ESMOLOL FOR THE MANAGEMENT OF PEDIATRIC HYPERTENSION AFTER CARDIAC OPERATIONS

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Objective: Hypertension frequently occurs during the immediate postoperative period in children after repair of aortic coarctation but may also occur after repair of other congenital heart defects. Nitroprusside has often been used to control blood pressure in this setting. Because hypertension after coarctation repair is frequently associated with elevations in catecholamines, esmolol, a short-acting β -blocking agent, may be an effective alternative. Therefore we undertook the first systematic investigation to determine the efficacy and disposition of esmolol in pediatric patients with acute hypertension after cardiac operations. **Methods:** Twenty patients aged 1 month to 12 years (median 25.6 months) with acute hypertension after cardiac operations received esmolol in an opened-labeled trial. Esmolol was titrated to a blood pressure less than or equal to the 90th percentile for age. **Results:** Ten patients had coarctation repair and the remaining patients underwent repair of other congenital heart defects. On final esmolol dose (mean $\pm$ standard deviation dosage $700 \pm 232 \mu\text{g/kg/min}$) there was a significant percent decrease in heart rate and systolic and diastolic blood pressures from postoperative values. Esmolol dose was significantly associated with percent reduction in systolic blood pressure. Final esmolol dose and total body clearance were significantly higher in patients after coarctation repair. There were significant associations between esmolol dose and esmolol blood concentrations at steady state. **Conclusions:** The dosage required to control hypertension in patients after repair of aortic coarctation was higher than patients who underwent repair of other congenital heart defects. Esmolol was effective in controlling blood pressure in 19 of 20 patients without adverse effects. (J Thorac Cardiovasc Surg 1998;115:890-7)

Acute postoperative hypertension occurs in 37% to 100% of patients after aortic coarctation repair^{1,2} but may occur after repair of other congenital heart defects.³⁻⁵ Sodium nitroprusside is frequently used to manage hypertension after cardiac operations because of its ease of titration and its rapid onset and offset of action. However, sodium nitroprusside is an indirect stimulator of the sympathetic nervous system.^{6,7} This may further aggravate

the increased sympathetic activity frequently present in patients who have had repair of aortic coarctation.^{1,8} In some cases nitroprusside may add to the tachycardia decreasing arterial oxygen saturation tension (PaO_2) and oxygen saturation.⁹ β -Adrenergic blockade would provide rational therapy in this setting but has been limited by the lack of a titratable intravenous agent that had a rapid onset and offset of action.

Esmolol is an intravenous, cardioselective, β -adrenoceptor antagonist with a short duration of action.^{10,11} It is easily titratable and has safely been applied in the critical care setting, where potential adverse effects (e.g., bradycardia, hypotension, or bronchospasm) can be rapidly reversed.¹² In adults, esmolol has been used for the acute management of supraventricular arrhythmias,¹³ ischemic heart disease,¹⁴ intraoperative and postoperative hypertension,^{15,9} and in other situations where brief adrenergic blockade is required.^{16,17} Esmolol has been

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Table I. Blood pressure (mm Hg) values for entry criteria and esmolol dosing threshold

Age	Significant hypertension (95th%)*	Severe hypertension (99th%)*	Normal blood pressure (≤ 90 th%)*†
Newborn	SBP ≥ 96	SBP ≥ 106	SBP ≤ 87
7-30 days	SBP ≥ 104	SBP ≥ 110	SBP ≤ 101
<2 yr	SBP ≥ 112	SBP ≥ 118	SBP ≤ 105
	DBP ≥ 74	DBP ≥ 82	DBP ≤ 68
3-5 yr	SBP ≥ 116	SBP ≥ 124	SBP ≤ 107
	DBP ≥ 76	DBP ≥ 84	DBP ≤ 68
6-9 yr	SBP ≥ 122	SBP ≥ 130	SBP ≤ 111
	DBP ≥ 78	DBP ≥ 86	DBP ≤ 70
10-12 yr	SBP ≥ 126	SBP ≥ 134	SBP ≤ 117
	DBP ≥ 82	DBP ≥ 90	DBP ≤ 75

SBP, Systolic blood pressure; DBP, diastolic blood pressure. Adapted from reference 22.

