Propranolol in acute intermittent porphyria

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Summary

Twenty cases of acute intermittent porphyria were studied during the acute phase. Cardiovascular manifestations were noted in all the cases, with tachycardia in 20 and with hypertension in 17. Propranolol in doses ranging from 20-200 mg was given to all the cases and produced adequate control of tachycardia and hypertension. At follow-up, smaller doses of propranolol were found to maintain the pulse rate and BP within normal limits and also to prevent acute attacks.

Introduction

Acute intermittent porphyria is an inborn error of metabolism characterized by symptomatology pertaining to various organ systems of the body, namely gastrointestinal, neuropsychiatric and cardiovascular. The disease can predominantly affect any one system or a combination of these. Asymptomatic individuals are not unknown but usually the course of the disease is punctuated by acute exacerbations comprising mainly of pain in the abdomen, vomiting, constipation and paralysis of the limbs. The most common cardiovascular manifestation is tachycardia which is an invariable finding during the acute attack. Hypertension has been described as occurring in as many as 50% of the patients during the acute attack. The gravity of cardiovascular manifestations lies in the fact that these may progress to left ventricular failure and hypertensive encephalopathy. To prevent such drastic events from occurring adequate and timely treatment is always worth considering. A large number of drugs have been used to this effect including *Rauwolfia* derivatives, tetraethyl ammonium chloride, tolazoline hydrochloride, guanethidine and bethanidine, but the results have not been encouraging. Propranolol, a β -adenergic receptor blocking agent, has been advocated for this purpose in the present study with significantly favourable results.

A similar study has been conducted by Beattie *et al.* (1973); they used propranolol and obtained a reduction in heart rate and BP in 4 cases of acute intermittent porphyria. In one of these cases a marked alleviation of abdominal pain was also achieved.

Materials and methods

Twenty cases of acute intermittent porphyria in the acute phase were studied. The diagnosis was suspected from the clinical and family history and was confirmed by urine examination for the detection of porphobilinogen using a modified Watson-Schwartz test (Todd & Sanford, 1974) and uroporphyrin and coproporphyrin fluorescence test (Derek and Henry, 1967). All the patients were observed until symptomatic relief was obtained, and followed-up for up to one year, the intervals being 2 months, 6 months and 12 months. Cardiac rhythm was recorded on an ECG and the heart size was measured by an antero-posterior chest X-ray at the time of admission. Propranolol was given to all the patients having tachycardia, hypertension and a normal heart size, in doses ranging from 20-200 mg/day depending upon the severity of their condition. A record of pulse rate and BP was made every 6 hr to check the progress of the disease and to follow the effect of propranolol.

Results

There was a strong clinical indication of acute intermittent porphyria present in all the 20 cases studied. Abdominal pain and constipation were present in all the cases. Family history suggestive of the disease was present in 18 cases. Urine examination revealed strongly positive modified Watson-Schwartz test and significant fluorescence.

Response to propranolol in doses ranging from 40 to 80 mg/day, was much less and, therefore, the doses had to be increased up to 200 mg in 3 cases. In young patients and in those having only mild hypertension or mere tachycardia, doses ranging from 20 to 80 mg/day sufficed. Adequate control of pulse and blood pressure was obtained on an average between the 10th and 15th day after which it was maintained on smaller doses. The results are given in Fig. 1.

All cases were given a course of promazine before propranolol therapy. Promazine caused symptomatic relief but had no effect on pulse rate and BP. Propranolol did not enhance the rate of alleviation of symptoms such as abdominal pain, nausea,

vomiting and constipation, but the general condition of the patient improved visibly from the first week of therapy. Patients taking 200 mg of propranolol/day complained of occasional fatigue and giddiness.

FIG. 1. Pulse and blood pressure response to propranolol in acute intermittent porphyria. —Mean systolic BP (mmHg); —mean pulse rate/min; ---- mean diastolic BP (mmHg).

Follow-up revealed a normal pulse rate and BP on maintenance doses of propranolol. Minor abdominal pain and constipation were complained of by 3 patients but none had any acute episode.

Discussion

The acute phase of acute intermittent porphyria is frequently associated with tachycardia and hypertension. This was first described by Melkersson (1925) and later Goldberg (1959) reported the incidence to be about 50%. Waldenstrom (1937) suggested that tachycardia was a good indication of the activity of the disease.

Although all cases do not require treatment, because of a possibility of their culmination into serious and fatal conditions such as hypertensive

encephalopathy and left ventricular failure, timely control of tachycardia and hypertension is indicated.

The pathogenesis of tachycardia and hypertension in acute intermittent porphyria is not exactly understood: increased levels of circulating catecholamines have been demonstrated by Beattie *et al.* (1973); and hypersensitivity of receptor sites to catecholamines have been considered by Gibson and Goldberg (1956). Bearing any of these mechanisms in mind it is logical to advocate a sympathetic receptor blocking drug such as propranolol for their control. The results from the use of this drug were evident in all the patients in this study and conform closely with the previous similar report by Beattie *et al.* (1973). Other drugs used, such as *Rauwolfia* derivatives, tetraethyl, ammonium chloride, tolazoline hydrochloride, guanethidine and bethanidine, although they have controlled BP in some cases, their effect has not always been satisfactory, and they have the additional disadvantage of certain side effects seen when increasing the dose and duration of therapy. α -Methyldopa is capable of controlling blood pressure but it induces the enzyme amino-laevulinic acid synthetase which is thought to be related to the triggering of the acute attack of acute intermittent porphyria. None of these disadvantages has been found with propranolol.

As acceleration of incipient cardiac failure and an increase in the severity of overt cardiac failure are known to occur with propranolol and other β -adrenergic receptor blocking agents, caution should be exercised and such conditions should be ruled out before starting therapy. One such fatality has been reported by Bonkowsky and Tshudy (1974).

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