Fatal pulmonary embolism (PE) is a major cause of mortality in patients with spinal cord injury. In order to ascertain those characteristics that might predict this event, we reviewed the records of all patients with autopsy-proven massive PE admitted to a regional spinal cord care center over a 5-year period. The information analyzed included patient age, sex, race, height, weight, type of accident, prior use of tobacco, alcohol, or narcotic drugs, level of injury, presence of spasticity, surgical procedures, infections, transfusions, and type of anticoagulant prophylaxis. Forty-two concurrently hospitalized patients with spinal cord injury served as control subjects. Significant differences between cases and control subjects were observed for level of injury (fewer thoracic and lumbar injuries in cases, \( p = 0.04 \)), less spasticity in cases (\( p = 0.01 \)), and greater body mass index in cases (\( p = 0.01 \)). There was also a trend toward more advanced age in the cases (\( p = 0.1 \)) and more frequent serious infections (\( p = 0.08 \)). Lastly, low molecular weight heparin had been used as thromboprophylaxis in a greater proportion of control subjects than cases (60 percent vs 22 percent, \( p = 0.07 \)), suggesting that low molecular weight heparin may be more effective in preventing fatal PE than unfractionated heparin.

Massive pulmonary embolism (PE) is a much dreaded event in clinical medicine. The subject is usually recovering from trauma or surgery when an activity, such as arising from bed or straining at stool, triggers the sudden onset of chest tightness, air hunger, and sense of impending death. Recognizing the association of PE with deep vein thrombosis has led physicians to use preventative measures such as early ambulation, compression boots, and anticoagulants, which have decreased the frequency of thromboembolic events. Nevertheless, fatal PE still occurs, especially in patients with spinal cord injury.

In 1963, Tribe[1] provided autopsy data on 150 subjects with spinal cord injury. Pulmonary embolism was considered the cause of death in 37 percent of those dying within 3 months of injury. In a subsequent report by the same investigator, fatal PE was noted in 15 of 500 (3 percent) spinal cord-injured patients.[2] In more recent studies of patients receiving thromboprophylaxis, 2 of 41 (5 percent)[3] and 2 of 48 (4 percent)[4] were reported with fatal PE.

We wondered whether there were any characteristics that might help identify those patients with spinal cord injury destined to have fatal embolism. Recognition of heightened risk would intensify efforts at thromboprophylaxis: for example, early insertion of an inferior vena cava filter or more aggressive anticoagulant prophylaxis. To determine if there are predictive factors for massive PE, we reviewed the charts of all patients who died of massive PE during a 5-year period, as well as a control group of patients seen concurrently who did not have thromboembolism.

METHODS

We conducted a retrospective chart review of patients admitted to Northwestern Memorial Hospital and Rehabilitation Institute of Chicago with the diagnosis of acute spinal cord injury between 1987 and 1992. Nine cases of autopsy-proven massive PE were encountered among 51 charts reviewed; the 42 non-PE cases were considered control cases, and consisted of all patients with complete motor paralysis with informed consent for chart review. The following patient characteristics were recorded: age, sex, race, height, weight, type of accident, prior use of tobacco, alcohol, or narcotic drugs, level of injury, and the presence of spasticity (defined either clinically or inferred from the prescription of spasmolytic drugs). Also recorded were surgical procedures during hospitalization, complications (infections, transfusions), the prophylactic regimen used for thrombus prevention, and the number of days between the injury and discharge or fatal PE. In addition, body mass index (BMI) (weight in kilograms divided by the height in meters squared) was calculated. Obesity was defined as a BMI [greater than]26.4 that corresponds to an excess body weight of [greater than]20 percent.[5]

Fatal and nonfatal cases were compared statistically using Fisher's exact test, the \([\text{chi}].\sup{2}\) test for categorical factors, and the unpaired student's t test for continuous factors. Statistical significance was indicated if two-tailed p
values were 0.05 or less.

RESULTS

Fatal PE occurred in eight men and one woman. The patients ranged in age from 17 to 67 years (mean, 37 years; median, 38 years); five were white, three were black, and one was Hispanic. Five were injured as a result of motor vehicle accidents, three by falls, and one by diving. Half the patients had a history of cigarette smoking, two were using alcohol at the time of the accident, and one was an intravenous drug abuser. Six became tetraplegic, one paraplegic, and two had no neurologic deficit. Six of the patients had spinal fusions, and in seven, the hospital course was complicated by infection (pneumonia in three, urinary tract infection in one, septic arthritis in one, and unspecified sepsis in one). The fatal emboli occurred from 8 to 73 days following injury (mean, 36 days; median, 38 days).

