Recall bias, MMR, and autism

N Andrews, E Miller, B Taylor, R Lingam, A Simmons, J Stowe, P Waight

Methods

While the data collected in the earlier study conducted in 1998 are unlikely to have been greatly influenced by the putative MMR-autism association, the data for the newly diagnosed cases in the study conducted in 2000 had the potential for parental recall bias concerning the age at onset of symptoms, particularly for those in whom regression was reported. The potential for this bias arises because details of symptom onset are usually recorded retrospectively at the time of autism diagnosis. In order to investigate whether this had occurred we compared RI estimates for children likely to have been diagnosed before and after the MMR-autism publicity. Since cases notes for children diagnosed up to 1998 (pre-hypothesis) could have been changed or updated subsequently, the data collected in 1998 for the five districts included in the 2000 study were used for the pre-hypothesis RI estimates. The study period for this cohort was from 1979 to the end of 1997. The post-hypothesis data set used information collected in the 2000 study and was restricted to those born from January 1995. This date was used because no child born from 1995 onwards had a diagnosis before 1997 and most had diagnoses between 1998 and 2000.

The self controlled case series method uses conditional Poisson regression to enable estimation of the RI using only cases by comparison of the frequency of events within and outside specified post-immunisation risk periods. In these analyses the risk periods for autism onset considered were within 2, 4, 6, and 12 months of MMR. Age was adjusted for by stratification into one month groups. In the first analysis, cases were restricted to the subset of children with core or atypical autism in whom parents reported developmental regression, with onset defined as the age at which regressive symptoms were reported to have occurred. In the second analysis, all core and atypical autism cases were included and onset was defined as the age at first parental concern, irrespective of whether regression was reported. Only cases with age at regression or age at parental concern under 50 months were included. This age restriction resulted in the exclusion of four cases. Since no onsets occurred after a second MMR dose the RI was only estimated for the first MMR dose.

Results

From the 1998 study, 86 cases with an age at regression from 0 to 50 months and 285 cases with an age at parental concern from 0 to 50 months were identified in the five districts. From the 2000 study in children born from January 1995, 26 cases had an age at regression from 0 to 50 months and 95 cases had an age at parental concern from 0 to 50 months. Table 1 shows the RI estimates for regression onset within 2, 4, 6, and 12 months of MMR for the two studies. The RI estimates in the 2000 study were greater than those in the 1998 study, although the confidence intervals were fairly wide and differences between estimates in the studies were not significant. None of the RI estimates in either study were significantly greater than one.

Table 2 shows the RI estimates for onset according to first parental concern within 2, 4, 6, and 12 months of MMR for the two studies. The RI estimates for the 2000 study were similar to those in the 1998 study. The <6 month analysis for the five districts analysed from the 1998 study showed a significantly raised RI, similar to that previously reported for eight districts in the earlier study.

Discussion

The results of this study are consistent with the existence of parental recall bias when reporting the onset of regression in relation to MMR immunisation in children with autism. Although the direction of the bias is as expected, the number of cases in the 2000 study with regression and born since 1995 was small, and the differences compared with the 1998 study were not significant. No evidence of bias was seen for reported age at first parental concern, consistent with the emphasis of the MMR-autism hypothesis on the subset of children in whom parents report developmental regression. The raised RI...
seen in the 1998 study in the <6 month period for first parental concern was not seen in the 2000 data. This suggests that the 1998 result was a chance finding because of the number of post-immunisation periods examined in the study.

The potential for bias needs to be considered in any study reliant on clinical histories obtained after a hypothesis has been publicised. This may be in the form of recall bias or biased reporting of cases fitting the hypothesis and may lead to false conclusions. Although the difference in RI estimates pre and post the hypothesis was not significant, this paper highlights the possibility that such a bias could affect future studies.

ACKNOWLEDGEMENTS

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Contributions: N Andrews conducted the statistical analyses and wrote the paper; E Miller and B Taylor also wrote the paper and designed the study. R Lingam, A Simmons, and J Stowe collated case note data.

Table 1 Relative incidence of onset of regression after MMR immunisation in children with childhood and atypical autism

<table>
<thead>
<tr>
<th>Risk period post-MMR (mth)</th>
<th>1998 study (n=86)</th>
<th>2000 study—born from 1995 (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RI (95% CI)</td>
<td>Cases in risk period</td>
</tr>
<tr>
<td>&lt;2</td>
<td>1.01 (0.38 to 2.63)</td>
<td>6</td>
</tr>
<tr>
<td>&lt;4</td>
<td>0.99 (0.48 to 2.09)</td>
<td>14</td>
</tr>
<tr>
<td>&lt;6</td>
<td>0.97 (0.49 to 2.04)</td>
<td>24</td>
</tr>
<tr>
<td>&lt;12</td>
<td>0.94 (0.44 to 2.02)</td>
<td>46</td>
</tr>
</tbody>
</table>

Table 2 Relative incidence of timing of first parental concern in relation to MMR immunisation in children with childhood and atypical autism

<table>
<thead>
<tr>
<th>Risk period post-MMR (mth)</th>
<th>1998 study (n=283)</th>
<th>2000 study—born from 1995 (n=95)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>RI (95% CI)</td>
<td>Cases in risk period</td>
</tr>
<tr>
<td>&lt;2</td>
<td>1.07 (0.58 to 1.98)</td>
<td>14</td>
</tr>
<tr>
<td>&lt;4</td>
<td>1.18 (0.76 to 1.83)</td>
<td>34</td>
</tr>
<tr>
<td>&lt;6</td>
<td>1.55 (1.05 to 2.29)</td>
<td>65</td>
</tr>
<tr>
<td>&lt;12</td>
<td>0.91 (0.61 to 1.34)</td>
<td>106</td>
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</tbody>
</table>

REFERENCES

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