Response

To the Editor:

We thank Teramoto and colleagues for their thoughtful and insightful comments regarding our recent article in CHEST (March 2009).1 They stated that most hospitalized patients with pneumonia (including those with community-acquired pneumonia [CAP] and hospital-acquired pneumonia) were elderly and that the incidence of aspiration pneumonia was high in those patients. They also mentioned the importance of assessing silent aspiration and their interpretation of the treatment of healthcare–associated pneumonia (HCAP).

Although they pointed out the age difference between patients with HCAP and CAP, we analyzed our data by adjusting the age distribution, and assessing the severity of illness in both patients with HCAP and CAP by the same clinical prediction rule.1 Taking into account these analytical backgrounds, the proportion of in-hospital mortality and the occurrence of potentially drug-resistant (PDR) pathogens were significantly higher among patients with moderate HCAP than among those that of CAP patients. Furthermore, the frequency of PDR pathogens was almost the same in patients with moderate and severe HCAP; whereas it was dependent on the severity of pneumonia in CAP patients; the occurrence of PDR pathogens was associated with the initial treatment failure and inappropriate antibiotic treatment. Therefore, as the first step to improve the outcomes of HCAP patients, our results suggest that HCAP, which has been categorized into CAP, should be identified as a distinct entity, as Teramoto and colleagues mentioned. Swallowing rehabilitation and oral care may improve the quality of the management for patients with HCAP.

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Financial/nonfinancial disclosures: The authors have reported to the ACCP that no significant conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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DOI: 10.1378/chest.09-1762

References


Heparin-Induced Thrombocytopenia

To the Editor:

Though elegant and scholarly, the recent review of heparin-induced thrombocytopenia (HIT) by Shantsibaba et al1 in CHEST (June 2009) pays scant attention to the weakness of the evidence supporting the diagnosis of HIT.

Heparin is invariably administered to individuals who have experienced a thrombosis or are at risk of one. Thus, a central question about HIT and thrombosis arises: is thrombosis in a heparinized patient because of the heparin or despite the heparin? Almost all published information is anecdotal; the exceptions are cited by Warkentin2 (see Table 1 in the article) and purport to show that the odds ratio for thrombosis in the presence of HIT, compared with that for thrombosis in heparinized patients without HIT, overwhelmingly favors a link.

However, thrombosis occurs in about 20% of patients who are at high risk despite heparin prophylaxis3, half of these patients have...
will have occult pulmonary emboli, and these may cause thrombocytopenia. Thus, the 1% of patients to whom heparin prophylaxis is administered and who are diagnosed as having HIT with thrombosis could be a subgroup of the 10% of patients with occult venous thrombosis and pulmonary emboli.

The seeming causative role of the heparin-platelet factor 4 antibody binding to platelets in provoking thrombosis must also be questioned because a positive test result for the antibody is overwhelmingly falsely positive. Moreover, while it is appealing to link the propensity for heparin to generate an antibody with consequent thrombocytopenia and thrombosis, that possible linkage remains to be proven. Antiplatelet antibodies may cause thrombocytopenia without thrombosis; idiosyncratic thrombocytopenia purpura, in which there is antibody-mediated thrombocytopenia but no thrombosis, is a clear example.

An additional complexity in evaluating the HIT literature is that there are relatively few events in any single series. For example, in one article evaluating 598 patients who were receiving heparin, there were 3 patients with thrombosis among those in a group of 5 patients with HIT. This was described as a 60% incidence. But three events in a sample of five patients (considering 2 SDs as the pertinent range) encompass an incidence rate of 0% to 100%. Speaking of these data as showing a 60% incidence is potentially very misleading.

Thus, the question “is heparin responsible for the thromboses that may occur in heparinized patients?” is, the author believes, unanswerable with the currently available data. This does not argue that the current paradigm is in error or that current management guidelines are misdirected. It does argue that both remain to be proven correct.

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DOI: 10.1378/chest.09-1494

REFERENCES


Response

To the Editor:

Pollack challenges the existence of heparin-induced thrombocytopenia (HIT) as an independent, clinically relevant entity. Admittedly, it may be difficult to establish precise pathophysiologic links in rare conditions such as HIT. However, a number of facts support the existence of a heparin-triggered, immune system-mediated platelet activation and thrombocytopenia phenomena, which are often accompanied by severe thrombotic complications.

The administration of heparin can increase platelet factor 4 levels 15-fold to 30-fold and often causes the formation of autoantibodies to heparin-platelet factor 4 complexes. Importantly, treatment with low-molecular-weight heparins rarely stimulates the formation of antibodies when compared with unfractioned heparin (ie, approximately 5% vs 20%, respectively), and, correspondingly, low-molecular-weight heparins have a much lower risk for the development of the syndrome defined as HIT.

We agree that heparin is often associated with a reduction in platelet count, irrespective of the immune system response. However, in the majority of cases, thrombocytopenia occurs during the first few days of heparin administration, and is mild, is not progressive, and ultimately is not associated with an increased risk of thrombosis. The prognosis becomes very different in those patients in whom thrombocytopenia develops following prolonged heparin administration (usually between 4 and 15 days), as discussed in our recent review in CHEST (June 2009). This type of thrombocytopenia is consistently linked to the presence of circulating heparin-platelet factor 4 antibodies and, as Pollack admits in his letter, with a dramatically increased risk of thrombotic complications.

Is it possible that the thrombotic risk associated with the syndrome described as HIT just reflects the natural risk of thrombosis that is attributable to the background disorders? Apparently not, as the risk of thrombosis in untreated HIT patients is estimated to be up to 50% and uniformly exceeds the probability of thrombosis related to background disorders. Of note, the risk of arterial thrombosis is also increased in patients with HIT, despite the presence of a very low platelet count.

These associations are further confirmed by the recognized ability of plasma from HIT patients to activate platelets from healthy donors. This phenomenon is not usually seen in patients with circulating heparin-platelet factor 4 antibodies and thus serves as a basis for diagnostic platelet activation tests (eg, the serotonin release assay). Additionally, HIT is more often seen with bovine heparin, when compared with porcine heparin, probably reflecting the different levels of immunogenicity of heparin derived from various species.

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Financial/nonfinancial disclosures: The authors have reported to the ACCP that no significant conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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DOI: 10.1378/chest.09-1753