A NOTE ON THE RELATIVE ANTIDIURETIC POTENCY OF BEEF- AND HOG VASOPRESSIN

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Van Dyke, Engel & Adamsons, Jr. (1956) recently demonstrated that arginine- and lysine vasopressin, when expressed in pressor units, were of equal antidiuretic potency after subcutaneous injection into rats. When injected intravenously into dogs, however, arginine vasopressin was about seven times more potent than its lysine analogue.

The findings in dogs were confirmed in rats by Thorn (1957) who, therefore, concluded that the difference between the vasopressins depends on the route of administration rather than on species differences.

On the basis of these findings it would appear that the antidiuretic assay of hog posterior pituitary extracts against the International Standard, containing resp. lysine- and arginine vasopressin, is a comparative rather than a dilution assay. This, of course, would not invalidate the assay provided the physiological responses of standard and test are sufficiently similar.

The following experiments were performed in order to demonstrate the absence of any such similarity.

MATERIAL AND METHODS

Hormone preparations: As purified substances were not available extracts of beef- and hog posterior lobes were chromatographed according to Potts & Gallagher (1944). The pressor fractions contained per 100 I. U. of vasopressin: Beef extract: 9 I. U. of oxytocin, Hog extract: ≤ 0.2 I. U. of oxytocin, determined after tryptic inactivation of the vasopressin.

Antidiuretic activity was studied in male rats with a slightly modified Dicker (1953) technique. The water load was maintained on an automatic balance, at about 7 per cent of the body weight. The urinary flow was recorded by means of an electronic drop counter, cf. Fig. 1. The drop size was constant, about 18 µl., allowing, when necessary, the conversion of number of drops per minute to volume per minute. The
Thorp impulse counter used for kymographic recording was tripped down at 2.3 minutes intervals. Doses were injected (polythene cannula in the femoral vein) in 100 µl. and washed in with 50 µl. of saline. The interval between injections was about 1/2 hour.

The experiments were performed as balanced four-point assays according to a randomized block design. Altogether 12 injections were given to each rat. The data from at least three rats were pooled and calculated as one assay.

RESULTS

A typical tracing of the actions of beef- and hog vasopressin is shown in Fig. 1. The substances are seen to differ markedly as regards the duration of the effect. Although the antidiuresis elicited by hog vasopressin is more marked, its duration is shorter than that of beef vasopressin. This dissimilarity recurs with surprising constancy in all experiments.

An even more convincing example is given in Fig. 2 which shows the plotted data from an assay obtained on 48 injections, forming 12 randomized groups.

Records of quite similar pattern were obtained from comparative assays of unfractionated hog posterior pituitary extract, the International Standard (beef hypophyses), the U. S. P. Reference Standard (beef hypophyses), and synthetic lysine vasopressin.

In order to rule out any possible interference from oxytocin a few experiments were done, in which synthetic oxytocin was added to the pressor fraction of posterior pituitary. No potentiation of the response to vasopressin was observed.

DISCUSSION

The experiments described above are open to the objection that non-specific effects of impurities in the extracts might interfere with the effect of vasopressin. It appears, however, rather improbable that such interference would

Fig. 1.
Fig. 2.

Data from a four point comparative assay of beef- and hog vasopressin.

Abscissa: period after the injection. 1 period is 2.3 minutes.

Ordinates: urinary flow rate, in per cent of the rate in a 2.3 min. period before the injection.

The values plotted are the means (± standard error) of 12 responses at each dose level. In the calculation of the standard error, the variation between animals was neglected.

A: Beef vasopressin 12.5 micro-units, hog vasopressin 20 micro-units.
B: " " 25 " " 40 " "

recur with any constancy in experiments with different samples of posterior pituitary powder.

It seems, therefore, justifiable to conclude that beef and hog vasopressin do in fact differ as regards the duration of action.

Moreover, one of Thorn's published assays lends some support to the same conclusion.

This investigation is of practical significance with regard to the (antidiuretic) bio-assay of hog vasopressin against the International (beef) Standard. Here, the "relative potency" will depend on the duration of the urine collection period on which the calculation of the size of the response is based. It is needless to add that such comparisons must be invalid, many of them also from a statistical point of view.

SUMMARY

Experiments with the intravenous, antidiuretic rat assay technique disclosed a difference between beef- and hog vasopressin with regard to duration of effect.

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Comparative assays of the two vasopressins are, therefore, biologically, if not always statistically, invalid.

Any statement on the relative potency of vasopressins must be considered with caution.

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REFERENCES

Dicker, S. E.: J. Physiol. 122, 149, 1953.