaccinations, collected in Tuscany, Italy, between 1 January and 31 December 2017. Patients' characteristics, suspected vaccines, and AEFI description were collected. Causality and preventability were assessed using WHO and Schumock and Thornton algorithms, respectively. Logistic regression was used to estimate the reporting odds ratios of potential predictors of AEFI seriousness in children.

Table 1 - Characteristics of all AEFI reports (top) and each AEFI (bottom) in general population.

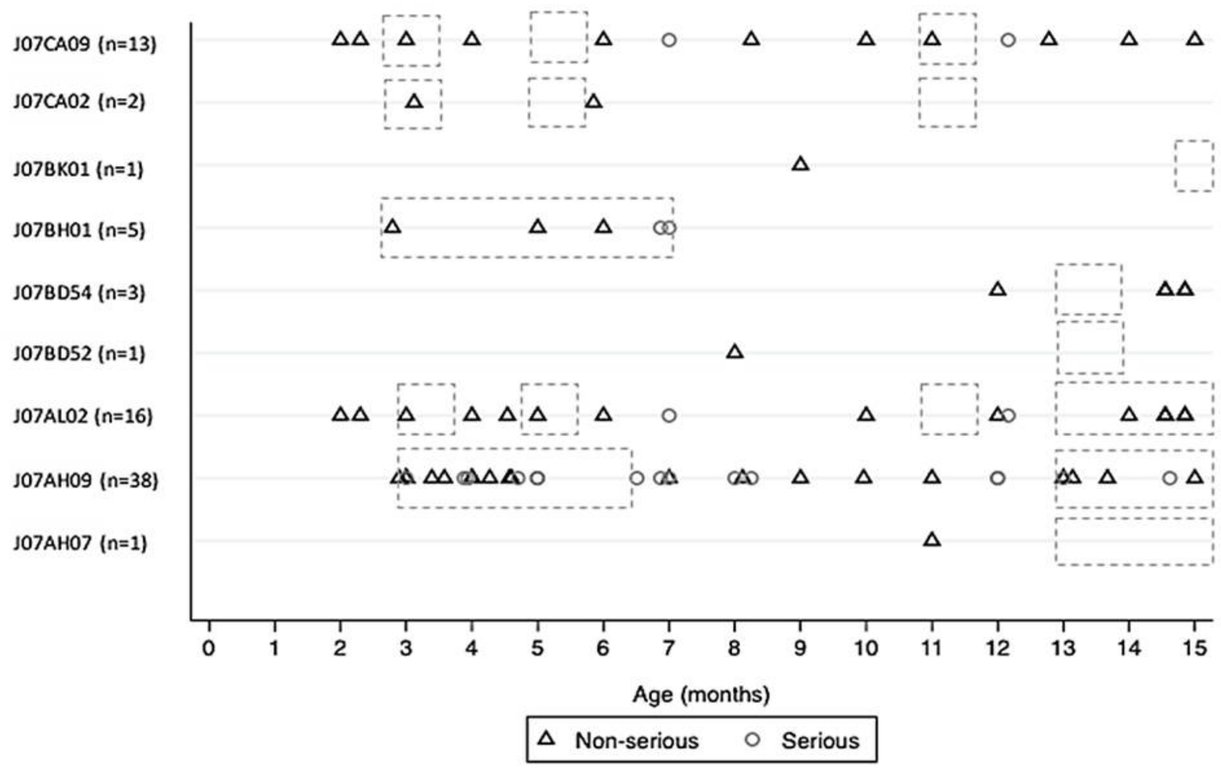
	Tot reports n=223 (%)	Non-serious n=171 (%)	Serious n=52 (%)	p-value
N AEFI for each report				
1	76 (34.08)	57 (33.33)	19 (36.54)	*0.503*
2	43 (19.28)	35 (20.47)	8 (15.38)	
3	49 (21.97)	40 (23.39)	9 (17.31)	
4+	55 (24.66)	39 (22.81)	16 (30.77)	
Age, years (overall)				
Median (IQR)	9.24 (1.14 – 42.17)	9.95 (1.24 – 44.25)	2.26 (0.84 – 22.28)	*0.091*
Pediatric age groups (FDA classification)				
Newborns (<1 month)	0	0	0	
Infants (1 month-2 years)	57 (25.56)	40 (23.39)	17 (32.69)	
Children (2-12 years)	73 (32.74)	56 (32.75)	17 (32.69)	
Adolescents (12-18 years)	12 (5.38)	8 (4.68)	4 (7.69)	
Adults (quartiles of age)				*0.664*
19-39 years	20 (8.97)	16 (9.36)	4 (7.69)	
40-49 years	21 (9.42)	18 (10.53)	3 (5.77)	
50-59 years	15 (6.73)	13 (7.60)	2 (3.85)	
Over 60 years	25 (11.21)	20 (11.70)	5 (9.62)	
Sex				
Female	102 (45.74)	84 (49.12)	18 (34.62)	***0.036***
Male	114 (51.12)	80 (46.78)	34 (65.38)	
Missing	7 (3.14)	7 (4.09)	0	
Ethnic group				
Caucasian	137 (61.43)	106 (61.99)	31 (59.62)	*0.880*
Others	14 (6.28)	10 (5.85)	4 (7.69)	
Missing	72 (32.29)	55 (32.16)	17 (32.69)	
Causality				
Consistent	153 (68.61)	129 (75.44)	24 (46.15)	***<0.001***
Inconsistent	24 (10.76)	7 (4.09)	17 (32.69)	
Indeterminate	44 (19.73)	33 (19.30)	11 (21.15)	
Unclassifiable	2 (0.90)	2 (1.17)	0	
Preventability				
No	207 (92.80)	162 (94.74)	45 (86.53)	***0.016***
Yes	16 (7.20)	9 (5.26)	7 (13.47)	
	Tot AEFI n=570	**Non-serious n=431**	**Serious n=139**	**p-value**
Number of suspect drug for each AEFI				
1	489 (85.79)	379 (87.94)	110 (79.14)	***0.002***
2	74 (12.98)	45 (10.44)	29 (20.86)	
3	7 (1.23)	7 (1.62)	0	
Concomitant drugs (not suspected)				
0	502 (88.07)	383 (88.86)	119 (85.61)	***0.023***
1	35 (6.14)	22 (5.10)	13 (9.35)	
2	23 (4.04)	21 (4.87)	2 (1.44)	
3	9 (1.58)	5 (1.16)	4 (2.88)	
4	1 (0.18)	0	1 (0.72)	
Tot strains/toxoids				
Median (IQR)	4 (4-7)	4 (3-7)	4 (4-6)	*0.815*
1	51 (8.95)	36 (8.35)	15 (10.79)	*0.940*
2-5	364 (63.86)	277 (64.27)	87 (62.59)	
6-9	53 (9.30)	40 (9.28)	13 (9.35)	
10-13	26 (4.56)	20 (4.64)	6 (4.32)	
14+	76 (13.33)	58 (13.46)	18 (12.95)	
Presence of allergens (in traces)				
Yes	222 (38.95)	180 (41.76)	42 (30.22)	***0.015***
No	348 (61.05)	251 (58.24)	97 (69.78)	
Seriousness (out of 139)				
Death	0	-	0	-
Persistent or significant disability/incapacity	8 (5.76)	-	8 (5.76)	
Congenital abnormalities/birth defects	0	-	0	
Hospitalization or prolongation	83 (59.71)	-	83 (59.71)	
Life-threatening condition	0	-	0	
Other clinically relevant conditions	48 (34.53)	-	48 (34.53)	
Outcome				
Complete resolution	247 (43.33)	184 (42.69)	63 (45.32)	***<0.001***
Improvement	119 (20.88)	98 (22.74)	21 (15.11)	
Still unresolved[#]	78 (13.68)	50 (11.60)	28 (20.14)	
Resolution with sequelae	5 (0.88)	5 (1.16)	0	
Unchanged/worsened reaction	2 (0.35)	2 (0.46)	0	
Death	5 (0.88)	0	5 (3.60)	
Missing°	114 (20.00)	92 (21.35)	22 (15.83)	
Interactions (DDIs + VDIs + VVIs)				
Not applicable (1 treatment)	450 (78.95)	346 (80.28)	104 (74.82)	***0.032***
No	106 (18.60)	78 (18.10)	28 (20.14)	
Mild	0	0	0	
Moderate	2 (0.35)	2 (0.46)	0	
Severe	12 (2.11)	5 (1.16)	7 (5.04)	

