Recent respiratory infection and the risk of myocardial infarction

T C Clayton, N E Capps, N G Stephens, J A Wedzicha, T W Meade

The mean age of participants was 63 years and 84% were men. All cases were interviewed within a week of admission, with 88% seen within the intended time period of four days. There was no evidence of an association between the primary definition of respiratory infection and MI (OR = 1.0, 95% CI 0.5 to 2.0, p = 0.98) (table 1). However, there was an unexpectedly high OR for the association of chest pain on breathing with infarction (OR = 17.5, 95% CI 3.6 to 85.6; p = 0.0001). For fever, there was also a strong association (OR = 5.9, 95% CI 2.0 to 16.8; p = 0.0004). Further analyses restricted to those participants reporting symptoms of both chest pain and fever, and thus with a seemingly certain diagnosis of lower respiratory infection, showed that all seven participants reporting both together were cases (p = 0.001). For five of these cases, the symptoms first appeared at least two weeks before the index event. To reduce the likelihood that chest pain might have been due to the early onset of MI, the data were also analysed by omitting patients who had chest pain on breathing (without fever) within the preceding week. There remained a strong association between pain and infarction (adjusted OR = 9.3, 95% CI 1.5 to 56.4; p = 0.009). There were also strong associations between chest pain on breathing or fever and symptoms of the primary definition of respiratory infection. Over time, the OR for chest pain or fever was 10.2 (95% CI 3.4 to 30.7) at 1–2 weeks before the MI, 8.2 (95% CI 2.3 to 29.5) at 3–4 weeks, and 0.9 (95% CI 0.4 to 2.1) at ≥1 month.

DISCUSSION

The numbers of participants in the study were not large but were nevertheless sufficient to show unexpectedly strong associations of reported chest pain on breathing with infarction. Recall bias by cases, who may have been more likely than controls to have recorded symptoms, has to be considered but this would have to have been extreme to account for the full extent of the odds ratios presented. Another possibility is that chest pain might in some cases have been a premonitory symptom of the infarct. Against this explanation is, firstly, that the association was still strong after cases whose pain had started within the week immediately preceding the MI were omitted. Secondly, pleuritic pain on breathing is not well documented as a premonitory symptom of MI and there was no evidence that the excess of chest pain in cases was caused by angina. Lastly, the association of chest pain with symptoms of the primary definition suggests that chest pain was part of the range of symptoms occurring in the respiratory infections reported.

Data from the general practice based IMS Disease Analyser-MediPlus database (IMS Health, London, UK) showed that only 0.023% of all consultations by men in the previous month were for pleuritic pain during the winter. Since <2% of all those aged 40 years or more on the practice lists were asked to participate, it is most unlikely that their initial selection as potential controls was connected with whether they had had recent pleuritic pain. In addition, controls reported primary symptoms with the same frequency as cases. Overall, our results are consistent with those of the GPRD studies, in contrast with which our study had the advantage of direct clinical histories of respiratory infection from cases and controls. We conclude that recent respiratory infection manifested by chest pain or fever may be a factor leading to MI. Several different pathways may be involved, including increased thrombogenicity, atherogenesis, and plaque rupture.1 3 If recent respiratory infection contributes to MI, the implications include further encouragement of a

Abbreviations: CI, confidence interval; GPRD, General Practice Research Database; MI, myocardial infarction; OR, odds ratio
high and more consistent uptake of influenza immunisation by older people and by those in vulnerable groups, as well as aborting infections at an early stage.

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