*Entry criteria for blood pressure.

†Esmolol dosing threshold or maximum of 1000 $\mu\text{g/kg/min}$.

shown to effectively attenuate the hemodynamic responses associated with stressful stimuli (e.g., endotracheal intubation) in the perioperative period.^{15, 18} Although the effects of esmolol are well characterized in adults, little information is known concerning its effects in children.¹⁹⁻²¹ On the basis of esmolol's pharmacologic profile, it may be a suitable alternative to sodium nitroprusside for the management of acute cardiac postoperative hypertension in pediatric patients. To date, trials evaluating esmolol as the sole agent in this clinical setting are lacking.

Specifically, the goals of this investigation were to (1) determine the dosing requirements and efficacy of esmolol in managing cardiac postoperative hypertension; (2) determine any associations between esmolol dose or blood concentration and hemodynamic parameters; and (3) determine the pharmacokinetic parameter estimates of esmolol in children.

Methods

The protocol was approved by the Institutional Review Board for Human Research. Written informed consent for participation was obtained from the patients' parents or legal guardians. Patients who had cardiac operations, from birth (term newborn) to 12 years of age, were considered for study enrollment if they had significant hypertension or were receiving sodium nitroprusside as an antihypertensive agent during the immediate postoperative period. Significant hypertension was defined as a blood pressure greater than the 95th percentile for age²² (Table I) on three or more consecutive arterial blood pressure recordings. For those patients receiving nitroprusside, the dose was weaned or discontinued and blood pressure assessed for 10 minutes or less. Other inclusion criteria were (1) an indwelling arterial catheter for esmo-

Table II. Esmolol dosing guidelines

Age	Dose* ($\mu\text{g/kg/min}$)	
	Starting	Titration
0-7 days	50	25-50 every 20 min
8 days to 1 mo	75	50 every 20 min
>1 mo to 1 yr	100	50 every 10 min
>1 yr to 12 yr	150	50-100 every 10 min

*Maximum dose: 1000 $\mu\text{g/kg/min}$.

lol blood sampling and continuous blood pressure monitoring and (2) an indwelling venous catheter for esmolol administration. A Spacelabs Monitor (model 90342; Spacelabs Inc., Redmond, Wash.) continuously displayed the electrocardiogram through lead V₂ or V₅, heart rate (HR), respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MAP). Patients with pulmonary disease, congestive heart failure, diabetes mellitus, hypoglycemia, receiving inotropic agents, or any antihypertensive agent other than sodium nitroprusside were excluded from the study.

Antihypertensive and antiarrhythmic medications were discontinued the day before the operation. Three or four preoperative HRs and blood pressures were obtained during the day before the operation and the mean determined for patients entering the study. Blood pressures were measured using a Dinemapp oscillometric blood pressure recorder (Critikon, Inc., Tampa, Fla.) applying standard techniques with patients in the supine or sitting position depending on patient age.²² Before the operation, a complete blood count with differential and serum electrolyte profile was obtained. Postoperative management was not influenced by the protocol. Standard sedation and analgesia management was morphine, 0.1 mg/kg intravenously every 1 hour, and lorazepam, 0.1 mg/kg intravenously every 6 hours as needed.

Esmolol (10 or 20 mg/mL) was prepared in dextrose 5% water²³ and administered intravenously by continuous infusion using a syringe pump (model 2001, Medfusion Inc., Duluth, Ga.). Esmolol dose was based on the patient age (Table II) and titrated until blood pressure was equal to or less than the 90th percentile for age (Table I) or 1000 $\mu\text{g/kg/min}$ was achieved. During esmolol infusion, arterial blood pressure and HR were recorded every 1 to 3 minutes depending on how rapidly these parameters were changing. MAP was calculated using the following equation:

$$\text{MAP} = \frac{(\text{SBP} - \text{DBP})}{3} + \text{DBP}$$

The final dose was maintained for 30 minutes to ensure steady-state conditions¹⁹ and then discontinued. Blood pressure and HR monitoring continued for 30 minutes after stopping esmolol. Esmolol or nitroprusside was restarted after the protocol was completed if clinically indicated.

