Short communication

RIVAROXABAN – THE CLINICAL SIGNIFICANCE OF PLASMA HALF-LIFE IN RELATION TO AGE

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INTRODUCTION

Rivaroxaban is one of the most widely used drugs from the group of "newer anticoagulants". In the form of the drug Xarelto, it accounts for most prescriptions in the Czech Republic. This drug is one of the few for which an age-dependent difference in plasma half-life ($t_{½}$) between younger and older subjects exposed to the drug is well documented. Both the SPC (summary of product characteristics) and the basic literature, including the registration documents, state that in "younger subjects", $t_{½}$ is 5–9 hours, and in "elderly subjects" (in the original), it is 11–13 hours. This is very interesting and important when determining an individual treatment plan, especially the dosage regimen and intervals. The terms "elderly subjects" and "younger subjects" undoubtedly require a more precise definition.

Situation

The Summary of Product Characteristics (SPC) of the original Xarelto product, under pharmacokinetic properties in the text section "5.2. Pharmacokinetic properties" (State Institute for Drug Control, 2023), states that rivaroxaban is eliminated from plasma with a terminal half-life of 5–9 hours in younger subjects, and 11–13 hours in older subjects.

The concept of elderly subjects must be seen in the light of the seminal work by Kubitza et al. (2008). This work is cited as a source in many other publications, particularly Mueck et al.'s seminal work on rivaroxaban (2014). It is listed here under citation number 41.

Only in this one paper (Kubitza et al., 2008), can we find how the authors perceive the term "elderly person", in the original "elderly subjects". The authors of the SPC undoubtedly share this idea for both Xarelto and Xanirva, and other "generics" of rivaroxaban. In their study, Kubitza et al. (2008) provide demographic characteristics with anthropometric data of the respondents. This study includes 52 people (elderly subjects), 27 men and 25 women, in the age range of 60.0–76.0 years, i.e., people older than 60 years. This is an interesting and important figure. In our cultural-political-professional environment, the age of 65 is commonly considered to be the beginning of "elderly age".

Therefore, if, in the SPC of a medicinal product with the active substance rivaroxaban, we read that in older adults the $t_{½}$ of rivaroxaban is 11–13 hours, this may be a difference of $t_{½}$ to 2.5 times compared to younger people. This applies to all patients over 60 if we consider the lower limit in younger people (5 hours) and the upper limit in older people (13 hours). Such significant differences in the length of the fundamental pharmacokinetic parameter, plasma $t_{½}$, i.e., in the behaviour of the drug during the "fate of the drug in the body", can affect the therapeutic and side effects of the active substance rivaroxaban.

Survey and its results

We asked what the age profile of patients who were prescribed rivaroxaban during 2024 at České Budějovice Hospital looks like.

There were 1,334 subjects, of whom 1,117, i.e., 83.73%, were older than 60. For approximately 84% of our patients "on rivaroxaban", a plasma half-life of $t_{½}$ of 11–13 hours must be expected. For the SPC, elderly subjects are older than 60, not 65. In the Czech Republic, persons aged 65 years and over are considered elderly.

CONCLUSION

Clinical significance of the findings

In our patients who were prescribed and dispensed a drug with the active ingredient rivaroxaban, 84% were people over 60. It can be reasonably assumed that the same will be true for patients treated in other healthcare facilities. The authors point out that in people over 60 years of age, it is necessary to assume that the plasma half-life $t_{½}$ of the active substance rivaroxaban will be 11–13 hours, not only in people over 65 years of age, as elderly patients in the Czech Republic are commonly referred to. This fact must be considered while prescribing.

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Further reading

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