Adherence to NOACs

Patricia van den Bemt

EAHP Hamburg 2015

Disclosure

- Unrestricted research grants from
  - Glaxo-SmithKline
  - Boehringer Ingelheim
  - Daiichi Sankyo
  - Bayer
  - Pfizer
- For research on medication safety and adherence
  - no product related studies

Question 1

- Non-adherence, defined as missed dosages, occurs more often with:
  a. NOACs – raise red card
  b. Vitamin K antagonists – raise green card
  c. Equal for both – raise no cards

Question 2

- Persistence is better for:
  a. NOACs – raise red card
  b. Vitamin K antagonists – raise green card
  c. Equal for both – raise no cards

NOACs, DOACs or NOACs

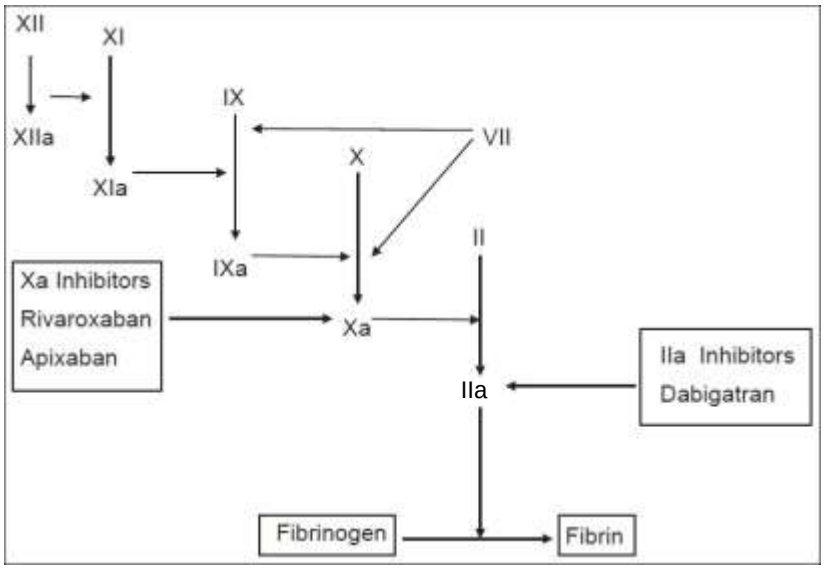
- New Oral Anticoagulants
- Direct Oral Anticoagulants
- Non-vitamin K Oral Anticoagulants

- Apixaban
- Dabigatran
- Rivaroxaban
- [Edoxaban]

Overview

Drug	Dabigatran	Rivaroxaban	Apixaban
Trade name	Pradaxa	Xarelto	Eliquis
Dosages	110/150mg (BID)	10/15/20mg (OD; VTE initially BID)	2.5/5mg (BID)
Action	thrombin inhibitor	factor Xa inhibitor	factor Xa inhibitor
T ½ (hours)	12-14	9-13	8-15
Time to Cmax (hours)	2	2-4	1-3
Bioavailability (%)	6.5	80	66
Interaction mechanisms	P-gp intestine	CYP3A4/P-gp	P-gp intestine
Protein binding (%)	35	>90	87
Renal clearance (%)	80	66	25
Linear kinetics	yes	no	yes

Mechanism of action



Summary study results

- Venous thrombo-embolism (*Thromb Res 2014;133:1145-51*)
  - Comparable efficacy vs. warfarin
  - Apixaban and rivaroxaban less major bleeding vs. warfarin
  - Indirect comparison NOACs: comparable regarding efficacy
  - Indirect comparison NOACs: apixaban potentially less bleeding

Summary study results

- Venous thrombo-embolism (*Thromb Res 2014;133:1145-51*)
  - Comparable efficacy vs. warfarin
  - Apixaban and rivaroxaban less major bleeding vs. warfarin
  - Indirect comparison NOACs: comparable regarding efficacy
  - Indirect comparison NOACs: apixaban potentially less bleeding

- Atrial fibrillation (*Thromb 2013;2013:640723*)
  - Comparable efficacy vs. warfarin
  - Less intracranial bleeding with NOACs vs. warfarin
  - May depend on quality of warfarin therapy (time in therapeutic range)

Real life…..