Esmolol blood samples (1.2 ml) were obtained at the following times: (1) just before starting the infusion; (2) before two dosage adjustments maintained for 20 minutes or longer; (3) at final dose; (4) just before stopping the

Table III. Demographic data

Patient	Age (mo)	Sex/race	Weight (kg)	BSA (m ²)	Diag.	HR* (BPM)	SBP/DBP (mm Hg)	MED. PTA†
1	5.2	F/B	3.1	0.20	ASD/VSD	126	81/58	Capt Furo
2	18.0	F/W	8.1	0.40	VSD/DCRV	123	102/54	Capt
3	24.2	M/W	12.0	0.53	CoA	108	116/64‡	Capt
4	8.4	M/B	8.0	0.36	CoA/PDA	109	111/54	Capt
5	36.0	M/B	11.5	0.53	TOF/Down's	112	107/52	
6	148.0	F/B	46.8	1.38	Ao Sten	88	113/61	
7	35.0	F/B	13.3	0.60	CoA	112	120/69‡	
8	1.2	M/B	3.7	0.23	Dup Ao Ar	180	95/53	
9	55.0	F/W	17.2	0.72	CoA	86	117/54‡	
10	2.4	M/W	6.2	0.30	CoA	127	153/79§	
11	55.0	F/B	22.0	0.83	CoA	90	127/68§	Aten
12	75.0	M/B	22.5	0.89	VSD	81	103/51	
13	32.0	F/B	12.7	0.55	ASD	103	106/45	
14	61.6	M/W	17.9	0.73	ASD	102	107/60	
15	21.5	F/W	10.0	0.44	CoA/PDA	129	114/62‡	Capt
16	1.0	M/W	1.8	0.15	CoA/PDA	145	99/54	Capt
17	15.5	M/W	13.2	0.53	CoA	118	107/57	
18	58.0	F/W	16.8	0.70	CoA	117	115/76	
19	27.0	M/B	12.8	0.58	VSD/PDA	113	126/70§	Dig Furo
20	16.4	M/B	9.2	0.41	VSD	105	104/43	
Mean ± SD	34.8 ± 34.6		13.4 ± 9.7	0.55 ± 0.28				

BSA, Body surface area; F, female; M, male; B, black; W, white; ASD/VSD, atrial septal defect/ventricular septal defect; DCRV, double-chambered right ventricular; CoA, coarctation of the aorta; PDA, patent ductus arteriosus; TOF/Down's, tetralogy of Fallot/Down syndrome; Ao Sten, aortic stenosis; Dup Ao Ar, duplicate aortic arch.

*HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure reported as mean of three consecutive preoperative measurements.

†PTA, Before admission; Capt, captopril; Furo, furosemide; Aten, atenolol; Dig, digoxin.

‡Significant hypertension ($n = 4$) (see Table I).

§Severe hypertension ($n = 3$) (see Table I).

infusion; and (5) at 2, 4, 6, and 10 minutes after stopping the infusion. Blood samples were obtained through an arterial line and immediately placed in test tubes containing sodium fluoride to prevent in vitro conversion of esmolol to its metabolite (ASL-8123).²⁴ A 1.0 ml aliquot was transferred to a test tube containing 3 ml of acetonitrile and the internal standard. Samples were vortexed and cold centrifuged (4000 rpm) for 10 minutes. The supernatant containing esmolol was extracted, placed on ice, and stored at -20°C until analysis.

Esmolol blood samples were analyzed by high-performance liquid chromatography using a similar technique as previously described.²⁵ The limit of sensitivity was 0.10 $\mu\text{g/ml}$. Standard curves were linear and reproducible over the range of 0.10 to 10 $\mu\text{g/ml}$ (correlation coefficients > 0.99). The mean $\pm$ SD interday and intraday coefficients of variation for the assay were $4.86\% \pm 2.13\%$ and $3.25\% \pm 1.77\%$, respectively.

