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Quantifying the effects of prior acetyl-salicylic acid on sepsis-related deaths: an individual patient data meta-analysis using propensity matching

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Background: Novel strategies for reducing deaths in patients with severe sepsis are needed as adjuvant therapies have failed to impact on mortality. The objective of this study was to conduct a meta-analysis on all published observational cohort data describing the association between acetyl-salicylic acid (aspirin) use prior to the onset of sepsis and mortality in hospitalised patients.

Material/methods: We searched MEDLINE, Cochrane and PubMed databases for English language articles published from inception to 1st July 2016. Selected studies reported mortality in patients on aspirin prior to the onset of sepsis, with a comparison group of untreated patients with sepsis. Sixteen studies were selected for inclusion. Fifteen studies described hospital-based cohorts (n=17,065), while one was a large insurance-based database (n=683,421). One hospital-based study was subsequently excluded as patients with sepsis could not be distinguished. It was not possible to disaggregate aspirin from other antiplatelet drug use in all studies. Individual level patient data were provided for all selected studies. Propensity analyses with 1:1 propensity score matching at the study level was performed, using the most consistently available covariates judged to be associated with aspirin / antiplatelet use. One-step and random effect two-step meta-analyses were performed to estimate the pooled average treatment effect of aspirin and of anti-platelet agents in general on sepsis-related mortality.

Results: Use of aspirin was associated with a 7% (95%CI, 2% to 12%, p=0.005) reduction in the risk of death by two-step meta-analysis (our primary analysis), with significant statistical heterogeneity (I^2=61.6%). Standardised re-analyses for anti-platelet agents (predominantly aspirin) found results from most hospital record-based studies to be consistent with no protective effect, but a significant effect was observed from analysis of the large insurance database. Pooled results showed a similar trend towards mortality risk reduction (4%, 95%CI -1% to 9%, p=0.11), with similar levels of heterogeneity (I^2=49.4%).

Conclusions: These results are consistent with effects ranging from 2% to 12% reduction in mortality risk in patients taking aspirin prior to sepsis onset. This association necessitates definitive study of the use of low-dose aspirin as a strategy for reduction of deaths in patients with sepsis.