Title: ELIMINATION OF POST BYPASS SECONDARY PEAKS OF FENTANYL BY PULSATILE CARDIOPULMONARY BYPASS

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Introduction. The option of pulsatile flow (PF) during cardiopulmonary bypass (CPB) has often been foregone because of the added complexity of the procedure and lack of substantial benefit. However, maintenance of liver blood flow and possible improved elimination of anesthetic drugs presented to the liver make the pulsatile option more attractive.[1,2] This study investigates the relationship of PF versus non-pulsatile flow (NPF) during CPB on the effective hepatic plasma flow (EHPF) and the resulting fentanyl levels post bypass.

Methods. With informed consent and approval from the Human Subjects Review Committee, we evaluated 24 patients scheduled for CABG surgery. Patients were excluded that were taking cimetidine, had ejection fractions of less than 50%, or had abnormal liver function studies. Each patient received morphine and lorazepam premedication calculated per kg of body weight. Standard monitoring procedures, including a Swan-Ganz catheter (SGC), were instituted before induction, at which time randomization to either PF or NPF flow occurred. Induction was performed with 50 mcg/kg of fentanyl (F) and an equal combination of 0.05 mg/kg of pancuronium and vecuronium. Maintenance of anesthesia consisted of F infusion of 0.5 mcg/kg/min and 100% O_2. CPB was performed with a Sarns 7400 MDX pump which had both a PF and NPF mode. Flows on pump were maintained between 2.2-2.4 L/m^2/min and perfusion pressures were between 50-70 torr. EHPF was determined using 0.5 mg/kg Indocyanine Green (ICG) given as a bolus through the central venous port SGC at 3 time periods: 20 min after induction, 20 min after aortic cross clamping, and 35 min after termination of CPB. Five blood samples were drawn from the radial artery at 3 min intervals during each time period. ICG concentrations were determined using ultraviolet spectroscopy. EHPF was calculated from semilogarithmic plots of ICG versus time. Plasma fentanyl concentrations were determined at 12 points during the study with the final sample being drawn at 30 min post-extubation. F analysis was by radioimmune assay accurate to 1 ng/ml. The results of EHPF and F plasma levels were correlated and analyzed by linear regression, analysis of variance, Fisher's exact test, and Pearson's product-moment correlation coefficient tests. Statistical significance was taken as a P value of less than 0.05.

Results. There were no demographic differences between the groups and no statistical differences between the calculated ICG dye volumes of distribution. With the initiation of CPB, EHPF was maintained at the prebypass level in the PF group while declining to nearly half (48%) that value in the NPF group. There was no statistical difference in plasma fentanyl level decline during CPB between the PF and NPF groups. There was a significant relationship between EHPF and PF which did correlate with lower F levels during bypass. Post bypass, the PF group had shorter half-lives that the NPF group, but this did not reach statistical significance. Significantly ($P<0.01$) more patients in the NPF group, 80% (12/15) had secondary plasma F peaks (five of these patients had multiple secondary peaks). Only 22% (2/9) of the PF patients had one plasma F level higher than the preceding one (no multiple peaks); whereas the NPF secondary peaks were characterized by two or more F levels greater than the preceding measured concentration.

Discussion. We determined that PF maintains EHPF at the prebypass level while NPF decreased EHPF by 48%. The maintenance of a higher EHPF did not greatly influence plasma fentanyl decline during bypass compared to NPF. This may have been due to the liver's high capacity for clearance of F even though flow was decreased. The significant difference that PF has on the elimination of plasma F peaks post bypass may be related to better maintence of perfusion via the PF improving deep compartment circulation allowing a steady clearance of F compared to the sequestered areas of F that may occur during NPF bypass.

References.
1. Koska AJ, Romagnoli A, Kramer WG. Effect of cardiopulmonary bypass on fentanyl distribution and elimination. Clin Pharmacol Ther 29:100-105, 1981.
2. Howie MB, Mortimer W, Rathburn S, Myers D, Dumond DA. Does pulsatile flow maintain liver blood flow during CPB? Anesthesiology 65:A52, 1986.

Figure 1 ACCUMULATIVE SECONDARY PEAK FENTANYL CONCENTRATIONS