COMPARISON OF TWO LABORATORY METHODS FOR THE DIAGNOSIS OF PHAEOCHROMOCYTOMA

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During the past 2 years, two short laboratory screening tests for phaeochromocytoma have been published. Both methods are based on the fact that patients with a phaeochromocytoma excrete increased amounts of pressor amines (adrenaline and noradrenaline) in the urine.[1]

The normal daily output of pressor amines is 15-30 μg., but it varies quite considerably under different conditions.[2] In essential hypertension the values are usually less than 100 μg., but values as high as 180 μg. have been reported.[3] After strenuous muscular work, which represents a form of stress, there is an increase in the excretion of pressor amines.[2]

In phaeochromocytoma the excretion of pressor amines is very much increased. Usually it exceeds 250 μg. daily and it may rise to 1-3 mg.

METHODS

In the method described by Moulton and Willoughby[4] untreated urine from a patient was injected into a cat, and the effect on the animal's arterial blood pressure was observed. The response to the injected urine was compared with the response to injections of standard solutions of adrenaline and of noradrenaline (0·1-0·2 μg., per ml.). A response greater than that to the standard solutions was indicative of phaeochromocytoma. Out of 250 cases, these authors identified 7 cases of phaeochromocytoma in which the values for pressor amines ranged from 0·3-3 mg. per day.

In Hingerty's method[5] the pressor amines from the patient's urine and from a standard normal urine to which noradrenaline has been added were adsorbed onto aluminium oxide, and eluted with acid. Ferricyanide was added to develop fluorescent products, and the difference of intensity of fluorescence between standard and test under an ultra-violet lamp was compared visually. The primary object of this semi-quantitative method was to detect the presence of more than 180 μg. of pressor amines in a 24-hour urine specimen, that being the concentration in the prepared standard. Hingerty[5] applied this method to 70 cases of suspected phaeochromocytoma. In the only case in which

the diagnosis was confirmed, the daily excretion of pressor amines was about 1,500 μg. The average excretion of the other 69 cases was 46 μg. per day.

RESULTS

Since it was first published, the cat test has been applied in this department to about 50 cases of suspected phaeochromocytoma. Two positive cases were found and confirmed by operation, unfortunately before the details of the fluorescence test were published. The cat test and the fluorescence test were done in parallel on 16 cases over a period of 4 months. The results for both methods were negative, the fluorescence test giving values ranging from 20-40 μg. per day. For the purpose of comparison, artificial positives were prepared by adding noradrenaline to normal urine to give values ranging from about 150 to 500 μg. per day; the amount recoverable was approximately 30%. Frazer[6] and Riley[7] reported the same finding. A direct comparison was made by preparing a urine containing the equivalent of 400 μg. noradrenaline per day. When injected into a cat, the arterial blood pressure curve was typical of one found in phaeochromocytoma and the fluorescence test indicated a value of 130 μg. per day, showing a recovery of about 30%. In the range of 200-400 μg. per day visual comparison was very difficult. Only when the values exceeded 500 μg. was the distinction clear cut.

DISCUSSION

Both methods have advantages and disadvantages.

The cat test requires experienced operators and adequate laboratory facilities. It is a reliable method, and one advantage is the fact that up to 20 assays can be performed on the same animal. The method also allows for exact repetition of the test on the same urine sample.

The fluorescence method requires no special apparatus, but exact repetition is not possible. Furthermore a 24-hour urine specimen is recommended for this method, whereas the cat test can be performed on random samples of urine.

As far as specificity is concerned, the fluorescence method is highly specific. The adsorption on aluminium oxide is specific for dihydroxyphenyl compounds like adrenaline and noradrenaline. Monohydroxyphenyl compounds such as ephedrine and tyramine are not adsorbed.[8]

Only catecholamines with a hydroxy group on the β carbon and a hydrogen on the α carbon of the side-chain are able to form strong fluorescent compounds. Isopropylnoradrenaline (Isuprel, Aludrin) gives a strong fluorescence, while Dopamine and 3 : 4 dihydroxynorephedrine (Corbasil, Cobefrine) gives only very weak fluorescence.[9] Under the circumstances there was little reason to expect any catecholamines with a hydroxy group in the side-chain, other than adrenaline and noradrenaline, to be present in the urine.

The cat test is less specific than the fluorescence test. Two substances, histamine and ephedrine, were found to give confusing results. Histamine caused a fall in the cat's blood pressure and adrenaline sometimes had a depressor action, depending on the sensitivity of the animal. Histamine could easily be distinguished from adrenaline by the injection of antihistaminics. Ephedrine had the same action as adrenaline. It is not easy to distinguish between ephedrine and adrenaline; only by reverting to the case history was it found that one patient had been taking ephedrine for asthma.

CONCLUSION

Our experience suggests that the fluorescence test may not be sensitive enough to detect border-line cases, and is of value only when the excretion of pressor amines is very much increased.

The cat test, although less specific and more likely to be influenced by the presence of various drugs in the urine, is the more reliable test for the screening of phaeochromocytoma.

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