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LETTER TO THE EDITOR

PRECAUTIONARY NOTE ON USE OF POLYETHYLENE GLYCOL AS A DRUG SOLVENT

Sir,

Polyethylene glycols (PEG 200-700) are used as solvents in various pharmaceutical preparations meant for both internal and external use (1,2). PEGs are incompatible with iodine, potassium iodide, sorbitol, tannic acid, metallic salts like bismuth, mercury and silver salts (2). Their systemic absorption in certain conditions may result in renal failure and CNS depression (3). Morbidity has been reported due to systemic toxicity. Being acidotic PEGs increase anion, osmolar gap, haemolysis and serum calcium (4). Topical application resulted in urticaria, delayed allergic eczematous reactions, cross sensitivity etc. (5). Inspite of the adverse side effects, it is still customary to use PEGs as solvents in conventional pharmacological screenings as they are claimed to be inactive ingredients. In this study during pharmacological screening it was observed that PEG400 exaggerated the effects of oxyphenonium bromide when administered intraduodenally.

Six male mongrel dogs weighing 10-15 kg were anaesthetized with pentobarbitone (30 mg/kg, ip). Blood pressure, respiration, intestinal movements, ECG (limb lead II) were recorded on a Grass Model 78D Polygraph. Responses of epinephrine (E), norepinephrine (NE), acetylcholine (ACh), left carotid artery occlusion and vagal stimulation (22Hz, 0.46sec duration and strength 5.6V) were recorded before and ½ hr, 1 hr and 2 hr after the intraduodenal administration of oxyphenonium (132 μg/kg) dissolved either in PEG400 or water (1 ml/kg). Drugs (E, NE, and ACh) were administered i.v. at the dose of 1-2 μg/kg. The dose of oxyphenonium was calculated from the human dose (100-200 μg/kg).

The vehicle (PEG400) itself did not produce any effect on the responses of blood pressure, respiration and intestinal movements; the cholinergic and adrenergic stimuli were unaltered. Responses to adrenergic stimuli were unaltered by oxyphenonium mixed in either vehicle. However oxyphenonium mixed in PEG400 had completely abolished the responses to ACh and vagal stimulation (Fig. 1-A). In the water solvent, oxyphenonium produced a minimal blockade of ACh (not significant) after 1 hr but the response to ACh returned to normal after 2 hr. However vagal stimulus was not blocked by oxyphenonium in water (Fig 1-B). ACh 1 μg/kg produced an increase in the respiratory rate but no change in the intestinal movements while the vagal stimulation produced an increase in both respiratory rate as well as the intestinal movements. Oxyphenonium in water vehicle did not alter the responses to ACh and vagal stimulation where as oxyphenonium in PEG vehicle had blocked both these responses.

The exaggerated blockade to both ACh and vagal stimulation by oxyphenonium in PEG400 may be due to enhanced rate of absorption and/or potentiation of the responses to oxyphenonium. Unless the drug levels are estimated and correlated with the responses, it is difficult to draw a conclusion. The potential blockade observed in this study is not reported anywhere else. Inclusion of this solvent can be definitely avoided or replaced with other inert vehicle in human medications. The aim of this publication is to caution that every investigator who uses this solvent as a tool to elucidate the drug effect may come across a relatively simple but clinically hazardous problem.

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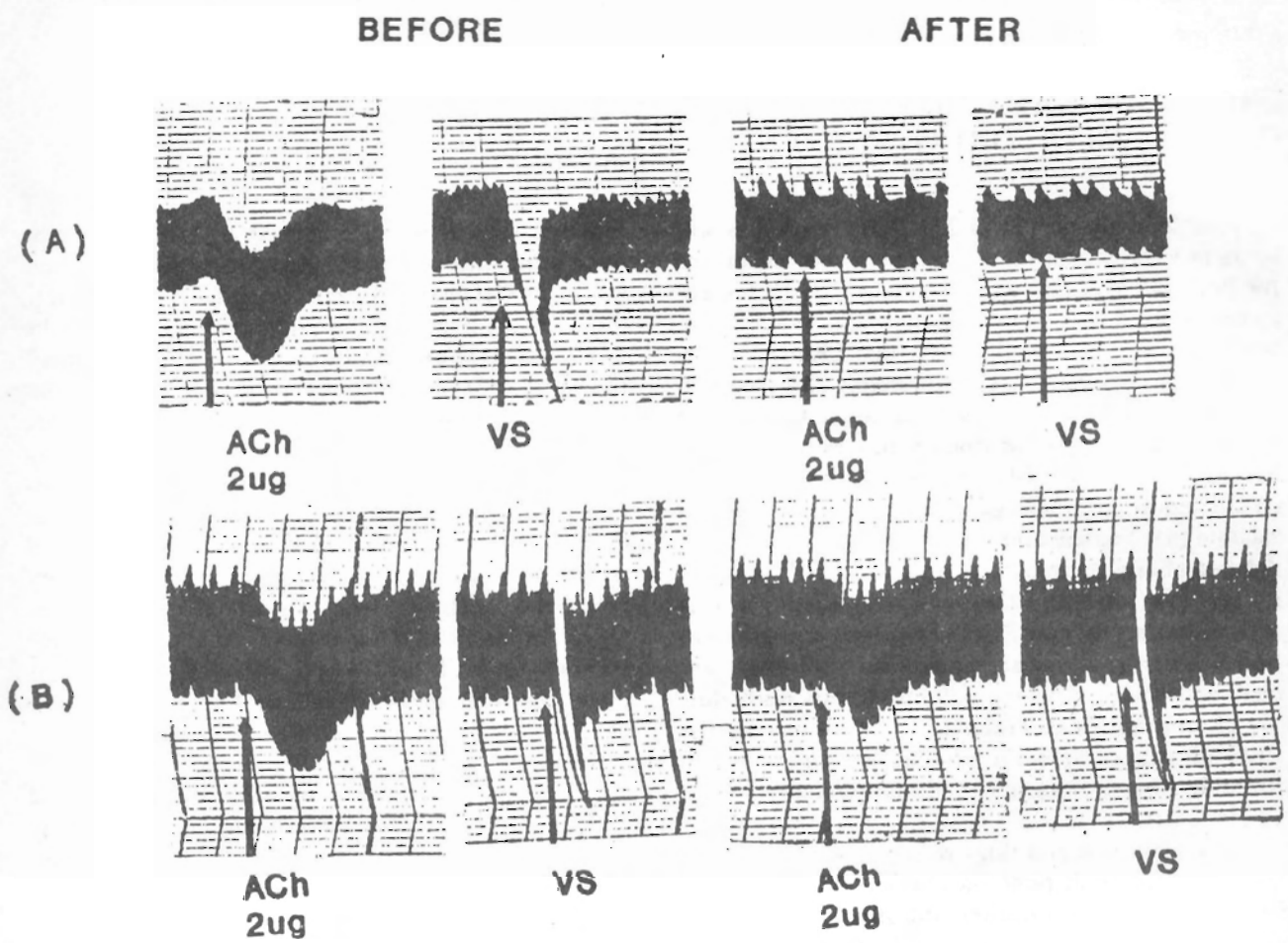

Fig. 1 : Effect of acetylcholine (ACh) & vagal stimulation (VS) on dog blood pressure before and 1 hr after oxyphenonium (132 μg/kg) in (A) polyethylene glycol (B) water.

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