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EDITORIAL

Switching among oral anticoagulants: is it logical?

It has almost been a century since the outbreak of sweet clover disease in North America which led to the discovery of warfarin and its derivatives. It was not known that a farmers' problem would turn out to be a useful treatment for many patients[1]. Today, oral anticoagulant (OAC) therapy is the cornerstone for stroke prevention in patients with atrial fibrillation (AF). The only available OACs have been the vitamin K antagonists (VKA) for more than 50 years but they have some well-known problems such as drug-drug, drug-food interactions and low therapeutic index. The development of direct oral anticoagulants (DOAC) changed the management of non-valvular atrial fibrillation (NVAF) patients dramatically in the last decade[2]. They have some advantages compared with VKAs, like fixed dose and predictable effects (i.e. no need for monitoring)[3].

One of the major problems with OACs is adherence. Anticoagulation should be a lifetime process in patients with NVAF; poor adherence will place these patients at a higher risk of stroke. Drugs work only if patients take them[4]. Patients on DOACs tend to have a better profile in terms of adherence compared with patients on VKAs which might partly explain the favourable effects of these drugs[5]. Among DOACs, apixaban treated patients were less likely to discontinue or switch to another OAC[6] which might also be an advantage for the drug.

The introduction of DOACs into clinical practice has resulted in another problem that has not been the case before, i.e. the option to switch from one OAC to another. While treatment changes from VKA to other OACs could be related to lower time in therapeutic range (TTR) values, changes from DOAC to another OAC could be related with a major clinical event. A Danish study has shown the most common reason leading up to a switch from DOAC to VKA was cardioversion[7]. Another study has also shown that switching among OACs was associated with increased rate of clinical events[4]. Patients who switch from one OAC to another might be at higher risk for clinical events which might explain the higher event rate. However, some studies have shown that switching from VKA to DOAC does not alter the risk of haemorrhagic complications in patients with NVAF[8]. Real-world outcome studies have shown that the annualized medical and total costs were lower with DOACs compared with VKAs although pharmacy costs were higher with DOACs[9]. Hence, it is not logical to switch from a DOAC to VKA because of higher pharmacy cost.

Elderly patients have an increased risk for stroke, however, OACs were generally less prescribed to these patients because of comorbidities[10]. Frailty, chronic renal disease and polypharmacy are the main contributors of elevated embolic and bleeding risk in these patients that have to be taken into consideration when making a decision on OAC therapy[11]. We showed that physicians tend to prescribe more OAC for elderly NVAF patients if they had elevated risk score for stroke and lower risk score for bleeding[10]. However, currently available risk scores are far from perfect. Hence the benefits and risks of OACs should be carefully evaluated and the management of NVAF should be individualized[12]. If a decision is made to anticoagulate an elderly patient, it should be known that the net benefit of DOACs seems consistent in pivotal DOAC trials and an even greater benefit of these drugs has been shown by real-world data[13]. Therefore, most of the elderly NVAF patients should be on an OAC and preferentially on a DOAC.

A recent study from the *Journal* reported that patients who switch from apixaban to another OAC had a twice higher risk for major bleeding related hospitalization rates compared with patients who continue apixaban treatment[14]. Interestingly most of the switchers had switched from apixaban to warfarin which might be a confirmation of the safety of DOACs and especially apixaban. However, they could not demonstrate any association between stroke/systemic embolization risk and switching among drugs. Major bleeding related medical costs, stroke/systemic embolism related medical costs and total all cause medical costs were higher for switchers. The results might not be unexpected as the costs went up if a patient had a clinical event. However, total all-cause healthcare costs were similar between switchers and continuers. This might be related to the pharmacy costs of apixaban as mentioned by the authors. One might expect that the drug costs would decrease but medical costs would increase with time. Hence, it is reasonable to avoid switching from apixaban to another OAC and probably from DOACs to VKAs.

Switching to different OAC might sometimes be an obligation because of worsening renal/hepatic function or starting an interacting drug. In this case, it is important to test the INR and to start the OAC in an appropriate time[2]. When switching from DOAC to VKA the INR should be checked and DOAC should not be stopped before INR $>$ 2 which usually takes 3–4 days. Patients are vulnerable in this period and early discontinuation of DOAC may lead to excess in thromboembolic event rates. The opposite is also true as early initiation of DOAC may lead to increased bleeding events. It is utmost important to follow the well-established guidelines when performing a necessary switch among OACs[15].

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