Br. J. clin. Pharmac. (1990), **29**, 254–256

The effect of autonomic blockers on heart rate: a comparison between two ethnic groups

E. C. MEYER, De K. SOMMERS, H. S. SCHOEMAN[1] & J. C. AVENANT
Department of Pharmacology and [1]Department of Statistics, University of Pretoria, P.O. Box 2034, Pretoria, 0001, South Africa

The influence of autonomic blockers on the heart rate of ten Bushmen and eight White volunteers was studied. There were significant differences in heart rate response to atropine alone between the White's and Bushmen. However, after prior β-adrenoceptor blockade, these differences were no longer significant. It is postulated that a varying pharmacogenetic sensitivity to autonomic blockers may result from inequality of vagal or sympathetic tone.

Keywords autonomic blockers heart rate ethnic differences

Introduction

Significant genetic differences in heart rate response to atropine have previously been reported between American Whites and Blacks (McGuigan, 1921; Paskind, 1921) and between White and Venda male volunteers (Meyer *et al.*, 1988). It has also previously been described (Meyer & Sommers, 1988) that prior β-adrenoceptor blockade accentuates the early and late bradycardic effect of small doses of atropine in White volunteers. The purpose of this study was to determine whether a varying pharmacogenetic sensitivity to autonomic blockers could be demonstrated in the Va'Sekele Bushmen. The Va'Sekele are a tribe of nomadic San Bushmen, who, owing to their isolated nomadic lifestyle are probably still a genetically homogenous group. Originally from Southern Angola, these people migrated South from their traditional habitat during the Angolan war in 1974–1975 and settled in the Caprivi strip.

Methods

After ethical approval and informed consent was obtained, a single-blind, placebo-controlled trial with eight healthy White and 10 healthy Bushmen male volunteers was carried out. The average age of the groups was 22.3 and 21.8 years, and the average masses 65.4 and 58 kg respectively. Volunteers fasted from the previous evening and remained fasting and supine for the duration of the trial. They rested for at least 30 min before control ECG (lead 2) and blood pressure readings were taken. Atropine 1.0 mg diluted to 2 ml with sterile water or placebo (2 ml sterile water) was given rapidly in a forearm vein.

The trial consisted of two phases at least 1 week apart, firstly with prior β-adrenoceptor blockade consisting of atenolol (Tenormin® Stuart) 100 mg the evening before and again 90 min before atropine or placebo administration and secondly without any prior β-adrenoceptor blockade.

Continuous ECG tracings were taken for the first 4 min, thereafter 30 tracings were made at 15 and 30 min, and then every 30 min for the trial duration of 5 h. Pulse-rate was calculated by counting the number of QRT complexes. For statistical analysis the differences between the atropine or atropine and atenolol and placebo values were calculated to determine the effect of atropine with and without prior β-adrenoceptor blockade on each group. The absolute change in pulse-rate (i.e. pulse-rate at specific time minus the base-line pulse was further calculated and the two groups compared to each other by means of an analysis of variance. Student's paired *t*-test was used to compare the effects of the drugs. A profile analysis using the Manova test criteria was done to compare the overall curves of

the Bushmen and White volunteers without atenolol, $P < 0.05$ being regarded as significant throughout.

Results

After placebo there was no significant changes in heart rate over time. The control heart rate values (Whites 64, Bushmen 67) did not differ significantly. After atenolol pretreatment the control heart rate values (Whites 51, Bushmen 62) differed significantly.

After administration of atropine 1.0 mg (Figure 1) the White volunteers developed a significant tachycardia during the first minute which lasted for 2 h. By the end of the trial the White volunteers had still not developed a bradycardia. The Bushmen developed a significant bradycardia during the first min. During the second min a significant tachycardia developed.

Heart rate values dropped back to control values at 120 min and at 210 min a significant bradycardia had developed. There were significant differences in the respective heart rate responses to the atropine at 1, 30, 270 and 300 min. The overall curves of the two groups also differed significantly. After prior β-adrenoceptor blockade (Figure 2) there were no significant differences in heart rate response to atropine between the Bushmen and Whites. Both groups developed a significant bradycardia within the first min, followed by a significant tachycardia. At 120 min heart rate dropped back to control values, at 180 min both groups developed a significant bradycardia. The Bushmen's increase in heart rate was significantly less than without β-adrenoceptor blockade at 30 min.

