Title : PROPRANOLOL REDUCES NITROPRUSSIDE DOSE AND CYANIDE LEVELS

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INTRODUCTION: Propranolol has been recommended as a useful drug for reducing sodium nitroprusside (SNP) dose-requirement and the risk of cyanide toxicity.[1] Concern has been expressed however, that use of propranolol might prevent tachycardia and thus mask an important sign of cyanide toxicity. This study was undertaken to determine the effects of propranolol on hemodynamic function, dose requirement for SNP and blood cyanide concentrations during SNP-induced hypotension in humans.

METHODS: The protocol for this study was approved by our human studies committee. Ten consecutive patients ranging in age from 8-18 years (Mean=13) received N_2O-morphine d-tubocurarine anesthesia for spinal fusion operations. After an hour of SNP-induced hypotension a bolus injection of propranolol 0.01 mg/kg IV was given. Heart rate, mean radial arterial pressure, and SNP dose-requirement were tabulated at 15 minute intervals throughout. Arterial blood gases and cyanide concentration[2] were drawn before beginning SNP, before giving propranolol, and an hour after propranolol. Data were analyzed by analysis of variance and Duncan's multiple range test. $P<.05$ was regarded as significant.

RESULTS: Before propranolol, SNP dose-requirement, heart rate and blood cyanide levels all increased significantly (figures 1 and 2). Heart rate slowed after propranolol in 9 patients, and this was associated with a reduction in SNP requirement, ($P<.05$). Cyanide levels also fell in each of these cases, unlike the usual response to SNP infusion where cyanide increases with time.[1]

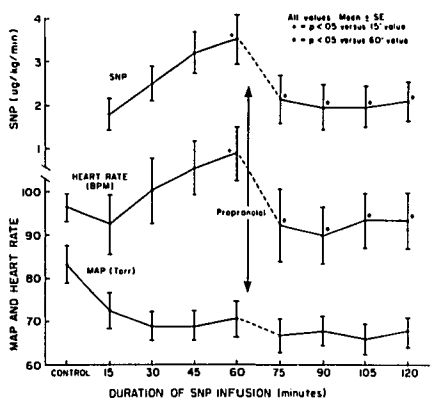

Fig 1. SNP requirement, heart rate and Mean arterial pressure in 9 patients who responded to propranolol. Heart rate and SNP requirement increased significantly during the hour before propranolol, and were reduced significantly following propranolol.

In one patient, (the fourth in the series) heart rate did not slow after propranolol and SNP requirement remained constant at 5.5 µg/kg/min. In this case the cyanide level increased from 6.8 µM/l after one hour of SNP to 9.6 µM/l after two hours of SNP. Since these data suggested that more than one dose of propranolol might be necessary to lower both heart rate and SNP requirement, two subsequent patients were given one and two additional increments of propranolol respectively as needed for a decrease in heart rate and SNP requirement. In each instance heart rate slowed gradually over several minutes, permitting a smooth reduction in SNP dose while a constant level of hypotension was maintained. Base excess increased significantly, probably reflecting a reversal of cyanide-induced metabolic acidosis, since no other measures were taken to correct acidosis after propranolol was given.

We conclude: Increasing SNP dose-requirement frequently occurs during induced hypotension with N_2O-morphine anesthesia in adolescents. Judicious administration of propranolol in a dose sufficient to lower heart rate during SNP-induced hypotension, reduces both the nitroprusside dose-requirement and also the likelihood of developing cyanide toxicity.

REFERENCES:

1. Vesey CJ, Cole PV, Simpson PJ: Cyanide and thiocyanate concentrations following sodium nitroprusside infusion in man. Br J Anaesth 48:651-660, 1976.
2. Rodkey FL and Collison HA: Determination of cyanide and nitroprusside in blood and plasma. Clin Chem 23:1969-1975, 1977.

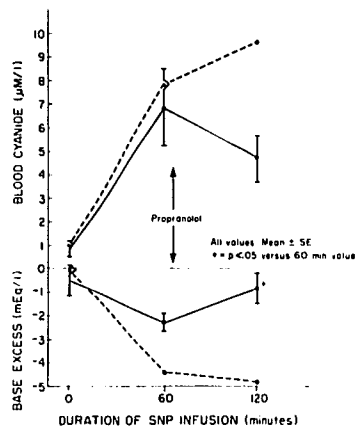

Fig 2. Blood cyanide increased and base excess decreased in all patients during the first hour of SNP infusion. Dashed line indicates patient who did not respond to a single propranolol dose.