Blood esmolol concentration-time profiles were analyzed by noncompartmental pharmacokinetics. The terminal elimination half-life ($t_{1/2}$) was determined from the slope of the terminal elimination phase. Total body clearance (TBC) was calculated by the following equation:

$$\text{TBC} = K_e/C_{ss}$$

where K_e was the final dose and C_{ss} was the mean of concentrations obtained at steady state. The volume of distribution at steady state ($V_{d,ss}$) was determined by dividing the elimination rate constant ($K_e = 0.693/t_{1/2}$) into TBC.²⁶

Statistical analysis. Baseline hemodynamic parameters were defined as the three consecutive measurements of blood pressures and HRs obtained the day before the operation. Percent change in hemodynamic measurements during the postoperative period and at final dose were determined from baseline values. Significant differences were determined using a paired t test. A Student's t test was used to determine significant differences between the group that underwent coarctation repair and those that underwent repair of other congenital heart defects for (1) mean TBC, (2) mean final dose, (3) mean steady-state esmolol blood concentrations at final dose, and (4) mean percent change in hemodynamic parameters during the postoperative period and on final esmolol dose.

Stepwise multiple regression analysis, using forward addition and backward elimination, was used to determine the association between esmolol dose and the mean percent change of measured hemodynamic parameters. The mean percent change in hemodynamic parameters

Table IV. Postoperative and final hemodynamic results

Patient	Postoperative			Final				After/esmolol*	
	HR (beats/min)	SBP/DBP (mm Hg)	%HTN SBP/DBP	HR (beats/min)	SBP/DBP (mm Hg)	%HTN SBP/DBP	Esmolol ($\mu\text{g/kg/min}$)	HR (beats/min)	SBP/DBP (mm Hg)
1	126	131/84†	17/14	126	99/57	-12/-23	500	126	121/68
2	135	143/81†	28/10	136	98/62	-13/-16	550	130	104/59
3	122	147/68†	31/-8	111	109/53	-3/-28	950	123	133/74
4	133	127/60†	13/-19	134	102/61	-9/-18	950	126	115/50
5	115	110/82‡	-5/8	112	90/63	-22/-17	300	111	94/61
6	129	146/81†	16/-1	114	102/70	-19/-15	300	118	130/82
7	140	144/93†	26/22	114	110/71	-5/-7	950	130	147/103
8	192	125/62†	12/-16	148	96/49	-14/-34	350	159	101/47
9	116	132/74†	14/-3	111	94/59	-19/-22	850	123	105/60
10	133	136/85†	21/12	124	118/66	1/-11†	1000	129	131/68
11	92	129/70†	11/-8	121	102/52	-12/32	950	130	110/51
12	105	128/74‡	5/-5	113	108/77	-12/1	500	111	118/82
13	153	131/73†	13/-4	125	106/64	-5/-14	700	134	129/74
14	115	124/67†	7/-12	102	100/59	-14/-22	800	108	119/71
15	150	120/72†	7/-3	120	102/60	-9/-19	750	131	108/60
16	165	111/79†	7/NA§	125	92/58	-12/NA§	600	155	100/65
17	159	118/75†	5/1	130	105/69	-6/-7	650	140	110/67
18	118	118/68‡	2/-11	107	105/66	-10/-13	650	116	112/70
19	129	126/65†	13/-12	117	94/52	-16/-30	1000	119	112/61
20	122	139/85†	24/15	116	95/58	-15/-22	700	119	117/59
Mean $\pm$ SD			13 $\pm$ 9/-1 $\pm$ 12			-11 $\pm$ 6/-18 $\pm$ 9	700 $\pm$ 232		

HR, Heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; %HTN, percent hypertension based on 95th percentile for age.

*Mean of three to four consecutive measurements immediately after esmolol.

†Severe hypertension (see Table I).

‡Significant hypertension (see Table I).

§NA, Not available.

(i.e., HR, SBP, DBP, and MAP) for all patients receiving the same dose, under steady-state conditions, was determined from a minimum of three measurements for each parameter. Steady state was defined as maintaining the same dose for 20 minutes or more. Least squares regression analysis was used to examine associations between the following: (1) patient age and pharmacokinetic parameters (TBC, $t_{1/2}$, and V_{dss}), (2) mean esmolol blood concentration and mean percent reduction in hemodynamic parameters for all patients on the same dose under steady-state conditions, and (3) dose and mean esmolol blood concentrations at steady state. Significance was defined as $\alpha = 0.05$.

