Antiplatelet drug use in a diabetic clinic

A. WOODWARD, D. BAYLEY, L. OVEREND and G. GILL

From the Department of Diabetes and Endocrinology, University Hospital Aintree, Liverpool, UK

Received 7 March 2007 and in revised form 3 May 2007

Summary

Background: There are definite indications for antiplatelet therapy in diabetes in the presence of large-vessel disease, but in the absence of large-vessel disease, the evidence is less clear. There is also evidence that antiplatelet therapy is under-prescribed.

Aim: To investigate the use of antiplatelet drugs in patients attending a diabetic clinic in a large teaching hospital.

Design: Retrospective case-note survey.

Methods: We examined the case-notes of 300 consecutive diabetic patients, to determine whether antiplatelet therapy was being used in appropriate patients, including those with established large-vessel disease, hypertension and nephropathy or microalbuminuria.

Results: The patients were of mean ± SD age 61 ± 13 years, diabetes duration 10 ± 8 years, BMI 31.4 ± 6.7 kg/m² and HbA1c 8.3 ± 1.5%; 276 (92%) had type 2 diabetes, and 162 (54%) were male. Antiplatelet drugs were being taken by 157 (52%) who fulfilled the survey standard for treatment; a further 83 (28%) met the survey standard but were not receiving treatment, of whom 48 (16% of the total group) had no valid contraindication.

Discussion: A significant minority of diabetic patients are being denied antiplatelet drugs despite good indications.

Introduction

Diabetic patients are at high risk of macrovascular disease, notably ischaemic heart disease (IHD), cerebrovascular disease (CVD) and peripheral vascular disease (PVD). When these complications are established, antiplatelet therapy (aspirin or clopidogrel) is unquestionably beneficial. However, the indications for such treatment without established macrovascular disease (i.e. primary prevention) are less certain, and this is reflected by somewhat variable guidelines. Currently, in the UK (Joint British Societies), it is suggested that all diabetic patients over 50 years should receive aspirin, and those under 50 years should be treated if they have had diabetes for over 10 years; or have hypertension, retinopathy or nephropathy. More recently, US guidelines (American Diabetic Association) recommend aspirin for diabetic patients over 40 years of age, or under 40 years with ‘additional risk factors’.

Shortly before the publication of JBS 2, we investigated antiplatelet therapy usage in the Diabetic Clinic of a large north Liverpool teaching hospital, to assess current practice in the climate of a weak evidence base and confusing guidelines.

Methods

We surveyed the case-notes of 300 consecutive patients who were attending the Diabetes Centre follow-up clinics at the University Hospital Aintree,
Liverpool, over a 3-month period between January and March, 2005. All types of diabetes were included. Data were recorded onto proforma by a research nurse and later transferred to an Excel 2000 spreadsheet (Microsoft). These data included demographic details, body mass index (BMI), glycated haemoglobin (HbA1c), diabetic complications, presence of hypertension, and antiplatelet drug usage. HbA1c was measured by a DCCT-aligned HPLC system (non-diabetic range 4.2–6.0%).

Definitions
Hypertension was diagnosed if the patient was on antihypertensive therapy. Our clinic criterion for the presence of microalbuminuria was at least two separate urinary albumin-creatinine ratio (ACR) values >2.5 mg/mmol in men, or >3.5 mg/mmol in women. Nephropathy was considered present if persistent macroalbuminuria (dipstix-positive) occurred with no definable non-diabetic cause, and retinopathy was present.

Survey standard
As a standard to judge performance against, we defined ‘high-risk’ patients suitable for antiplatelet therapy as having any one of the following characteristics: (i) established large-vessel disease (IHD, PVD or CVD); (ii) hypertension (blood pressure controlled to <150/90 mmHg); (iii) nephropathy or microalbuminuria. We did not include risk factors such as dyslipidaemia and smoking, because of a weak evidence-base.

Statistics
We used a StatsDirect biomedical software package. Results were expressed as percentages for proportionate data, and means ± SD for quantitative data.

Survey registration
The project was registered with the Audit Department of University Hospital Aintree NHS Trust.

Results
Patient characteristics
The 300 patients were of mean ± SD age 61 ± 13 years, diabetes duration 10 ± 8 years, BMI 31.4 ± 6.7 kg/m² and HbA1c 8.3 ± 1.5%. There were 162 (54%) males, and 276 (92%) had type 2 diabetes.

Table 1 Complication details of study group (n = 300)

<table>
<thead>
<tr>
<th>Complication</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrovascular disease</td>
<td>109 (36%)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>77 (26%)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>25 (8%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>37 (12%)</td>
</tr>
<tr>
<td>&gt;1 macrovascular disease</td>
<td>30 (10%)</td>
</tr>
<tr>
<td>Microvascular disease</td>
<td></td>
</tr>
<tr>
<td>Retinopathy</td>
<td>88 (29%)</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>29 (10%)</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>77 (26%)</td>
</tr>
<tr>
<td>&gt;1 microvascular disease</td>
<td>22 (7%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>214 (71%)</td>
</tr>
</tbody>
</table>

There were 240 patients (80%) with two or more complications, and 134 (45%) with three or more.

