

PAIN RESPONSE TO M-M-R VACCINATION IN 4 - 6 YEAR OLD CHILDREN

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ABSTRACT

Background

Differences in pain response to two different M-M-R products have previously been demonstrated in 12-month old infants and in 4 – 6 year old children.

Objective

To determine if the acute and immediate pain response to two licensed M-M-R vaccine products (using a self-report measure) in children 4-6 years of age was similar to that demonstrated in younger infants.

Methods

Randomized, double blind, study. Subjects were randomly allocated to Priorix[®] (SmithKline Beecham) or M-M-R II[®] (Merck Frosst). The primary outcome measure was pain response to vaccination quantified using a self-report OUCHER pain scale. Secondary outcome measures included pain measurement by proxy (physician and parent) using a visual analog scale (VAS) and measurement of cry and cry duration immediately post-vaccination.

Results

Of the 60 subjects enrolled, 30 received Priorix[®] and 30 received M-M-R II[®]. There were no significant differences between the two groups on age, sex, or previous painful procedure. Post-vaccination, children in the M-M-R II[®] group had higher median pain scores compared with children in the Priorix[®] group for VAS (12.5 vs. 2.0, respectively by paediatricians, $p=0.017$; 18.5 vs. 5.0, respectively by parents, $p=0.235$), OUCHER (20 vs. 0.00, respectively, $p=0.047$). The median duration of crying post M-M-R II[®] was higher compared with Priorix[®] (6 vs. 0 seconds, respectively, $p=0.020$).

Conclusion

Priorix[®] was associated with significantly less pain compared with M-M-R II[®], at the time of injection.

Key Words: *Vaccination, pain, measles-mumps-rubella vaccine*

Parental preference is to avoid the pain and emotional distress associated with childhood vaccination.¹ Reducing vaccine-associated pain may therefore increase uptake. Differences in immediate pain response to two different M-M-R products, administered to 12-month old infants, have been demonstrated.²

The objective of this study was to determine if the acute pain response to two licensed M-M-R vaccine products, using a self-report measure in

children 4-6 years of age, was similar to that observed in younger infants.

Participants and Methods

Healthy pre-school children (4–6 years) receiving their second M-M-R vaccination in an urban primary care paediatric practice were enrolled. Ethical approval was granted by the Hospital for Sick Children, Toronto, Canada, Research Ethics Board, and informed consent was obtained from

all parents of enrolled subjects. A randomized, double blind study design was used. The randomization schedule was prepared off-site by the study statistician. A random numbers table was used to create a randomization schedule for vaccine allocation Priorix[®] (SmithKlineBeecham, Pharma, Oakville, Ontario) or M-M-R II[®] (Merck Frosst Canada & Co, Montreal, Quebec). Vaccine allocation was placed in numbered and sealed opaque envelopes. Subjects were consecutively assigned a study number on recruitment that was linked to the number on the randomization envelopes. To maintain blinding, a clinic nurse reconstituted the vaccines in 3.5 ml syringes and wrapped the barrel with an opaque adhesive label. Neither the paediatrician performing the injection (MI or MG) nor the parent of the child being vaccinated was aware of which vaccine was being administered. Children were vaccinated while sitting on the examination table. The vaccine material was injected subcutaneously according to standard recommendations.³ The needle was inserted by a rapid plunge into a pinched-up fold of skin and subcutaneous tissue. Parents were told that they could do whatever they would normally do to comfort their child after the vaccination.

The primary outcome was pain response to vaccination using a self-report measure. A sample size of 30 per group provided 80% power to detect a difference of 50% in pain scores between the two groups (at an alpha level of 5%). The primary validated scoring method used was the OUCHER pain scale, which was completed by the child post-vaccination. This scale measures pain

intensity using six photographs depicting facial expressions ranging from no hurt (score 0) to biggest hurt (score 100).⁴ A visual analogue scale (VAS) was used as a secondary outcome measure and was completed by the parent and paediatrician pre-vaccination (5 seconds) and post-vaccination (within 15 seconds) using a linear 100 mm scale, where 0 mm denoted no pain and 100 mm denoted maximal pain. For the VAS parent and paediatrician scores, the median difference in pain scores (post minus pre) for each group were calculated and compared. Other secondary outcomes used a videotape recording of the procedure to measure whether the subject cried (yes or no), and the duration of the cry post-vaccination. The non-parametric Mann Whitney U-test was used to test for differences in median pain scores between the two groups (Priorix and M-M-R). A chi-square test was used to test for differences in frequency of crying between the two groups. A p-value <0.05 was considered significant.

