The effect of prior statin use on outcomes following admission with community acquired pneumonia to acute medicine.

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Abstract

Community acquired pneumonia (CAP) is a significant cause of morbidity and mortality. Statins have pleiotropic effects and may improve survival in patients with pneumonia. We investigated if patients on statin therapy had altered outcomes in CAP. The impact of dosage was assessed as a secondary endpoint.

Methods

Following ethical approval, medical records of patients admitted to an acute medical unit in an NHS hospital between 2010 and 2012 were reviewed retrospectively. Inclusion criteria was a coded diagnosis of CAP confirmed by a respiratory consultant who reviewed electronic notes for symptoms and chest radiographs to ensure patients met BTS definitions of a community acquired pneumonia. Demographics, co-morbidities, CURB-65 score, medications and outcomes were recorded. The cohort (n=2068) was divided according to prior statin use. The predicted probability of death (PPoD) was calculated using binomial logistic regression, controlling for age and gender. Patients taking statins were then stratified according to statin dose. Since most patients within the cohort were taking Simvastatin, dose response analysis was performed for Simvastatin alone.

Results

A total of 2068 patients were included within the study, of which 634 patients were taking a statin prior to their hospital admission. Group demographics were similar in terms of gender and severity of pneumonia, as defined by their CURB score. The statin use group were older than the statin free group and had a higher frequency of cardiovascular disease and diabetes (Table 1).

458 of those admitted with pneumonia died during their admission. 83% of statin users survived to discharge compared with 75% of those who did not take a statin on admission (Figure 1). The PPoD, based on age and statin use, was lower in the statin group than those who were statin free (OR=0.525 p=0.006) (Fig2).

Subgroup analysis revealed the reduction in PPoD is dose dependent, with the most significant reductions being seen in those taking greater than 40mg of Simvastatin per day (Fig3).

Conclusion

We describe greater survival in patients with pneumonia who were on statin therapy prior to admission despite this cohort being older with more comorbidities. There appears to be a dose dependent relationship with greater reduction in mortality at higher doses. This supports findings of animal models but is the first time it has been described in CAP.

Introduction and Aims

Community acquired pneumonia (CAP) is considered the leading cause of death from infectious disease in developed countries. Increased mortality is associated with systemic manifestations and complications of CAP with sepsis being the most common and challenging. Sepsis increases in incidence with age and age is a predictor of outcome in patients with pneumonia.

CAP associated mortality has not improved for twenty years, despite successful international campaigns to improve the rapid instigation of anti-microbial therapies and supportive measures. A recent study suggested 73% of community associated infectious deaths and 60% of community associated infective-related deaths were associated with non-antibacterial species, suggesting that new antibiotic strategies alone may be insufficient to improve outcomes. New therapeutic approaches are needed to improve outcomes.

HMCoSA Reductase inhibitors (statins) are classically utilised to lower cholesterol in subjects with increased risk of cardiovascular morbidity. There is a body of evidence suggesting that statins may prevent or influence outcomes in sepsis both in prevention and treatment cohorts, although there is still uncertainty as to the benefit of statin initiation or continuation during septic episodes. There is also uncertainty as to the most efficacious dose of statin if therapeutic trials were to be designed.

The aims of the current study were 2 fold.

1. To determine if statin use was associated with improved outcomes in patients admitted to a secondary care hospital with pneumonia

2. To determine if there was a dose response between outcomes and statin dose

Methods

Following ethical approval, medical records of patients admitted to an acute medical unit in an NHS hospital between 2010 and 2012 were reviewed retrospectively. Inclusion criteria was a coded diagnosis of CAP confirmed by a respiratory consultant who reviewed electronic notes for symptoms and chest radiographs to ensure patients met BTS definitions of a community acquired pneumonia. Demographics, co-morbidities, CURB-65 score, medications and outcomes were recorded. The cohort (n=2068) was divided according to prior statin use. The predicted probability of death (PPoD) was calculated using binomial logistic regression, controlling for age and gender. Patients taking statins were then stratified according to statin dose. Since most patients within the cohort were taking Simvastatin, dose response analysis was performed for Simvastatin alone.

Conclusions

1. We present decreased mortality in patients admitted with community acquired pneumonia with a prior history of statin use compared with patients not on a statin prior to admission. This was seen despite statin users being older and having more co-morbidities.

2. A clear dose response was also seen, with a lower PPoD was seen with higher doses of statins. The PPoD decreased sharply with increasing simvastatin dose suggesting that higher statin doses were associated with decreased mortality.

3. These results are consistent with animal studies which have suggested that statins may have pleiotropic effects which modulate neutrophil function, reducing acute lung injury, cytokine release and vascular permeability in acute infections. Previous human studies have also suggested that statins may improve outcomes in pneumonia, however this is the first time a positive dose response has been reported.

4. Further work is needed to study patient characteristics within each group in detail to determine if other clinical factors or treatment regimens may have impacted on survival.

5. Further work should also determine if there were any negative effects on liver function or muscle enzymes with the continuation of a statin during an acute admission of pneumonia.

6. Although this study has been conducted retrospectively at a single center, we consider the substantial reduction in PPoD in the patients taking higher doses of statins to be sufficient grounds to investigate the relationship further by conducting a randomized controlled trial of statin therapy in community acquired pneumonia. Recruitment for this study (i.e. SIMPACT) is currently underway funded by the British Lung Foundation.

Table 1 – Patient demographics, co-morbidities and outcomes. Mann-Whitney U-test conducted for continuous variables and X2 test for categorical variables. Data presented as mean±SD or number (% of group).