Results

Twenty patients aged 1 month to 12 years (median 25.6 months) were enrolled in this investigation. Patient characteristics are described in Table III. Ten patients underwent repair of aortic coarctation. The remaining patients had repair of other congenital heart defects. Seven patients had preoperative hypertension (6, coarctation repair; 1, ventricular septal defect/patent ductus arteriosus) (Table III). Postoperatively, 12 (6, aortic coarctation) patients had systolic hypertension, 1

patient had diastolic hypertension, and the remainder had both. Seventeen patients had severe hypertension (>99 th percentile for age) and three patients had significant hypertension (>95 th percentile for age) (Table IV). Mean time from completion of the operative procedure to study entry was 4.7 hours (range 2.0 to 9.5 hours). Eighteen patients were receiving nitroprusside (mean dose 3.5 $\mu\text{g/kg/min}$; range 1 to 7 $\mu\text{g/kg/min}$) during the immediate postoperative period. Nitroprusside was discontinued and esmolol was begun in 17 patients. In the remaining patient (patient 11), nitroprusside was discontinued after achieving an esmolol dose of 700 $\mu\text{g/kg/min}$. The mean esmolol dose required to normalize blood pressure was 700 $\mu\text{g/kg/min}$ (range 300 to 1000 $\mu\text{g/kg/min}$). Final esmolol dose requirements in patients undergoing coarctation repair (mean dose $\pm$ SD: 830 $\pm$ 153 $\mu\text{g/kg/min}$; 18,608 $\pm$ 4,905 $\mu\text{g/m}^2/\text{min}$) was significantly ($p = 0.01$) higher than patients having repair of other congenital heart defects (mean dose $\pm$ SD: 570 $\pm$ 230 $\mu\text{g/kg/min}$; 12,766 $\pm$ 5,559 $\mu\text{g/m}^2/\text{min}$). No signif-

Fig. 1. Scatterplot showing the association between esmolol dose and blood concentration at steady state, as well as the predicted blood concentration by dose (solid line) and 95% confidence limits (dashed lines).

icant difference was found in steady-state esmolol blood concentrations at final dose between these groups.

The pharmacokinetic parameter estimates for all patients were (mean $\pm$ SD): $V_{d_{ss}}$ (L/kg) = 0.53 ± 0.33 ; TBC (ml/kg/min) = 126 ± 37 ; $t_{1/2}$ (min) = 2.7 ± 1.3 . Patient age and pharmacokinetic parameters $V_{d_{ss}}$ and $t_{1/2}$ were not significantly associated ($r^2 = 0.18$, $p = 0.07$; $r^2 = 0.06$, $p = 0.28$, respectively). A weak but significant inverse association was found between age and TBC in ml/kg/min ($r^2 = 0.28$, $p = 0.02$). A significant association was found between esmolol dose in both $\mu\text{g}/\text{m}^2/\text{min}$ (Fig. 1) and $\mu\text{g}/\text{kg}/\text{min}$ ($\mu\text{g}/\text{kg}/\text{min} = 143.9 + 89.5 \times \text{blood concentration}$; $r^2 = 0.63$; $p = 0.001$) and esmolol blood concentrations at steady state. TBC (ml/m²/min) in patients undergoing coarctation repair (mean $\pm$ SD: TBC = 3271 ± 835) was significantly ($p = 0.006$) higher than in patients having repair of other congenital heart defects (mean $\pm$ SD: TBC = 2396 ± 571); TBC in ml/kg/min approached significance ($p = 0.076$) between these groups.

A significant percent increase in postoperative hemodynamic measurements was found when compared with baseline values. On final esmolol dose a significant percent reduction ($p \leq 0.005$) (Fig. 2) in HR and blood pressure was noted from postoperative values. Percent change between baseline and

final hemodynamic measurements was significant for SBP ($p = 0.001$) (Fig. 2). A smaller percent decrease was found in SBP on final esmolol dose in patients who underwent coarctation repair than patients having repair of other congenital heart defects (-8.5% vs -14.2% ; $p = 0.001$, respectively). No other significant differences were found in hemodynamic measurements between these groups. By multiple stepwise regression analysis, esmolol dose was only significantly associated with percent change in SBP (Fig. 3).

