Serum concentration of Non-vitamin K antagonist oral anticoagulants (NOACs) in older hip fracture patients

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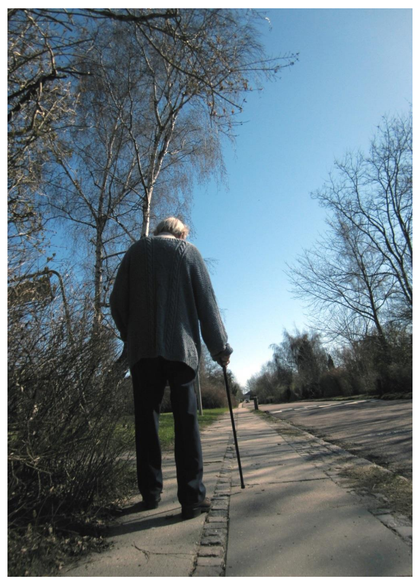

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Background and Objective:

To determine use of NOACs in older hip fracture patients by objective detection in serum(s) at hospital admission compared with medication lists and, also, to estimate the elimination half-life (T½) in NOAC users. Further, to study the impact of NOAC use on waiting-time for surgery and need for blood transfusions. Finally, to assess detected s-concentration in relation to reference ranges of NOACs.

Design:

A prospective study of older (≥65 years) hip fracture patients admitted to an orthogeriatric unit, October 2015 to February 2016. Medication reconciliation (MR) was performed. Time for last consumed dose of NOAC, start of surgery and need for blood transfusions were recorded and compared to warfarin-users. Blood samples from admission and next to surgery were analyzed for s-concentration of NOACs, and these were compared with the information from MR. T½ of NOACs was estimated using two s-concentration measurements prior to surgery (T ½ = ln2/kel, kel = elimination constant).

Results:

We included 167 patients (median age 84 years, 73.1 % women). NOAC use was detected by serum analysis in 11 patients (6.6 %; 100% coherent with MR), while 15 patients (9.0%) used warfarin. 7 of the 11 NOAC users (63.6%) had s-concentrations of NOACs above the reference range at admission, and 5 patients (45.5%) had s-concentrations within the reference range before surgery. Patients using NOAC had significantly longer median waiting-time for surgery than warfarin-users (50 vs 36 hours, p=0.004). Blood transfusions were given to 36.4 % of NOAC-users vs 21.4 % of warfarin-users (p=0.651). Mean estimated T½ of NOACs were 33, 16.5 and 14.5 hours for dabigatran (n=2), apixaban (n=4) and rivaroxaban (n=2), respectively.

NOAK-patient	Waiting-time for surgery	Fall in Hb	Blood transfusions
Apixaban			
1	32	2.8	0
3[1]	41	2.9	2
5	40	0	0
6[1]	46	2.3	4
7[1]	52	2.3	2
9	64	1.4	0
Rivaroxban			
4	35	1.7	0
8[1]	55	2.1	2
11	45	0.6	0
Dabigatran			
2	22	0.3	0
10[1]	43	2.2	0

Overview of waiting-time for surgery, time from 2.test to surgery, fall in hemoglobin (Hb) and need for blood transfusions for the patients

(n=11) included in the study at Diakonhjemmet hospital
NOAC: Non-vitamin K oral anticoagulants
[1] Patients used lower doses of NOAC: Apixaban 2.5 mg x 2, rivaroxaban 15 mg x 1, and dabigatran 110 mg x 2, respectively

Apixaban-patient	S-cons 1 (nM)	S-cons 2 (nM)	Estimated half-life (normal 12 h)[1]
1	383	161	14.4
3[2]	576	140	16.2
5	LOQ		
6[2]	684	156	18.3
7[2]	509		
9	302	76	17.1
Rivaroxaban-patient	**S-cons 1 (nM)**	**S-cons 2 (nM)**	**Estimated half-life (normal 11-13h)**
4	168	26	11.1
8[2]	1053		
11	2332	382	18.0
Dabigatran-patient	**S-cons 1 (nM)**	**S-cons 2 (nM)**	**Estimated half-life (normal 12-14h)**
2	155	LOQ [3]	7.0
10[2]	28	17	54.9

Overview of serum concentrations (s-cons) and estimated half-life for patients (n=11) included in the study at Diakonhjemmet Hospital

Reference area: apixaban and rivaroxaban: 50-300 nM, dabigatran 100-300 nM
Blank: no blood available for analysis
NOAC: Non- vitamin K oral anticoagulants
LOQ: s-cons below limit of quantification. For dabigatran LOQ = 4 nM
[1] Normal half-life for elderly patients given in the SPC
[2] Patient used reduced dose of apixaban 2.5 mg x 2, rivaroxaban 15 mg x 1, dabigatran 110 mg x 2, respectivel.
[3] Estimated by assuming s-cons = LOQ = 4nM

Conclusion:

MR is effective in detecting NOAC use in older hip fracture patients, but importantly s-concentrations are higher than expected in this population prior to surgery, even though the waiting-time is longer than for non-NOAC users. The tendency of more need for blood transfusions, in NOAC vs. warfarin users, is also of importance. Further studies on pharmacokinetics in the elderly hip fracture patients are needed.

Diakonhjemmet Sykehus

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No conflict of interest