

Date :
Title : PATTERNS OF SERUM COBALAMINS DURING NITROPRUSSIDE ADMINISTRATION IN MAN
Author : N.R. Fahmy, M.D.
Affiliation: From the Anesthesia Services of the Massachusetts General Hospital and the Department of Anaesthesia, Harvard Medical School, Boston, Massachusetts 02114

Introduction

It has been suggested that cobalamin (vitamin B₁₂) may play an important role in cyanide metabolism.¹ Since sodium nitroprusside (SNP) is metabolized in man releasing cyanide, we decided to study the patterns of serum cobalamins during SNP administration.

Methods

Twelve patients undergoing major orthopedic procedures under general anesthesia and induced hypotension (to reduce blood loss) were randomly assigned to receive SNP or pentolinium. The SNP and pentolinium (control) groups had six patients each. Following premedication with morphine and scopolamine, anesthesia was induced with thiopental. Endotracheal intubation was facilitated by succinylcholine. Intravenous morphine (average dose 26 mg), nitrous oxide-oxygen and d-tubocurarine were used for maintenance of anesthesia. Ventilation was controlled to maintain arterial PCO₂ between 35 and 40 mm Hg. SNP or pentolinium was administered in sufficient doses to lower and maintain mean systemic arterial pressure at 50 mm Hg. Arterial blood samples were obtained before and at hourly intervals for 4 hours during hypotension and two hours postoperatively. Samples were analyzed for blood cyanide and plasma thiocyanate concentrations (colorimetric methods), total serum B₁₂ concentration (radioisotope dilution assay), serum cobalamins (thin-layer chromatography and bioautography), serum electrolytes, blood lactate and pyruvate concentrations (enzymatic method), and PO₂, PCO₂ and pH (standard electrodes).

Results

SNP Group: Blood cyanide increased significantly ($P < 0.001$) from 3.2 ± 0.9 (pre-infusion) to 71.5 ± 14.1 μg per 100 ml (4 hours after SNP); it was still significantly elevated two hours postoperatively. Plasma thiocyanate did not change significantly during hypotension; it was increased ($P < 0.05$) postoperatively, however. Total serum B₁₂ decreased significantly ($P < 0.001$) from 558 ± 64 to 324 ± 52 pg per ml. An important change in the pattern of serum cobalamins occurred with SNP administration. Methylcobalamin (MeCbl) and adenosylcobalamin + hydroxocobalamin (AdoCbl + OHcbl) concentrations decreased, whereas cyanocobalamin concentration increased significantly after SNP. The same pattern persisted postoperatively. A significant negative correlation existed between blood cyanide and total serum B₁₂ concentration.

Pentolinium Group: Blood cyanide, thiocyanate and B₁₂ concentrations were not changed. These variables, however, were not significantly different between the two groups before arterial hypotension

was induced. Other measured variables were not significantly changed in either group.

Infusion rate of SNP was 5.16 $\mu\text{g}/\text{kg}/\text{min}$. Total dose of pentolinium was 22 mg. Durations of hypotension were comparable in both groups.

Discussion and Conclusions

These results demonstrate that cyanide released from therapeutic doses of SNP decreased serum B₁₂ concentration and altered the pattern of serum cobalamins. The drugs employed and induced hypotension *per se* had no effect on the results, since no changes were detected in the pentolinium (control) group. The observed increases in blood cyanide levels are in agreement with those reported previously.² Plasma thiocyanate concentrations were not significantly changed, indicating that this variable is not an important indicator of cyanide toxicity during short-term SNP infusion.

A striking feature of these results is the decrease in serum B₁₂ concentration, most probably resulting from loss of B₁₂ in urine. This is apparent from examination of changes in the pattern of serum cobalamins, i.e., decreased MeCbl, AdoCbl + OHcbl and increased CNCbl. These findings also suggest the involvement of B₁₂ in cyanide metabolism. Cyanide released from SNP combines with OHcbl and other cobalamins to form CNCbl. The latter (normally absent or present in trace amounts), being less firmly bound to plasma proteins, is readily excreted in urine. Similar findings were found by Linnell *et al.*¹ in heavy smokers (high cyanide intake).

Thus, serum B₁₂ levels should be monitored during long-term use of SNP. Moreover, hydroxocobalamin can be an important adjuvant during SNP administration; it raises serum cobalamin levels and can prevent potential cyanide toxicity from SNP.

References

1. Linnell JC, Smith ADM, Smith CL, *et al.* Effect of smoking on metabolism and excretion of vitamin B₁₂. *Br Med J.* 1968; 2: 215-216.
2. Vesey CJ, Cole PV, Simpson PJ. Cyanide and thiocyanate concentrations following sodium nitroprusside infusion in man. *Br J Anaesth.* 1976; 48: 651-660.