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TITLE: Post-bypass Hypothermia: Prevention and Clinical Benefit

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Inadvertent hypothermia following apparently adequate rewarming during hypothermic cardiopulmonary bypass (CPB) is a common intra- and postoperative problem. Administration of sodium nitroprusside (SNP) plus increasing pump flows during the rewarming phase of CPB was recently reported to result in a 42% amelioration of the average nasopharyngeal temperature (NPT) decrease by 80 minutes post-CPB.<sup>1</sup> The present study was conducted 1) to determine whether this effect of vasodilation could be quantified with a dose-response relationship; 2) to determine whether peak great toe temperature (GTT) during rewarming could be used to assess adequacy of rewarming when such vasodilation and increased pump flow therapy is used; and 3) to determine the postoperative clinical significance of these intraoperative therapy changes.

#### Methods

Ten adult patients undergoing hypothermic CPB for coronary artery bypass grafting procedures (Group I) were given as much SNP as possible during rewarming, within the constraints of maintaining mean radial artery pressure  $\geq 70$  mmHg. At the same time, pump flow was increased until arterial inflow line pressure reached 250 mmHg. Narcotics only were administered during the pump run. NPT and GTT were measured each minute during rewarming and every five minutes from the termination of CPB until the patient reached the intensive care unit. In the ICU, NPT and GTT were measured hourly until NPT reached 37°C. Blood loss and blood transfusion were recorded for the first eight postoperative hours. Cardiac index (dye dilution) was measured and complications such as excessive bleeding, need for inotropic support, etc. were noted. A second group (N=10, Group II), matched for age, sex and operation were rewarmed without vasodilation or increased pump flows.

#### Results

Post-bypass NPT decreases of  $> 1.5^\circ\text{C}$  after 80 minutes were considered to be failures of therapy. Seven of the 10 patients treated with SNP and increased pump flows during rewarming were "successes", with post-bypass NPT decreases of  $< 1.5^\circ\text{C}$ , ranging from 0-1.4°C. Of the three "failures", one patient failed to significantly vasodilate in response to non-toxic doses of SNP and two had peak SNP doses of  $> 4 \mu\text{g}/\text{kg}/\text{min}$ . Peak SNP dosage for the patients in whom NPT decrease was  $< 1.5^\circ\text{C}$  at 80 minutes averaged  $3.4 \pm .15 \mu\text{g}/\text{kg}/\text{min}$ . Analysis of the dose-response data indicates the optimum range of SNP dosage to be between 2.8 and 4.0  $\mu\text{g}/\text{kg}/\text{min}$ .

Group I overall average NPT decrease at 80 minutes post-CPB was  $0.98 \pm .73^\circ\text{C}$ , and at ICU admission was  $1.28 \pm .34^\circ\text{C}$ ; while Group II average NPT decrease at ICU admission was  $3.3 \pm .34^\circ\text{C}$  ( $p < .001$ ). Time required for NPT to reach 37°C after arrival in the ICU was  $2.3 \pm .19$  hours for Group I vs.  $3.1 \pm .73$  hours Group II,  $p < .02$ . These data do include the three "failures" in Group I.

Great toe temperature (GTT) increased during rewarming in all Group I patients, and the increase averaged  $6.2 \pm .74^\circ\text{C}$ . While GTT increased in Group II, the magnitude was significantly less ( $2.0 \pm .43^\circ\text{C}$ ,  $p < .001$ ). GTT increases during rewarming of  $> 3.5^\circ\text{C}$  were associated with NPT decreases of  $< 1.5^\circ\text{C}$  in Group I patients except those who received  $> 4 \mu\text{g}/\text{kg}/\text{min}$  of SNP during rewarming and the single patient who failed to vasodilate in response to SNP. In contrast, GTT increases of  $> 3.5^\circ\text{C}$  occurred in only two Group II patients; and in these patients, NPT decrease post-bypass was numerically less than in the overall group as expected.

Cardiac index at ICU admission, along with blood loss and blood replacement for the first 8 postoperative hours, are shown in Table 1. Postoperative CI was significantly greater in Group I. Although blood loss and replacement averaged numerically less for Group I, the difference was not significant. Additionally, shivering in the ICU was not observed in any of the patients who were pharmacologically vasodilated during rewarming, while shivering occurred in 2 of 10 of Group II patients. No patient in either group required reoperation for excessive bleeding. Inotropic support in the ICU was used in three Group II patients and no Group I patients.

#### Conclusions

- 1) The most efficacious dosage range for SNP administration during rewarming was 2.8-4.0  $\mu\text{g}/\text{kg}/\text{min}$ . A definite dose-response relationship was established.
- 2) Great toe temperature increases of  $> 3.5^\circ\text{C}$  during rewarming were associated with NPT decreases of  $< 1.5^\circ\text{C}$ , when SNP was used during rewarming and pump flows were increased to a point at which arterial inflow line pressure reached 250 mmHg.
- 3) Postoperative CO and CI were significantly greater in patients who received SNP and increased pump flows during rewarming. In addition, no shivering was seen in the ICU in these patients, eliminating the potentially increased  $\dot{V}\text{O}_2$ .

#### References

1. Noback CR, Tinker JH: Heat dosage vs. distribution during rewarming on CP bypass. *Anesthesiology* 51: S134, 1979

Table 1: Postoperative Comparison

	Group I (SNP, n=10)	Group II (no SNP, n=10)	
CO (l/min)	$5.38 \pm .31^*$	$3.5 \pm .28$	$p < .001$
CI (l/min/m <sup>2</sup> )	$2.68 \pm .15$	$1.85 \pm .14$	$p < .001$
Blood loss (ml) <sup>+</sup>	$305 \pm 49$	$446 \pm 100$	NS
Transfusion (ml) <sup>+</sup>	$406 \pm 89$	$660 \pm 147$	NS
Inotropic support (#)	0	3	
Reoperation (#)	0	0	

\*mean  $\pm$  SEM

<sup>+</sup>in the first 8 hours postop