Clinical Efficacy of Aspirin and Dextran for Thromboprophylaxis in Geriatric Hip Fracture Patients

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Summary: The clinical efficacy of thromboprophylaxis with aspirin and dextran 40 was compared in a prospective review of 530 geriatric hip fracture patients treated surgically. All patients were also treated with early mobilization with weight bearing as tolerated and above-knee elastic stockings. In addition to clinical efficacy in preventing thromboembolic complications (deep vein thrombosis (DVT), pulmonary embolism (PE)), safety and cost-effectiveness were also assessed. The overall incidence of clinical thromboembolic disease was 2.8% (DVT = 0.4%, PE = 2.4%). The incidence of DVT (0.5%) and PE (2.6%) in the aspirin group was essentially the same as the incidence of DVT (0.3%) and PE (2.4%) in the dextran group. The in-hospital mortality rate (aspirin 4.6%, dextran 3.8%), wound drainage (aspirin 1.5%, dextran 0.9%), deep wound infection (aspirin 0.5%, dextran 0.3%), gastrointestinal bleeding (aspirin 2.1%, dextran 1.5%), and congestive heart failure (aspirin 2.6%, dextran 1.8%) did not differ significantly between the two groups. The intraoperative transfusion rate was similar in both groups (aspirin .65 units, dextran .55 units). However, postoperatively, the transfusion rate was significantly higher in the dextran group (aspirin .26 units, dextran .41 units, p < .05). The treatment of thromboembolic complications was the same for each group and therefore represents similar treatment costs. However, the cost of prophylaxis with dextran was $309 per patient and with aspirin was $1.79 per patient. Our findings suggest that, based on clinical diagnostic criteria, aspirin and dextran are equally effective thromboembolic prophylactic agents in geriatric hip fracture patients. The safety, cost, and ease of administration of aspirin may make its use more desirable. Key Words: Hip fracture, geriatric—Aspirin—Dextran 40—Thromboprophylaxis.

Geriatric hip fracture patients may be at increased risk for thromboembolic complications because of their increased age, recumbency, precedent trauma, and the required surgical management. The incidence of clinical thrombophlebitis following hip fracture has been reported as 5 to 40%, and the incidence of pulmonary emboli (PE) (fatal and nonfatal) has been reported as 4 to 24% of patients (10).

Preventive measures fall into two basic categories: first, physical methods that include early ambulation, elastic stockings, elevation of the lower limb, lower extremity sequential compressive devices, and vena cava filter; second, pharmacologic methods including antithrombotic drugs like heparin, dextran, aspirin, and warfarin (5,6). There have been a number of investigations using a combination of these methods. Advocates of many of these methods have based their conclusions on comparative studies using physical exam as well as invasive and noninvasive studies to detect thrombi (5,10,11, 16).
Dextran 40 is a branched polysaccharide that contains D-glucose units in a predominantly 1-6 linkage. It promotes a dissolution of thrombi without significantly altering the function of coagulation factors contained in plasma. This is accomplished by decreasing blood viscosity, inhibiting aggregation of platelets, and coating vascular endothelium. The complications associated with dextran 40 therapy include volume overload with a potential risk of congestive heart failure, anaphylaxis, and acute renal failure (9).

Aspirin in low doses (<1000 mg per day) interferes with platelet function by blocking the production of thromboxane A₂. Complications of aspirin use include gastrointestinal bleeding and wound hematoma (9,14).

We evaluated the efficacy, safety, and cost of thromboembolic prophylaxis used in our hospital between August 1985 and June 1990 following hip fracture in the geriatric population. The purpose of this study was to compare the efficacy, safety, and cost of thromboprophylaxis regimens used in the treatment of geriatric hip fracture patients.

MATERIALS AND METHODS

All patients admitted to the Hospital for Joint Diseases between August 1985 and June 1990 for the treatment of a fracture of the proximal femur were evaluated for inclusion in the study. For inclusion, patients had to be ≥65 years of age with a fracture of nonpathological origin; ambulatory before fracture with or without assistive devices; sufficiently cognitively intact to participate in the postoperative rehabilitation program; have no history of thromboembolic events [deep venous thrombosis (DVT) and PE]; and have received postoperative thromboprophylaxis consisting of either dextran 40 or low dose aspirin combined with early weight-bearing ambulation and elastic stockings.

Patients who met these criteria were followed prospectively, and all pertinent information was entered into a computerized database. Patients were divided into two groups based on the thromboprophylactic regimen utilized: dextran 40 versus low dose aspirin. The regimen chosen was not randomized but was based on the surgeon’s preference. In general, aspirin was avoided in patients with a history of peptic ulcer disease or gastrointestinal bleeding; and dextran 40 was avoided in patients with a history of congestive heart failure, pulmonary edema, or significant cardiac insufficiency. However, the most important factor determining the choice of thromboprophylaxis was surgeons’ preference.

