

Title : PLASTIC ABSORPTION ADSORPTION OF NITROGLYCERIN SOLUTION

Authors : J. K. Ingram, M.D., J. D. Miller, M.D.

Affiliation: Department of Anesthesiology, University of California, Los Angeles, UCLA Center for the Health Sciences, Los Angeles, California 90024

Introduction. It has long been recognized that the volatile sublingual compound of nitroglycerin (NTG) lost potency in various binders, containers and packing materials. The present study deals with the question of absorption/adsorption of intravenously administered NTG solution onto various plastic carriers and reservoirs, with resultant loss or variability of potency. The study was prompted by our own observations of NTG's seeming variability of effect when given intravenously, and by a correspondence in the New England Journal of Medicine¹ where evidence of Viaflex bag adsorption of NTG without the appearance of breakdown products was presented.

Methods. NTG solution was prepared by dissolving NTG tablets in normal saline to final dilutions of 50 and 200 micrograms/cc. The kinetic assay of Fung² was used to identify a chromophoric intermediate whose absorbance at 328 mμ has been shown to be proportional to the initial NTG concentration present in the reaction mixture. NTG solution was placed into glass syringes, plastic syringes and various plastic intravenous reservoirs and tubings. NTG concentrations were determined from samples taken over five hours from both standing and infused (Harvard Pump) solutions. Infused amounts were chosen based upon clinical doses reported in the literature.

Results. In assessing reservoirs with standing solutions, we found NTG concentration remained unchanged in glass and plastic (polypropylene) syringes over a five hour sampling period. Solutions placed in a Buretrol (cellulose propionate) experienced ongoing decrements in concentration reaching a 40% loss at two hours. The polyvinylchloride (PVC) tubing of the Buretrol exerted an additive adsorptive effect with a 70% loss of original NTG concentration at two hours. After standing in the Buretrol for four hours, the NTG solution was drained and fresh solution replaced. For both concentrations tested, adsorption continued but at a slower rate, indicating non-saturation of the Buretrol's adsorptive capacity. An immediate 80% loss was noted when NTG was placed into a plastic Viaflex bag (PVC). Infusion studies utilizing a Harvard Pump and polypropylene syringes showed that uptake of NTG was pronounced in conduits composed of polyvinylchloride but absent for polyethylene (COBE Hi-Pressure). The uptake of NTG in standing solutions in PVC conduits (extension tubing, CVP catheters, Swan-Ganz catheters and "T" connectors) ranged from 65-75% in less than one hour. During infusion, PVC uptake was shown to be rate and concentration dependent. Delivering 5 grams of NTG/hour through a PVC T-connector, we found that a 50 ug/cc solution at 100 cc/hr reached a transient

adsorption maximum of 12% at fifteen minutes whereas 200 ug/cc at 25 cc/hr reached a maximum of 37% at the same time. Slower infusion rates were associated with more pronounced and prolonged decrements in NTG concentration. Eventually the NTG concentration rose toward initial values in the PVC conduits after having reached a nadir within the first hour.

Discussion. Our studies show that the amount of NTG reaching a patient during intravenous infusion may vary substantially with time, introducing a further complicating variable upon the process of titration of agent versus patient response. Materials shown to have adsorptive capacity for NTG include cellulose propionate, PVC and siliconized rubber (Holter chamber). Materials free of adsorptive capacity include glass, polypropylene and polyethylene. A safe, rational system of administering vasodilators requires knowledge of the delivered agent's concentration. An ideal infusion system for NTG would incorporate the non-adsorptive carriers and conduits mentioned; however, if adsorptive material need be used - dilute, rapidly infused NTG minimizes adsorption. Also, minimum durations for standing solution exposure to plastic is desirable though immediate uptake is well documented in our studies.

References.

1. Crouthamel, W.G., et.al. Loss of Nitroglycerin from Plastic Intravenous Bags. New England Journal of Medicine. 299:262, August 3, 1978.
2. Fung, et.al. Factors Affecting the Kinetic Assay of Nitroglycerin in Dosage Forms. American Journal of Hospital Pharmacy 32:1039-1042, October 1975