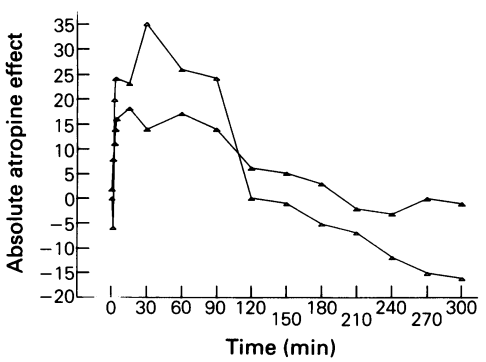

Figure 1 Heart rate changes after administration of atropine 1 mg to two ethnic groups, i.e. Whites ($n = 8$) ▲ and Bushmen ($n = 10$) △. Absolute atropine effect: Difference between effect obtained with placebo and with atropine alone.

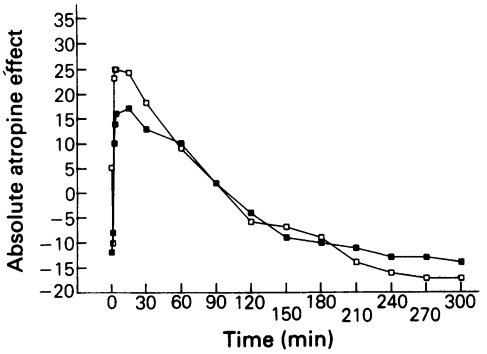

Figure 2 Heart rate changes after administration of atropine 1 mg after prior β-adrenoceptor blockade (atenolol 100 mg) to two ethnic groups, i.e. Whites ($n = 8$) ■ and Bushmen ($n = 10$) □. Absolute atropine effect: Difference between effect obtained with placebo and with atropine after prior β-adrenoceptor blockade.

Discussion

It is very clear that atenolol prior treatment accentuated the early and late bradycardic effects of atropine on the heart rate of White volunteers, while having no effect on the bradycardic response of the Bushmen volunteers to atropine. Their tachycardic response was, however, significantly decreased.

It is well-known that the effect of atropine may differ greatly between individuals at equivalent doses (Crawford, 1923). Vagal tone is thought to be the most important determinant of effective dose (Chamberlain & Turner, 1967). It has been shown that Black volunteers have a significantly higher intrinsic parasympathetic tone (Venter *et al.*, 1984) than White volunteers. We found the Whites to have significantly higher basal sympathetic tone than the Bushmen volunteers.

It would appear that the Bushmen have a high resting parasympathetic and relatively slight sympathetic tone, while the Whites have a high resting sympathetic and relatively slight parasympathetic tone.

The differences in reaction of heart rate after atropine administration between the groups cannot be explained on physical grounds alone. Although it is known that the dose of atropine sufficient to cause striking cardiac acceleration in an untrained individual may be relatively ineffective in an athlete (Kauf, 1926), all the volunteers were young fit persons who exercised regularly. The difference may be due to a difference in requirements resulting from an inequality of vagal or sympathetic tone. The

Bushmen volunteers may possibly have a lower basal level of circulating catecholamines owing to a less stressed, rural and relatively relaxed way of life. Genetic differences in sensitivity to atropine may be responsible—patients with Down's syndrome respond with abnormally great mydriasis and increased sensitivity to atropine's cardioacceleratory effects (Harris & Goodman, 1968). These results do, however, warrant further investigation regarding ethnic and possibly genetic differences in response to autonomic blockers.

References

Crawford, J. H. (1923). The influence of the vagus on the heart-rate. *J. Pharmac. exp. Ther.*, **22**, 1–19.

Chamberlain, D. A. & Turner, P. (1967). Effects of atropine on heart-rate in healthy man. *Lancet*, **ii**, 12–15.

Harris, W. S. & Goodman, R. M. (1968). Hyperreactivity to atropine in Down's syndrome. *New Engl. J. Med.*, **279**, 407–409.

Kauf, E. (1926). Ueber die Einwirkung von Atropin und Adrenalien auf das Herz Sporttreibender. *Wien. Klin. Wschr.*, **39**, 212–214.

McGuigan, H. (1921). The effects of small doses of atropine on heart-rate. *J. Am. med. Ass.*, **76**, 1338–1340.

Meyer, E. C., Sommers, De K., Schoeman, H. S. & Avenant, J. C. (1988). The effects of atropine on heart-rate: a comparison between two ethnic groups. *Br. J. clin. Pharmac.*, **25**, 776–777.

Meyer, E. C. & Sommers, De K., (1988). Possible mechanisms for anti-cholinergic induced bradycardia. *Eur. J. clin. Pharmac.*, **35**, 503–506.

Paskind, H. A. (1921). Some differences in response to atropine in White and coloured races. *J. lab. clin. Med.*, **7**, 104–108.

Venter, C. P., Joubert, P. H. & Strydom, W. J. (1984). Ethnic difference in response to pharmacological denervation of the heart. *I.R.C.Sc.J. med. Sci.*, **12**, 963–964.

(Received 31 March 1989, accepted 5 September 1989)