- ….is no clinical study
- Concerns about adherence
  - Warfarin: INR reveals adherence problems
  - NOACs: no monitoring…..

Monitoring is no guarantee

- It will DETECT potential adherence problems
- …..but it will not PREVENT them

Monitoring is no guarantee

- It will DETECT potential adherence problems
- …..but it will not PREVENT them

- Study 200 patients on warfarin, mainly for VTE and AF
- 15% non-adherent (10% self reported; 15% based on refill rate)
- Refill rate was associated with time in therapeutic range (TTR)

J Thromb Thrombolysis 2013;36:416–21.

Monitoring is no guarantee

- It will DETECT potential adherence problems
- …..but it will not PREVENT them

- Study 200 patients on warfarin
- 15% non-adherent (10% self reported; 15% based on refill rate)
- Refill rate was associated with time in therapeutic range (TTR)

- Study 8000 patients on warfarin for long-term treatment VTE
- 75% non-adherent based on refill rate
- 50% non-persistent
- association with outcome

Manag Care Pharm 2013;19:291-301.

All OACs are equal…

- 364 patients: 204 warfarin and 160 dabigatran
- Self reported adherence
  - 0.65 missed warfarin dosages/month vs 0.63 dabigatran

Pat Pref Adher 2014;8:167-177.

All OACs are equal…

- 364 patients: 204 warfarin and 160 dabigatran
- Self reported adherence
  - 0.65 missed warfarin dosages/month vs 0.63 dabigatran

- 101801 patients: from NOAC trials – NOAC vs comparator
- Comparator mostly warfarin; ACS-trials placebo; one trial aspirin
- VTE: persistence NOAC = warfarin
- AF: persistence NOAC = warfarin
- ACS: persistence NOAC < placebo

Mayo Clin Proc 2014;89:896-907.

….but some are more equal

- 1775 warfarin vs. 3370 dabigatran for AF
- 1745 matched pairs using propensity score matching
- Persistence after 6 months and 1 year
  - Warfarin 53% and 39%
  - Dabigatran 72% and 63%

Circ Cardiovasc Qual Outcomes 2013;6:567-574.

Non-comparative studies

- 159 patients on dabigatran for AF
- Monocenter study: large academic center
- Medication possession ratio (MPR)
  - Mean 0.63
  - 43% of patients MPR<0.8 (mean in this subgroup 0.39)

J Manag Care Pharm 2014;20:1028-34.

Non-comparative studies

- 159 patients on dabigatran for AF
- Monocenter study: large academic center
- Medication possession ratio (MPR)
  - Mean 0.63
  - 43% of patients MPR<0.8 (mean in this subgroup 0.39)

- 5376 patients on dabigatran for AF
- Veterans Health Administration database
- Proportion of days covered (PDC; comparable to MPR)
  - Mean 0.84
  - 28% of patients PDC<0.8
  - Poor adherence associated with increased risk of stroke

Am Heart J 2014;167:810-17.

Interim conclusions

- Adherence problems not unique to NOACs
- Comparable to warfarin
- But less visible (no monitoring)
- Persistence potentially better with NOACs (limited evidence)

Risk factors

- Potential risk factors:
  - Age (younger age, higher risk of non-adherence!)
  - Low income
  - Psychiatric comorbidity
- But…… no consistent predictors
- Rely on general factors known to be of influence on adherence
  - Knowledge / information
  - Forgetfulness
  - Dosages schedules

Improving adherence to NOACs

- Inform patient on indication
  - Beliefs in medicine – necessity
- Inform patient on potential side-effects and what to do
  - Belies in medicine – concerns
- Frequently reassess potential non-adherence
- When suspected:
  - Motivational interviewing (necessity/concerns)
  - Change to NOAC with once daily dosage regimen
  - When forgetfulness plays a role:
    - Technical solutions, such as SMS reminders
- If all else fails:
  - Change to VKA enabling monitoring

Question 1

- Non-adherence, defined as missed dosages, occurs more often with:

  a. NOACs

  b. Vitamin K antagonists

  c. Equal for both

Question 2

- Persistence is better for:
  - a. NOACs
  - b. Vitamin K antagonists
  - c. Equal for both