Table 1 examines the characteristics of patients with spinal cord injury, comparing those with fatal PE to those without this event (control subjects). Factors such as age, sex, race, use of alcohol, tobacco, and narcotic drugs were similar in the two groups. Obesity (BMI $\geq 26.4$) was present in four of the cases (44 percent) and only five of the control subjects (15 percent). Cervical spine injury with tetraplegia was present in six of the nine cases; thoracic and lumbar spine injury was less prevalent than in the control subjects. Spasticity was present in none of the cases but more than half of the control subjects $p = 0.01$. There were no differences in the frequency of surgical procedures, transfusions, and complications, although there was a trend toward more pulmonary and other serious infections in the fatal PE cases.

All subjects received heparin prophylaxis by subcutaneous injection; unfractionated heparin was given in a dose of 5,000 U every 8 h and low molecular weight heparin (LMWH) in a dose of 3,500 U once daily. While only 2 of the 9 cases (22 percent) received LMWH, 25 of the 42 control subjects (60 percent) were treated with this agent $p = 0.07$.

DISCUSSION

This retrospective study of fatal PE in patients with spinal cord injury has shown that injury level, BMI, and absence of spasticity are significant factors predicting this event. Cervical spine fracture with tetraplegia was present in 67 percent, obesity in 44 percent, and none had developed spasticity. Other characteristics in this population were somewhat older age and more infections during hospitalization. Given the limitations of a retrospective study, a prospective analysis using predefined categories of risk factors should be conducted to confirm these observations.

In a recent review, Weingarden[6] observed that over the last 30 years, 8 studies had reported 222 instances of deep vein thrombosis and PE in 1,362 patients, for an incidence rate of 16.3 percent. This estimate was based on clinical evidence, which significantly underreports the true incidence of these disorders. When patients are systematically studied by venography, many who have no clinical evidence of venous thrombosis are found to have clots. In a series of 147 patients with acute spinal cord injury, 20 had clinical evidence of deep vein thrombosis, and an additional 29 had venographic evidence of thrombosis.[7] The authors further reported that there were 6 cases of fatal PE among the 328 patients in their files, an incidence of 1.5 percent.

There is surprisingly little published data on patient characteristics that may predict PE. In the Framingham study,[8] 46 subjects with autopsy-proven PE were analyzed with regard to age, blood pressure, cholesterol and glucose levels, cigarette use, and weight. Of these several variables, only weight was significantly and independently associated with PE, and only among women. In patients with spinal cord injury, the location and severity of the lesion predict risk; PE is more common in patients with tetraplegia than paraplegia and complete than incomplete paralysis.[9] In addition, the factors identified in the present investigation--high level of injury, increased BMI, lack of spasticity--contribute to venous stasis and increase thromboembolic risk.

Given these risk factors, how should the clinician attempt to prevent fatal PE in this patient population? One option would be the insertion of a vena caval filter as soon after injury as possible.[10] While this approach is associated with a high rate of success in preventing PE (from 95 percent to 97.3 percent effective in patients with proven deep vein thrombosis[11]), it requires venography and skilled personnel to place the device, thus increasing costs. In addition,
thrombi present in the iliofemoral vein may propagate proximally and extend through the filter, resulting in vena caval and/or renal vein occlusion. Migration of the filter and bowel perforation have been reported in some tetraplegics.[12]

A simpler approach may be through intensifying anticoagulant prophylaxis. While increased doses of unfractionated heparin may lead to bleeding, the LMWHs are accompanied by a low frequency of hemorrhage.[13] In previous studies in spinal cord-injured patients, only 1 of 68 (1.5 percent) had bleeding.[3] In that investigation, the LMWH was given in a daily fixed dose of 3,500 U subcutaneously; this is the dose received by the two patients shown in Table 1. It is possible that if the LMWH was given on a body weight basis (for example, 50 U/kg), efficacy might be improved. It should be noted that in a recent study of thromboprophylaxis in patients with hip surgery, the dose of LMWH was 75 U/kg, and bleeding was infrequent.[14] Since an increase in BMI was characteristic of the patients with fatal PE, dosing anticoagulants on a body weight basis would seem preferable and might save lives.

REFERENCES


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