ANTICOAGULANTS: EVALUATION OF RISKS/BENEFIT RATIO

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ABSTRACT

Anticoagulants have been part of our life for over a hundred years. During this time, scientists, chemists and physicians have introduced several life saving drugs, none of which is 100% safe. Whenever a physician treats a patient with an anticoagulant, he/she is always faced with a dilemma: "I want to have the most benefit and none of the risks following the use of these agents". We have researched the risk and benefit profile of warfarin and DOACs in this presentation.

INTRODUCTION

Management of VTE is always a challenge. One of the treatment options is the prescription of anticoagulants. Besides being beneficial, the anticoagulants also possess one challenge: safety. By assessing the risk-benefit ratio of different anticoagulants, including warfarin and DOACs, one can develop a good understanding of which anticoagulant will be the best option to treat their VTE. We have researched the risk and benefit profile of warfarin and DOACs in this presentation. We recommend that each physician should utilize his or her expertise in making a careful selection of the anticoagulant based on the efficacy and safety profile.

RISK-BENEFIT RATIO

1. The risk-benefit ratio involves a careful decision by a physician for every patient when using a drug for management of a condition.
2. No drug is safe by any means, and each drug has some safety issues.
3. The physician is thus left with a very fine line decision between to treat the patient with the drug to relieve the symptoms, and yet there should be minimal, or no side effects.
4. Without a careful process between the risk and the benefits, the patients could be exposed to significant safety issues.
5. We selected warfarin and the Direct Oral AntiCoagulants (DOAC's) for our research.

WARFARIN

1. Warfarin is used to treat or prevent blood clots, which can reduce the risk of stroke in patients with atrial fibrillation, VTE, and prosthetic valves.
2. Acts by inhibiting the action of Vitamin K.
3. In patients taking warfarin, the INR must be adjusted.
4. Significant dietary restrictions exist for the use of warfarin.

DOAC'S

- In recent years, Direct Oral AntiCoagulants (DOACs: dabigatran, rivaroxaban, apixaban and edoxaban), have been introduced for stroke prevention.
- DOAC is a generic term for a group of anticoagulats that act directly against certain coagulation factors.
- DOAC's include direct thrombin inhibitors (DTIs, dabigatran) and direct factor Xa inhibitors (rivaroxaban, apixaban, edoxaban, betrixaban).
- No need for INR monitoring .
- No dietary restrictions.
- Used in the management of VTE, atrial fibrillation, and stroke.

DOAC'S IN MANAGEMENT OF VTE

1. DOAC's are effective in reducing stroke risk in atrial fibrillation (AF).
2. Apixaban, dabigatran and rivaroxaban have shown different results:
3. Apixaban reduces risk of stroke without increasing risk of major bleeding or intracranial hemorrhage.
4. Dabigatran 150 mg reduces risk of stroke with similar bleeding risk, but slightly increases gastrointestinal bleeding and myocardial infarction risk.
5. Rivaroxaban may be as effective as warfarin in preventing stroke or systemic embolism.
6. The DOAC's also have risks such as: major bleeding, fatal bleeding and intracranial hemorrhage.

MULTI CRITERIA DECISION ANALYSIS (MCDA) AND ANTICOAGULANT AGENTS

1. MCDA is a method for supporting decisions for assessing risks and benefits of medical therapies.
2. MCDA applies 3 levels of criteria (top level criteria, mid-level criteria, bottom level sub-criteria) relating to 3 key domains (a) burden of disease, (b) beneficial effect, (c) safety profile.

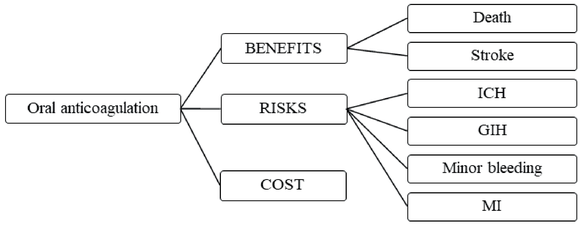

Figure 1: Display of benefits, risks, and costs

MULTI CRITERIA DECISION ANALYSIS (MCDA) AND ANTICOAGULANT AGENTS

The MCDA analysis scores were:
Apixaban 33 (safest, most effective, but costly) .
Dabigatrán 25
Warfarin 18 (most toxic, least effective, very inexpensive).
Rivaroxaban 14 (toxic, least effective in the DOAC class, but costly).

Table 1: Comparison of warfarin, Apixaban, Dabigtran and Rivaroxaban for benefits, risks and cost

	Criterion	Warfarin	Apixaban	Dabigatrán	Rivaroxaban
Benefits	Risk of Stroke	1.10	0.88	0.91	1.10
	Risk of death	0.33	0.29	0.20	0.28
Risks	Risk of ICH	0.66	0.29	0.31	0.39
	Risk of GIH	0.89	0.58	1.54	1.56
	Risk of MB	11	9	13	17
	Risk of MI	0.68	0.49	0.80	0.71
Cost	Cost[¶]	$14	$327	$222	$222

- The scores above reveal the most preferred and the less preferred option, considering the benefit-risk ratio and drug costs altogether.
- Apixaban therefore should be considered as the preferred anticoagulant option -due to a better benefit-risk balance and a minor cost influence, followed by dabigatran, warfarin and rivaroxaban.

Table 2: Warfarin and DOAC's: Side effects and treatment of side effects

Name of Anticoagulant Agents	Side effects of Anticoagulant Agent	Treat side effects of Anticoagulants
Warfarin	Headache, stomach pain, bleeding, discomfort, vomiting	Fresh frozen plasma, Vitamin K
DOAC's	Uncontrolled bleeding, severe pain	DOAC antidotes Idarucizumab, andexanet alfa and ciraparantag. Idarucizumab is the only approved antidote and is specific for dabigatran.

ARE ALL ANTICOAGULANTS SAFE?

1. Anticoagulants are not safe, and despite their benefits, they do possess side effects, which in some cases could be very serious.
2. The experienced physicians will need to put their medical and clinical background to test to make sure that the patients get the most benefit and least side effects out of an anticoagulant agent.

WHAT ARE THE BENEFITS OF ANTICOAGULANTS?

- The main benefit of anticoagulants is that they help prevent blood clots as well as keep clots from growing.

CONCLUSIONS

1. The physician needs to make a very careful decision when selecting an anticoagulant agent, when it comes to efficacy (benefit) and side effects (risk).
2. The lifesaving benefits of some of the anticoagulants such as Apixaban often outweigh the potential dangers.
3. These benefits truly help patients who have suffered from DVT, PE, stroke, blood clots, etc.
4. Although there are a few risks to taking anticoagulants, the benefits of these often exceed the risks.

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FUTURE DIRECTIONS

In the future, we plan to research the risk-benefit ratio of heparin, one of the most widely used anticoagulants that has been in therapy over 100 years.

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