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Sudden Unexpected Deaths and Vaccinations during the First Two Years of Life in Italy: A Case Series Study

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Infanrix Hexa Periodic Safety Update Report (PSUR) to the EMA Compliments the Findings of Deaths with the Hexavalent Vaccine

Posted by Puliyel on **15 Oct 2016 at 10:55 GMT**

With reference to the paper by Traversa and collaborators (1) we commend the monumental work, their meticulous collection of data and analysis. We however would like to make a few observations about the conclusions they have arrived at especially in the light of contemporaneous global data that has come in to the public domain recently.

1. The Italian court of Justice Nicola Di Leo recently ordered that the GlaxoSmithKline Biological Clinical Safety and Pharmacovigilance report to the regulatory authority (periodic safety update reports (PSUR) 15 and 16 (data up to 22 October 2011) to the EMA) on Infanrix hexa, be made public and this is now available on the internet (http://autismoevaccini.fi...). This gives the global background to what Traversa et al have observed looking at more detailed data from Italy on sudden unexplained deaths (SUD) and vaccination in the first 2 years.

2. '''Data from Italy and Germany not Comparable'''
The authors point out that their relative risk (RR) of SUD (for any vaccine and any risk periods), while it was greater than 1, was almost an order of magnitude lower than the estimates from Germany (seen after the 4th dose). They found the increase in RR confined to the first dose and they suggest it may be partially explained by a residual uncontrolled confounding effect of age.

In Germany a fourth dose is given in the 2nd year where as in Italy only 3 doses are given mostly in the first year. In the absence of the 4th dose in Italy it is not surprising that the mortality seen in the second year in Germany was not seen in Italy. The two data are not comparable

The German study quoted found 3 deaths within 48 hours of vaccination in the second year, and the standardized mortality ratio (SMR) was 23. The background rate of SUDS in the second year is much lower than the background rate of SIDS in the first year. An increase of 3 deaths was sufficient to increase the SMR by 23 times. The same increase of 3 deaths in infancy where the background rate of SIDS is much higher will not show up as statistically significant.

The PSUR 16 documents that the observed deaths on day 1 and 2 after immunization were higher than expected in the children vaccinated in their 2nd year (5 observed against 3.96 expected on day 1 and 6 observed against 5.94 expected on day 2) (Please see pages 246-249 of the uploaded document).
(Source: Table 36 The GlaxoSmithKline Biological Clinical Safety and Pharmacovigilance 16th PSUR report to Regulatory Authority)

If the 15th and 16th PSUR are compared it will be noticed that 'expected death rate' was doubled in the 16th report and yet the observed deaths exceeded the expected!

The 16th report states "It can thus be estimated that 75% of all recipients of Infanrix hexa were in their first year of life, and 20% were in their second year of life (5% were not attributable because the age at vaccination was unknown). Therefore the number of doses (since launch) was estimated to be 54,7 in infants under 1 year and 14,6 millions over the age of 1 year." The

estimate of the number of doses in the second year was suddenly pushed up from 9.4% in the 15th PSUR (page 782 of the uploaded document) to 20% in the 16th report. Had the PSUR 15 distribution of doses over 1 year been used for the 16th report, the expected deaths would have be halved and the observed deaths would have been double what were expected for the first 4 days and actual death would exceed expectation in the first 7 days. The observed deaths on day 0 was 2 where only 1 was expected, it was observed in 5 on day 1 when only 1.86 was expected, there were 6 deaths up to day 2, where 2.79 were expected and 6 deaths on day 3 where 3.72 were expected, 7 deaths on day 5 where 5.58 were expected using the PSUR 15 expectation rates.

One may consider the change to 20% from 9.4% as a correction made for what was historically wrongly calculated at 9.4%. The 20% figure is valid only if all children receiving the vaccine, receive 4 doses and of them 1 was after the age of 1 year. Pragmatically the figure of 20% is not tenable. Countries like Italy (the second largest market for the vaccine) advise only 3 doses and all the doses are given under 1 year.

3. '''Health Vacinee Effect Negated'''
Traversa found deaths with other vaccines in the first 7 days less than 1. This is exactly what is expected if the vaccine itself does not kill. Healthy children are taken for vaccination and mortality of children taken for vaccination is less than normal in the week of vaccination, compared to the population as a whole. In contrast to the situation with other vaccines Traversa found a doubling of deaths in the week after administering the first dose of Hexavalent vaccine. This is clearly remarkable.

4. '''Residual uncontrolled confounding?'''
Traversa et al write, 'The comparison between risk periods (days closer to the vaccine shot) and control periods (more distant days) is influenced by the decreasing trend of the basal rates of SUD. Thus, our RRs may be at least partly affected by the residual uncontrolled confounding effect of age.'

The doubling in deaths with the first dose cannot be residual uncontrolled confounding effect of age as in the in period 80 to 100 days the vaccine risk period usually falls in the middle between 90 and 97 days. Carpenter et al examining unexplained infant death in 20 regions in Europe (2) report that the highest mortality is around 10 weeks (around day 70) and any residual uncontrolled confounding should have resulted in less deaths not more deaths.

5. Traversa and colleagues found more deaths in the period 0-7 days but not in the period 0-14 days. This does not blunt the importance of their finding of increased deaths in the first week. If most of the deaths from vaccine occur in the first week, the increase may show up as statistically significant in the first week but it may not be significant within a larger window of 0-14 days. The impact of the increased deaths in the first week gets diluted within the background death rate as the window is enlarged.

6. Traversa found increase in deaths after the first dose and not with subsequent doses. It may be implied that if the deaths were due to vaccine it must be seen with the same magnitude with each exposure to the vaccine.

This need not be so. If vaccine deaths are a form of hypersensitivity to the vaccine components, we can expect it will pick up most of those who are sensitive with the first dose. If one survives the first dose it means they are not sensitive and problems will be less with subsequent doses. This will explain the higher incidence with the first dose.

A lay person may enquire why, if that is so, the German data showed so much increase in deaths with the fourth dose. Examination of the PSUR table will explain this seeming paradox. There were 29 deaths in the first 2 days in first year and only 5 deaths in the second year. However expected deaths are also much higher in the first year than in the second year. Thus although there were fewer deaths with the 4th dose (as expected from our explanation of hypersensitivity) those (few) deaths reached statistical significance because expected deaths were so much lower.

7. In May 2005, Zinka and colleagues reported six cases of sudden infant deaths caused by Hexavac (3) Marketing authorization in the European Union was withdrawn in August 2005 (Doc.Ref.EMEA/207369/2005) quoting decreased immunogenicity of the hepatitis B component. The findings of Traversa validate the observations of Zinka and colleagues.

'''Conclusion'''
The data from Traversa point to a real risk of death with the hexavalent vaccine. The data pertains mostly to children under 1 year of age. It doubles the risk of death in the week after the first dose of vaccination. It must be read in conjunction with the data on deaths in the second year from Germany and the PSUR 16 report. The data suggests that the vaccine is probably causing unnecessary deaths.

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No competing interests declared.

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