The dextran 40 group received 50 g of dextran 40 in 300 to 500 cc of saline administered i.v. during surgery followed by a similar dose daily until the day of discharge. The aspirin group received ≤325 mg in tablet form starting on the day of surgery until the day of discharge. On postoperative day one, the patients were mobilized out of bed to chair. Weight bearing as tolerated with ambulation was started on postoperative day two. This early mobilization program was followed in the majority of cases. Changes in this approach were required in a small percentage of patients and generally included those who required monitoring in the intensive care unit during the early postoperative period.

During the hospitalization, all patients were examined daily by the orthopaedic staff. When DVT was suspected clinically, a venogram was ordered. If a PE was suspected, a ventilation/perfusion scan was obtained. If this was inconclusive, a pulmonary angiogram was performed. If a diagnosis of either DVT or PE was confirmed, the patient was started on heparin anticoagulation followed by conversion to oral warfarin. Coagulation status was followed by serial partial thromboplastin time and prothrombin time. Patients were allowed to resume ambulation after adequate anticoagulation was obtained. The treatment of thromboembolic complications was the same for both thromboprophylaxis groups.

In addition to the prospective data collection, the charts of all patients with DVT or PE were carefully reviewed to ascertain the details of treatment. Statistical analysis was performed using the chi-square test with Yate’s correction to evaluate for significance.

RESULTS

A total of 530 patients fulfilled the criteria for inclusion in this study: 338 in the dextran 40 group and 192 in the aspirin group. Each group was characterized with respect to multiple prefracture hospitalization characteristics including age, sex, number of co-morbid conditions, number of medications, length of surgery, anesthetic type, surgery type, and hospital length of stay. This data is summarized in Table 1. There were no significant differences between the two groups except for the number of co-morbid conditions, which was greater in the aspirin group (p < .004).
TABLE 1. Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Dextran 40</th>
<th>Aspirin</th>
<th>NS</th>
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</thead>
<tbody>
<tr>
<td>Average age</td>
<td>79.6</td>
<td>80.7</td>
<td></td>
</tr>
<tr>
<td>No. patients</td>
<td>338</td>
<td>192</td>
<td></td>
</tr>
<tr>
<td>No. men</td>
<td>66 (19.5%)</td>
<td>33 (17.2%)</td>
<td></td>
</tr>
<tr>
<td>No. women</td>
<td>272 (80.5%)</td>
<td>159 (82.8%)</td>
<td></td>
</tr>
<tr>
<td>Average length of</td>
<td>118.5 min</td>
<td>114.0 min</td>
<td>NS</td>
</tr>
<tr>
<td>surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average no. of</td>
<td>1.46</td>
<td>1.82</td>
<td>(p &lt; .05)</td>
</tr>
<tr>
<td>co-morbid conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average ASA rating</td>
<td>2.25</td>
<td>2.29</td>
<td>NS</td>
</tr>
<tr>
<td>Average length of</td>
<td>22.2 days</td>
<td>24.0 days</td>
<td>NS</td>
</tr>
<tr>
<td>stay in hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fracture type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femoral neck</td>
<td>174 (51.5%)</td>
<td>93 (48.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>Intertrochanteric</td>
<td>164 (48.5%)</td>
<td>99 (51.6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Surgery type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORIF</td>
<td>203 (60.1%)</td>
<td>134 (69.8%)</td>
<td>NS</td>
</tr>
<tr>
<td>Endoprosthesis</td>
<td>135 (39.9%)</td>
<td>58 (30.2)</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, not significant; ORIF, open reduction-internal fixation.

Thromboembolic complications were similar in each group. The incidence of thrombophlebitis was 0.3% in the dextran group and 0.5% in the aspirin group. Nonfatal PE occurred in 1.5% of the dextran group and 0.5% of the aspirin group (p < .05). Fatal PE occurred in 0.9% of the dextran group and 2.1% of the aspirin group. This difference was not statistically significant. Total inhospital mortality was 3.8% in the dextran group and 4.6% in the aspirin group (p > .05). Analysis of this data for men and women within each group also did not show any significant differences for thromboembolic complications.

The medical records of all 22 patients who died in the hospital were reviewed. The cause of death was determined by clinical information; no autopsies were performed. Of these 22 patients, the cause of death was PE in four and other nonthromboembolic complications in 15 patients. There were three patients for whom a cause of death could not be established. Two of these patients were in the aspirin group and one in the dextran group. These deaths were considered secondary to thromboembolic complications so that we would not be underestimating the incidence of fatal PEs. These results are summarized in Table 2.

Complications most commonly associated with aspirin used included gastrointestinal bleeding and mild renal insufficiency. Dextran may cause volume overload (congestive heart failure), renal failure, and anaphylaxis. Comparison of the incidence of these complications and others between the two groups showed no significant difference (Table 3). The intraoperative transfusion rate was similar in both groups (aspirin .65 units, dextran .55 units). However, the postoperative transfusion rate was significantly greater in the dextran group (aspirin .26 units, dextran .41 units, p < .05).

