Dr Reshmi Raychaudhuri – Impact on congenital pneumonia in neonates

The background has already been alluded to in a great amount of detail, but secondary to prematurity and its complications, congenital pneumonia and early onset sepsis are the most important causes of neonatal morbidity and mortality and we know that GBS infection is the commonest cause of early onset sepsis in neonates. Early onset GBS infection most frequently presents with sepsis and pneumonia and over the last 25 years we've seen how, with maternal screening of GBS carriage and intrapartum antibiotic use, there has been a significant reduction in the incidence of invasive early onset GBS disease in many countries.

The incidence in the UK of early onset GBS infection is variable by geographical areas, but in 2013 an incidence of 0.38 or 0.4 cases per 1000 live births was stated by the Public Health England, However is this just the tip of the iceberg? Our colleagues at St Georges, including Dr Bedford Russell, prospectively collected data for one year of all neonates who required a septic screen in the first 72 hours of life. Including definite culture proven sepsis and probable early onset GBS infection, which was defined as babies with clinical signs of sepsis with negative cultures but positive deep ear swabs for GBS suggestive of colonisation, revealed an almost hundred fold increase in the incidence of 3.6 per 1000 live births. If we look at this estimate it indicates much greater disease burden in the UK than that suggested by culture proven sepsis and this lends to the support for an urgent need of greater prevention strategies.

Based on this data we hypothesised that the introduction of a universal maternal GBS screening programme and intrapartum antibiotic use would reduce the incidence of not only invasive early onset GBS disease, but also early onset neonatal sepsis as a whole and congenital pneumonia.

Our objective was to review the number of cases of congenital pneumonia and early onset sepsis before and after the introduction of a universal maternal screening programme in March 2014. We used the National Neonatal Database. The interrogation platform is called Badgernet which collects data on all neonatal admissions and discharges and this data is used to inform the National Neonatal Audit Programme. We identified cases by searching for diagnoses of sepsis, suspected sepsis, presumed sepsis, unwell with negative microbiology, GBS sepsis or congenital pneumonia. Once we identified cases we reviewed the electronic and paper case notes, where available, of all these cases covering a period from March 2011 to April 2015. We included all babies born at Northwick Park Hospital after March 2011 and admitted to the Neonatal Unit. We included all babies born at or greater than 35 weeks gestation and cases which met our criteria for early onset sepsis and congenital pneumonia.

It is difficult to find an objective and widely accepted definition of neonatal sepsis due to the variable clinical presentation and low yield of cultures. We did a literature review and defined early onset sepsis according to a definition set by the expert meeting on neonatal and paediatric sepsis which was housed by the European Medicines Agency. This was a meeting which convened to define neonatal sepsis in a way that could be used to run clinical trials. The definition we used defines early onset sepsis as under 72 hours of life with 2 clinical and 2 laboratory criteria associated with sepsis in the presence of suspected or culture proven sepsis. Similarly it is difficult to find a gold standard definition of congenital pneumonia and after a literature review we included cases which had all 3 of the following: signs of respiratory distress, abnormal inflammatory markers as well as chest X-ray changes consistent with infection.

Looking at our total infection data we identified 60 cases from April 2011 to March 2015. We excluded more than half of these cases as they were either external transfers from other hospitals, they did not meet our case definition or they were from March 2014 which is the period during which the screening programme was still being rolled out. We included three years of data before screening was introduced from April 2011 to February 2014 and we have eleven months of data post screening from April 2014 to March 2015. If you look at the total infections you can see there are quite small numbers. We had ten total infections in the first year. In the next year we had eight, six and then three after screening was introduced. Looking at the total infection rate, expressed as per 1000 live births, you can see that there's a general downward trend in the rate of infection, however this is a much more marked drop in the year after screening was introduced and it has dropped to 0.63.

Breaking down this information further into early onset sepsis cases only we identified 38 cases and excluded 24. You can see very small numbers are involved. In the first year, in April 2011, we had six cases. Of these four were culture proven GBS sepsis. One case was of GBS bacteraemia and congenital pneumonia and another case was of GBS bacteraemia and meningitis. This year, the infection rate was 1.16 per 1000 live births. Since March 2011 we have had no culture proven cases of early onset sepsis. The rate post screening was 0.62.

Coming to now congenital pneumonia we identified 22 cases of which nine were excluded. In the first year we had four cases of congenital pneumonia and with slightly higher cases in the second year of seven. Two of these cases had negative cultures, but were colonised with GBS with positive skin swabs. The year prior to screening we had two cases, but interestingly after screening was introduced no cases were identified at all.

To summarise our findings, this table represents total infections of early onset sepsis and congenital pneumonia. We have collated the pre-screening rate expressed as the rate per 1000 live births and this has amalgamated the three years pre-screening data from April 2011 to February 2014. We have our post screening rates. The ratio in the fourth column

refers to the rate of reduction, which is the post screening rate divided by the pre-screening rate and the relevant P value. Looking at total infections you can see that the rate of infections post screening fell to more than a third compared to pre-screening rates, however this has not reached statistical significance. There was no significant change in the rate of early onset sepsis cases. For congenital pneumonia we have identified no cases of congenital pneumonia after screening, however for the purposes of statistical analysis we included a few cases. Nevertheless the rate of reduction is not statistically significant at the moment.

So what does this data tell us?

We can say that the introduction of a universal maternal GBS screening programme at Northwick Park Hospital has been associated with the reduction in the number of cases of infections and congenital pneumonia and we have not identified any cases of congenital pneumonia after screening. The rates of reduction are not statistically significant currently, but we have only presented preliminary data with eleven months' worth of data since screening was started and our numbers are very small. If we consider the incidence of early onset GBS disease and early onset sepsis this is perhaps understandable. In terms of confounders, the most important confounder would probably be the changes in antibiotic practice both on maternity and the neonatal side, however currently we are unaware of any difference or change in policy with our antibiotic practice.

To conclude, if we consider the Bradford Hill criteria for causation, we have possibly shown a temporal association with the reduction in rates of total infections and congenital pneumonia since the universal GBS screening was introduced. We have certainly biological causability in what we know about the disease process and coherence with other studies. However at the moment we are only able to show you preliminary data and currently it lacks power in statistical significance so further studies are necessary to confirm our initial observations. We are continuing to collect data and hope to expand on our findings in the near future.