Therapeutic Levels of Recombinant Hirudin

G.	Nowak
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Max-Planck-Gesellschaft, Research Unit for Pharmacological Haemostaseology, Jena, FRG

Dr. G. Nowak, Institute of Pharmacology and Toxicology, Medical Academy Erfurt, Nordhäuserstrasse 74, D-O-Erfurt (FRG)

Dear Sir,

In volume 21, suppl. 1/91, of Haemostasis, expected circulating levels of recombinant hirudin in various clinical indications were stated by Walenga et al. [1, table 3, page 52]. These therapeutic levels were also discussed in the text, with respect to an optimized therapy. However, it must be emphasized that these statements will not bear closer experimental or clinical examination.

Beginning with prophylaxis, a blood level below 2.5 µg/ml is recommended. I am absolutely sure that a substantially lower blood level will be sufficient. For therapeutic anticoagulation a blood level of 5-10 µg/ml is recommended. Again, I am quite sure that 20-50 times lower levels will be entirely sufficient. For hemodialysis the authors recommended 3-8 µg/ml; in our studies we demonstrated that a blood level of 0.5 µg/ml was entirely sufficient to perform hemodialysis without any problems in patients.

Furthermore, the authors re-recommend a blood level of 10-30 µg/ml for major surgery and cardiovascular bypass surgery. Within a range like this, blood has already become unclottable; hence, such levels cannot be regarded as appropriate in clinical use because of the imminent fatal bleeding they will provoke.

It is indeed advisable to correct the data and revise them in accordance with the available clinical data.

In the present stage of introduction of recombinant hirudin into clinical use (clinical phase II studies), in my opinion, such blood levels are simply unacceptable because they will definitely lead to extremely dangerous situations, particularly as long as there is no antidote.

Furthermore, as to the assay methods for recombinant hirudin, the assay range is much too high [1, table 4, page 61]. In my opinion, it should be 50 times lower.

There are enough data from animal experiments which may be useful in clinical therapy with respect to recombinant hirudin levels in various indications.

Taking into consideration the forthcoming introduction of hirudin into clinical therapy, will you please ask the authors in your journal to answer the critical remarks mentioned above.

Reference

Walenga JM, Hoppensteadt D, Koza M, Wallock M, Pifarre R, Fareed J: Laboratory assays for the evaluation of recombinant hirudin. Haemostasis 1991;21 (suppl 1):49-63.