RESULTS

Table 1 shows the baseline characteristics of the two groups. As shown in Table 2, pain scores were higher for M-M-R II[®] vs. Priorix[®] for all outcome measures. Children in the M-M-R II[®] group had significantly higher OUCHER scores and were more likely to cry post-vaccination, compared with the Priorix[®] group.

TABLE 1 Baseline characteristics of the two groups

CHARACTERISTIC	M-M-R II [†] (N=30)		Priorix [‡] (N=30)		p-value
	N	%	N	%	
Sex (male)	15	(50)	13	(43)	0.605
Previous painful experience*	14	(47)	12	(40)	0.602
Circumcision, males (yes)	10/15	(67)	7/13	(54)	0.488
Paediatrician (MI)	23	(77)	21	(70)	0.559
Mean age in months (SD)	54	(6.9)	55	(6.1)	0.844

[†] Merck Frosst Canada & Co., Montreal, Quebec [‡] SmithKlineBeecham, Pharma, Oakville, Ontario

* Surgery, fracture, burn etc.

TABLE 2 Outcome Pain Measurements M-M-R II[®] vs. Priorix[®]

OUCHER (0 – 100)	M-M-R II[†] (N=30) Median (inter-quartile range)	Priorix[‡] (N=30) Median (inter-quartile range)	p-value
Post-vaccination	20.00 (0 – 60)	0.00 (0 - 20)	0.047
VAS (0 – 100) (VISUAL ANALOGUE SCALE)			
Parent, Difference (post-pre)	18.50 (0 – 34)	5.00 (0 – 17)	0.235
VAS (0 – 100) (VISUAL ANALOGUE SCALE)			
Paediatrician, Difference (post-pre)	12.50 (2 – 60)	2.00 (0 – 16)	0.017
CRYING Yes (%)	17 (57)	8 (27)	0.018
Median cry duration (seconds)	6 (0 – 40)	0 (0 – 0)	0.020

[†] Merck Frosst Canada & Co., Montreal, Quebec

[‡] SmithKlineBeecham, Pharma, Oakville, Ontario

DISCUSSION

These findings – higher pain scores immediately post-vaccination in the M-M-R II[®] group, compared with the Priorix[®] group – confirm similar findings in previous studies involving infants² and toddlers.⁵ The assessment of acute pain in infants and children is difficult to measure because pain is difficult to quantify. In infants, validated behavioral scales (facial expression, crying, and body movement) and physiological measures (heart rate, respiration, sweating, and endorphins) have been used extensively. In older, verbal children, self-report of pain using validated tools such as the OUCHER, has contributed to the accuracy of pain measurement and reinforces the findings of this study.

It has been observed that self-reports in adults are better estimates of the patient's experience than behavioural or physiological measures.⁴ In children, the OUCHER agrees with results obtained by other measures, and is one of many validated instruments available to evaluate paediatric pain.⁴ Another instrument used to assess pain in children is the Faces Pain Scale-

Revised⁶, which was used in a study similar to ours of 4–6 year old children receiving two MMR vaccines.⁷ The results of that single blind study confirmed our findings that Priorix[®] was associated with significantly less pain than M-M-R II[®] (marketed in France as RORVax by Aventis Pasteur-MSD).

The results of this study suggest that the pain of vaccine injection is potentially preventable by improving the tolerability of the vaccine. In other words, differences in the physicochemical properties of the vaccines may contribute to the differential pain experienced by the recipients^{2,8} and may be a factor that can be modified by vaccine producers. With many vaccines currently being recommended for routine childhood immunization, the burden of pain and distress may interfere with parental compliance and aggravate the already prevalent anti-vaccine sentiment.⁹ Additional research is warranted to determine the modifiable vaccine components that contribute to vaccination pain.

CONCLUSION

Priorix[®] was associated with significantly less pain compared with M-M-R II[®], at the time of injection in 4–6 year old children.

Conflict of Interest and Funding

This study was unfunded. The principal investigator (MI) has received grant funding in the past from GlaxoSmithKline.

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