Draft

Minutes of meeting of causality assessment meeting held at LHMC on 15-Feb,13

- All the 14 death cases following pentavalent vaccination in Kerala were discussed and analysed during the meeting. The draft Kerala report by the central team and state AEFI causality assessment report was also reviewed.
- References from Brighton, Nelson and other research articles were reviewed.

To summarise:

1. Reported deaths (AEFI cases) are sporadic from different part of the state, there is no clustering, and adverse events have not been reported from other children who have received the vaccine from the same vials. Programme errors therefore appear unlikely.
2. In 8 cases, death was reported after 1st dose, in 4 cases – after 2nd dose, in 1 case- after 3rd dose and in case- (Easy4 – not known). Eleven infants were females.
3. Eleven deaths occurred beyond 12 hours of administration of the vaccine and in 2, vaccine was administered in less than 12 hours (within 5-6 hrs) before the death. In one child interval between vaccine administration and death was not available.
4. In six cases, co-morbidities were present that could have contributed to death
5. The clinical manifestations, age group, season, and time of the death in 8 infants were consistent with presumptive diagnosis of SIDS (Sudden Infant Death Syndrome)
6. There is also seasonality in death cases: 5 cases were during April – October while 9 cases were during December – February (cooler months).
7. Post mortem was done in 4 cases. The tissues from these children should be subjected to more detailed analysis for histopathology, immunological, molecular and toxicology testing to complement our current understanding and help in arriving at a more specific diagnosis in the context where deaths have occurred. These tissue samples may be sent to institutions like AIIMS, New Delhi and possibly WHO/CDC for further testing (if required).
8. From the available tissues, possibilities of genetic studies may be explored to determine association with SIDS.
9. All cases had received PCM prior to death. PCM related hypersensitivity although rare in children < I year, the possibility needs to be investigated.
10. A request to CDSCO may be sent for vaccine quality audit.

Finally, the overall assessment of the 14 reported deaths by causality assessment committee, it appears that the vaccine is unlikely to be contributing to the cause of these deaths. However, the causality assessment committee shall meet again to review the detailed investigations from PM cases.

Technical update on reported deaths following administration of Pentavalent vaccine

1. Government of India introduced a liquid pentavalent into the routine immunization schedule on 14 December 2011 to replace the DPT and Hepatitis B vaccines and introduce Hib vaccine. Since its introduction, about 400,000 children have received the vaccine in 2 states: Kerala and Tamil Nadu.
2. Within India, the national Technical Advisory Group on Immunization (NTAGI) 'strongly recommended that Hib vaccine should be immediately introduced in India's UIP" and the Indian Academy of Pediatrics (IAP) stated in 2012 that "(the committee of immunization) strongly supports the Government of India's efforts to introduce the vaccine in all the states of the country."
3. A total of 79 AEFI cases reports with Penta vaccine of which 19 are death (24%) and 60 cases (76%) are of hospitalization.
4. Annual breakup is as follows:

Year	Death	Hospitalization	Total
2011	1	4	5
2012	14	42	56
2013	4	14	18
Total	19 (24%)	60 (76%)	79

5. The states reporting the 22 death are as follows:

Year	State	AEFI death reported
2011	Kerala	1
2012	Kerala	10
	Tamil Nadu	4
	Total	14
2013		
	Kerala	3
	Haryana	1
	Total	4
	GRAND TOTAL	19

6. Causality classification of AEFI deaths is as follows:

S No.	State	Program error	Vaccine reaction	Injection reaction	Coincidental	Unrelated	Total
1	Kerala	0	0	0	6	8	14
2	Tamil Nadu	0	0	0	4		4
3	Haryana	0	0	0	1		1
	India	0	0	0	11	8	19

7. AEFI deaths reported following pentavelent vaccine in Kerala state were reviewed by state AEFI committee and a central team was also sent to facilitate the process. The cases were further reviewed by the causality assessment subcommittee of the National AEFI committee which confirmed that for the 14 reported deaths, 6 had co morbidities and 8 other cases were unrelated to the vaccine. It reported

a. For the 14 penta related AEFI deaths there is seasonality in death cases with almost a third of the deaths having been reported during the cooler period from December – February.
b. The clinical manifestations, age group, seasons, and time of the death in 8 infants were consistent with presumptive diagnosis of SIDS (Sudden Infant death Syndrome). Post-mortem samples are available from 4 cases and the central investigation team has requested for a more detailed analysis for histopathology, immunological, molecular, toxicology and genetic testing to complement current understanding and help in arriving at a more specific diagnosis in the context where deaths have occurred and to determine association with Sudden Infant Death Syndrome. (SIDS).
c. All cases received PCM prior to death, PCM related hypersensitivity although rare in children < 1 year; the possibility needs to be investigated.

Finally, the overall assessment of the 14 reported deaths by causality assessment committee; it appears that the vaccine is unlikely to be contributing to the cause of these deaths. However, the causality assessment committee shall meet again to review the detailed investigations from PM cases.

8. As directed further histo-pathological analysis of the post mortem samples of 3 cases was sought at Pathology Department AIIMS, Delhi under the leadership of Dr S K Panda had a review meeting was conducted soon after.

9. The histopathological review concluded that the deaths were due to vasogenic shock. The cause of the shock could however not be determined with the current evidence available and the previous conclusion of the causality committee holds.

10. Haemophilus influenza type B (Hib) is a bacterium which causes severe pneumonia, meningitis and other life-threatening conditions in children less than five years of age. Conjugate Hib vaccine has proven to be one of the best tools to prevent infections caused by Hib vaccine globally. WHO recommends Hib conjugate vaccines for all children, noting “in view of their demonstrated safety and efficacy, conjugate Hib vaccine should be included in all routine infant immunization programmes”. Although safe and effective, the Hib vaccine was available to only a small portion of children in India through the private sector.

11. These deaths though sad and unfortunate, are sporadic from different parts of the state. There is no clustering, and adverse events have not been reported from other children who have received the vaccine from the same vials.

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