Table 2 - Association between serious AEFI risk and different factors expressed as Reporting Odds Ratio (ROR) within pediatric population stratified according to the age classes of the National Vaccination Plan 2017–2019

	0-15 months		16 months-12 years		12 -18 years	
	Adjusted ROR (95% CI)	p-value	Adjusted ROR (95% CI)	p-value	Adjusted ROR (95% CI)	p-value
Sex						
Female	Ref.					
Male	1.26 (0.48 – 3.27)	*0.639*	2.29 (1.10 – 4.76)	***0.027***	0.20 (0.02 – 2.39)	*0.203*
Concomitant drugs (not suspected)						
No	Ref.					
Yes	3.20 (0.96 – 10.70)	*0.059*	6.88 (1.42 – 33.43)	***0.017***	-	-
Tot strains/toxoids						
1-6	Ref.					
6+	0.16 (0.02 – 1.30)	*0.087*	2.14 (0.97 – 4.74)	*0.060*	-	-
Presence of allergens (in traces)						
No	Ref.					
Yes	0.31 (0.04 – 2.56)	*0.280*	0.94 (0.45 – 1.98)	0.873	-	-

Results: A total of 223 suspected AEFI reports were collected, and the majority of them were defined as non-serious (76.7%). Reports were mostly related to one vaccine, and to a median of 2-5 strains/toxoids. The total number of simultaneously administered strains/toxoids and the presence of allergens did not correlate with AEFI seriousness. Considering vaccines with a high number of administered doses (≥60,000 doses), the rates estimated for serious AEFI reports were always very low, ranging between 0.01 and 0.2/1,000 doses. Twenty-four vaccines (8,993 doses) were not related to any AEFI.

Figure 1 - Distribution of AEFI reports (non-serious and serious) collected for mandatory and non-mandatory vaccinations performed between 0 and 15 months of age, according to the National Vaccination Plan 2017-2019 (dashed areas).



Discussion and Conclusion: Results of present study showed that AEFI were very rare, the vast majority of them was non-serious and, despite the claims of anti-vaccination movements, the simultaneous administration of vaccines was safe and did not influence the risk of reporting a serious AEFI, particularly in children.

Reference: Lombardi N, Crescioli G, Bettiol A, Tuccori M, Rossi M, Bonaiuti R, Ravaldi C, Levi M, Mugelli A, Ricci S, Lippi F, Azzari C, Bonanni P, Vannacci A. Vaccines Safety in Children and in General Population: A Pharmacovigilance Study on Adverse Events Following Anti-Infective Vaccination in Italy. Front Pharmacol. 2019 Aug 30;10:948.

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