The treatment of thromboembolic complications was essentially the same in the two groups. Intravenous heparin therapy was started immediately at a dose that maintained the partial thromboplastin time to two times control. Coumadin was begun 3 to 5 days later and maintained at a dose to elevate the prothrombin time to 1{1/2} times control. The cost for the treatment of this complication was essentially the same for both groups.

However, based on the average hospital length of stay for each group, the cost of prophylaxis was $309 for dextran and $1.79 for aspirin. The cost estimates include the drug, i.v. fluid, tubing, and angiocatheter. However, the estimate did not include personnel costs associated with administration of the medication or caring for and changing i.v. lines, which would obviously be significantly greater for the dextran group.

DISCUSSION

The incidence and significance of thromboembolic complication following hip fracture has been a frequent subject in the literature over the past three decades. In general, the reports have been variable and confusing, especially concerning the incidence of these complications. It has been assumed since the autopsy study of Sevitt and Gallagher in 1959...
that prophylactic anticoagulation treatment was required in hip fracture patients to reduce the reported 18% incidence of PE and 29% incidence of DVT to 2% and 3%, respectively, with prophylaxis (17). One of the reasons confusion exists is that some studies have documented the incidence of asymptomatic and symptomatic thrombi while others have reported only symptomatic thrombi. For example, Johansson (12) reported a 12% incidence of asymptomatic DVT while Bergqvist (4) found a 64% incidence of asymptomatic DVT. Neither study used prophylaxis. Recently, Løtke and Day have questioned the need for antithrombic prophylaxis. They cite a low incidence of clinically significant DVTs and PEs (<1%) in untreated patients and question the risk–benefit ratio for prophylaxis with ≤20% wound complication rate with the use of warfarin or dextran. They also question the causative relationship between DVT and PE (8,13).

When prophylaxis has been used, the effectiveness of the different regimens has been variable. Alho compared aspirin, warfarin, and heparin in a prospective randomized trial utilizing clinical diagnosis as the indication for venography or V/Q scan. He found warfarin (DVT 2.5%, PE 0.5%) and aspirin (DVT 3%, PE 0.5%) equally effective and only marginally better than heparin (DVT 4.2%, PE 2.1%) in preventing PE (2). Other studies have reported conflicting data with the use of aspirin (2,7, 10). Although some reports have demonstrated the effectiveness of dextran, other authors have reported a mean incidence of 8.5% for DVT and 3% for PE with the use of dextran. However, these results were significantly better than the incidence of thromboembolic complications found in their control groups (1,3,10,12,15).

Our results demonstrate a low incidence of thromboembolic complications compared to other reports. This was true for both treatment regimens. Recognition of the importance of early mobilization starting on the first postoperative day with weight bearing as tolerated thereafter may be one reason for the decreased incidence of thromboembolic complications when comparing studies from the 1960s and 1970s in which mobilization was often delayed. In addition, our incidence of DVT was based on the clinical suspicion of DVT which may have resulted in an underestimation. However, our incidence of fatal PE may be overestimated because we included all sudden deaths of unknown cause in this category. Although both treatment groups had a low incidence of thromboembolic complications, this study did not include patients without prophylaxis. An important treatment group for comparison would be early mobilization and antiembolic stockings without prophylaxis.

The incidence of complications of treatment was low in each treatment group. Overall, only 2.1% developed congestive heart failure and 1.9% developed gastrointestinal bleeds. Because this was not a randomized study, the choice of dextran or aspirin was made by the surgeon. In general, when patients had a history of congestive heart failure, aspirin was used.

The increased transfusion rate postoperatively in the dextran group may be due either to increased postoperative bleeding in the dextran treated patients or possibly to hemodilution with dextran and therefore unnecessary transfusions.

It is important to emphasize that although all data in this study were collected prospectively, it was not a prospective randomized study. The decision to utilize aspirin or dextran was based on surgeon preference, which reflects an inherent bias. Better methodology would have been to utilize a prospective randomized study design including an objective assessment of thrombophlebitis (i.e., venogram, ultrasound, etc.). A design of this type would be expected to produce stronger and more incisive conclusions than the present study.

Based on the clinical results reported, aspirin is as effective as dextran 40 for prophylaxis in geriatric hip fracture patients. Dextran 40 has not gained wide acceptance because of its high cost, need for i.v. administration, and potential for side effects. Aspirin is better accepted and relatively free from side effects. Considering the added costs and discomfort associated with dextran administration as well as the increased transfusion rate in these patients, it is our feeling that aspirin is preferred over dextran 40 for thromboprophylaxis in geriatric hip fracture patients.

REFERENCES

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