PILOCARPINE AS AN ANTAGONIST TO THE UNDESIRE EFFECTS OF GANGLION-BLOCKING AGENTS IN THE TREATMENT OF HYPERTENSION

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A disadvantage in the use of ganglion-blocking agents for the reduction of hypertension is that they block conduction not only through sympathetic but also through parasympathetic ganglia. The desired lowering of blood pressure is due to the action on the former, the undesirable effects mainly to the action on the latter. It would be a clear advantage if the effects on parasympathetic ganglia could be neutralized.

It seemed to us that this ought to be readily done by the use of pilocarpine. This drug acts peripherally on the post-ganglionic terminals, and its action should not be prevented by simultaneous paralysis of the pre-ganglionic fibres to the ganglia. In medicinal doses it has no action on the post-ganglionic sympathetic terminals, so that it should not diminish the hypotensive action for which the ganglion-blocking drug is given. A preliminary trial on a suitable patient has confirmed this anticipation.

Case Report

The patient, a woman aged 45, had been treated since March, 1953, first with hexamethonium bromide intramuscularly, and later, for the past five months, with pentolinium tartrate ("ansolysen") orally. Both treatments gave very satisfactory results in reducing the hypertension and concomitant symptoms, but in doses sufficient to maintain an adequate reduction of blood pressure the side-effects were distressing. These were of the usual type: dryness of the mouth, leading to interference with speaking and swallowing; constipation and loss of appetite; dryness of the eyes and loss of accommodation; and, especially with hexamethonium, difficulty with micturition.

The patient was given orally a tablet containing 1/10 gr. (6.5 mg.) of pilocarpine nitrate. Within half an hour she reported that "instead of my mouth being parched, I can do nothing but spit." As the salivation was unnecessarily copious, half a tablet was next given. This produced slight moistening of the mouth, but not enough. A dose of about 1/13 gr. (5 mg.) (three-quarters of a tablet) has subsequently proved adequate for keeping the mouth in a satisfactory state of moistness. On this dosage the side-effects of pentolinium tartrate have largely disappeared. Certainly the dryness of the mouth and eyes is relieved, and appetite and digestion have improved. This has made a great difference to the patient's sense of well-being, which has been maintained for five weeks on a dose of pilocarpine of 1/10 to 1/13 gr. (6.5 to 5 mg.), during which time she has led a normally active life. The dryness of the mouth, an effect easily appreciated, disappears regularly within half an hour of swallowing the pilocarpine and returns in six to ten hours, depending on the dose. The patient has also remarked, without questioning, that the constipation has been less.

Comment

Pilocarpine, by stimulating all parasympathetic nerve-endings (or by some action equivalent to this), has a wide-

spread action on involuntary muscle and on secreting glands, and is a potential antagonist to all the effects which result from paralysis of parasympathetic ganglia. It would presumably have this effect in the case of any ganglion-blocking agent. In smaller doses it acts more on glands than on muscle, and might therefore be expected to antagonize the effects of ganglion-blocking agents on secretions more readily than those on muscle.

The loss of tone and of contractions of the alimentary tract which often occurs with ganglion-blocking agents is no doubt mainly due to blockage of the motor impulses to the muscle, but the diminution of salivary, gastric, and intestinal secretions can hardly fail to aggravate the constipating effect. Some improvement of this condition may therefore occur even if the dosage of pilocarpine is only high enough to act on secretions. In larger doses it powerfully stimulates intestinal muscle. It has also some action on ganglia, but this could hardly occur with medicinal doses. To what extent it could be safely used to antagonize the various muscular and glandular effects resulting from parasympathetic ganglion-block would require detailed exploration. It would be a question not only of dosage but probably to some extent also of individual variations in quantitative response. Fortunately, medicinal overdosage with pilocarpine can be readily antagonized with atropine should need arise.

We have not encountered in the literature any mention of pilocarpine having been tried for the purpose we have indicated, other than a passing reference by Smirk (1953). Our object in submitting this note is to suggest that it may prove of value for counteracting some at least of the undesirable side-effects which often mar the desired depressor effects of ganglion-blocking agents.

REFERENCE

Smirk, F. H. (1953). *N.Z. med. J.*, 52, 325.

THE ROLE OF SMOKING IN BRONCHITIS

BY

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Many factors which are responsible for the development or aggravation of bronchitis, such as climate, atmospheric impurities, hereditary predisposition (Oswald *et al.*, 1953), and infection (Stuart-Harris *et al.*, 1953), are difficult to control or eradicate. It is important, therefore, to assess the role of factors, such as smoking, which are more easily controlled. This investigation was undertaken to assess the incidence of bronchitis in a group of smokers compared with a similar group of controls who were non-smokers.

The patients studied consisted of a consecutive group of 422 males who were admitted to the Middlesex Hospital during the period from September, 1950, to September, 1952, for elective repair of inguinal hernia or a partial gastrectomy for chronic peptic ulcer. There were 310 smokers and 112 non-smokers.

Method

I examined each patient before the operation, and a postero-anterior radiograph of the chest was taken. The age, the place of residence, and a past history of diseases likely to predispose to the development of bronchitis were noted. Table I shows the distribution of these factors in the groups.