Table 2 Indications for antiplatelet drugs in 83 (28% of total) untreated patients

<table>
<thead>
<tr>
<th>Indication</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrovascular disease</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>8 (3%)</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>18 (6%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>41 (14%)</td>
</tr>
</tbody>
</table>

Thirty-one patients (10%) had more than one of the above indications.

Complications
Large- and small-vessel complications are shown in Table 1. The commonest complications were IHD (26%), retinopathy (29%) and microalbuminuria (26%). There were 214 (71%) with hypertension.

Antiplatelet drug use
Antiplatelet drugs were used in 162 (54%) patients, 157 (52%) of whom fulfilled our survey standard. The remaining five were on treatment because of dyslipidaemia (i.e. requiring a lipid-lowering drug). Of the total 157 patients on antiplatelet drugs, 140 (89%) were on aspirin, 11 (7%) on clopidogrel, 5 (3%) on aspirin and clopidogrel, and 1 (<1%) on dipyridamole.

Under-use of antiplatelet drugs
As well as the 157 (52%) on antiplatelet drugs, there were 83 (28%) not receiving treatment, but who fulfilled the survey standard. Their indications for treatment are shown in Table 2. Of particular concern, 16 (5%) of these patients had established
macrovascular disease. Hypertension was the commonest indication 41 (14%), and 31 (10%) of patients had more than one indication for antiplatelet therapy. We examined the notes of this group of patients carefully, as at least some may have had valid contraindications to antiplatelet drug use (Table 3), but there remained 48 patients (16%) with no valid contraindication: 8 with established macrovascular disease, 18 with microalbuminuria and 22 with hypertension.

Discussion

The current evidence base for the use of antiplatelet drugs in diabetes is confusing. Their benefit in secondary prevention (with established large-vessel disease) is unquestioned, and there is also evidence that aspirin is beneficial with type 2 diabetes and hypertension, without macrovascular disease. An extreme view is that all type 2 patients should have aspirin for primary prevention, as they have similar coronary risk profiles to non-diabetic subjects with established IHD. However, UK data on coronary mortality in type 2 diabetes suggest a lower risk than from the original Finnish data that supported this view. Other authors have reported ‘aspirin resistance’ in patients with type 2 diabetes, resulting in a lower effect of primary prevention, thus suggesting a need for large-scale controlled studies in diabetic patients. A further problem from the literature is that there is little or no direct or indirect information concerning antiplatelet usage in type 1 diabetes. Finally, the place of clopidogrel is uncertain—there is some evidence that it may be superior to aspirin in diabetic patients, but this has not generally been translated into common clinical practice, perhaps because of cost issues.

Our survey was done shortly before the recently published UK and US guidelines for antiplatelet drug usage in diabetes. We therefore based our survey standard on guidelines in place at the time: (i) presence of established macroangiopathy; (ii) hypertension without macroangiopathy; and (iii) nephropathy or microalbuminuria. Some guidelines also used an estimated 10-year coronary event risk of 15% or more as an indication for antiplatelet drugs, but as this criterion was not evidence-based, and was rarely available to clinicians in busy diabetic clinics, it was not used in our survey standard.

In our large group of predominantly type 2 diabetic patients, antiplatelet drug use was common (54%), with most (89%) on aspirin. A further 83 (28%) of the group were not on antiplatelet drugs, but fulfilled our survey standard criteria. However, a number of these had valid contraindications; though there was still a substantial proportion (48, 16%) who had no clear reason not to be on antiplatelet drugs, including eight who should have received therapy for secondary prevention.

Under-use of aspirin in UK diabetic clinics has been highlighted previously, and the authors of this report and others have drawn attention to the lack of evidence for antiplatelet drug benefits in type 2 diabetes. Similar findings have been reported outside the UK, suggesting ambiguity amongst prescribers regarding the role of aspirin. This may lead to clinical confusion, mistrust of current guidelines (which include non-evidence-based indications), and general under-use of these drugs.

We believe that the survey standard guidelines we adopted were suitable and reasonably evidence-based; despite this, 16% of eligible patients were denied the simple and inexpensive prescription of aspirin. Since this survey, in our patient clinic records we have inserted an antiplatelet box on the clinic proforma sheet, which is completed each time the patient attends. Diabetic clinics could make active efforts to ensure that patients are considered for antiplatelet therapy.

Acknowledgements

This study was sponsored by an unrestricted educational grant from Sanofi Pharma Bristol-Myers Squibb SNC.

References