The mean time to normalize blood pressure was 1.65 hours (range 0.6 to 3.6 hours). One patient (patient 10) did not achieve an SBP at the 90th percentile or less for age with an esmolol dose of $1000 \mu\text{g}/\text{kg}/\text{min}$.

Hemodynamic measurements (SBP, DBP, and HR) were significantly ($p \leq 0.02$) elevated after discontinuation of esmolol when compared with final esmolol dose values. Eight patients received one to three doses of morphine during the protocol (number of doses: 1 [$n = 6$], 2 [$n = 1$], and 3 [$n = 1$]). Four patients received one dose of lorazepam whereas two patients received one dose of lorazepam and morphine. Ten patients were restarted on esmolol within 10 to 17 minutes of the conclusion of the study. For two patients, esmolol was restarted at 1 and 2 hours. Esmolol was continued for 6 to 48

Fig. 2. Bar graph comparing postoperative and final hemodynamic measurements. Systolic blood pressure (SBP) was the only parameter significantly ($p = 0.000$) different among preoperative, postoperative, and final (+) measurements. HR and DBP indicate HR and diastolic blood pressure, respectively. *Indicates significant difference ($p \leq 0.005$) from final measurement.

hours. Four patients were started on an angiotensin-converting enzyme inhibitor and the remainder were placed on nitroprusside after the study. No adverse effects were associated with esmolol.

Discussion

Acute postoperative hypertension occurs in 37% to 100% of patients after aortic coarctation repair^{1,2} but may occur after repair of other congenital heart defects.³⁻⁵ The pathogenesis of paradoxical hypertension after coarctation repair involves the activation of the sympathetic nervous system (first phase) and renin-angiotensin system (second phase). In the first phase, postoperative norepinephrine concentrations have been found to increase 750% within 12 hours, leading predominantly to a rise in SBP.^{1,8} In the second phase, plasma renin activity increases 24 to 72 hours postoperatively producing significant elevations in DBP.¹ This phase may be prematurely activated when hypertension is controlled by sodium nitroprusside. Renin levels have been shown to increase fivefold within 30 minutes of induction of hypotension with sodium nitroprusside.⁶ The resulting increased angiotensin II vasoconstrictive activity would also increase sympathetic outflow from the

adrenal glands and central nervous system.⁷ Considering these physiologic changes a β -blocker, such as esmolol, should have a major influence on some of the cardiovascular changes after coarctectomy. However, plasma catecholamine and renin concentrations were not determined in this investigation. The mechanism for elevations in blood pressure after repair of other congenital heart defects is not clear but may be related to changes in renal blood flow and/or delay in autoregulatory response to a changed aortic blood flow.⁴

In this study, patients who underwent repair of aortic coarctation had paradoxical hypertension, with 6 of 10 patients having systolic hypertension only. This is consistent with the first phase of hypertension after coarctation repair.^{1,8} Patients with coarctation repair had a smaller decrease in their SBP while receiving a higher esmolol dose than patients undergoing repair of other congenital heart defects. The higher doses required in patients with coarctation repair may be related to their increased norepinephrine concentrations, increased TBC, or both. Theoretically, with higher esmolol dosing, β_1 -blocking selectivity would be lost, leaving norepinephrine to act on α -receptors unopposed. This would main-

Fig. 3. Scatterplot showing the relationship between percent change in systolic blood pressure and esmolol dose, as well as the predicted change in systolic blood pressure by dose (solid line) and 95% confidence limits (dashed lines).

tain or likely elevate systemic vascular resistance, requiring a higher esmolol dose to reduce cardiac output and lower blood pressure.

The mean esmolol dose required to normalize blood pressure was $700 \mu\text{g/kg/min}$. In a previous investigation the mean dose to produce β -blockade (defined as a 10% reduction in HR or MAP) was $535 \mu\text{g/kg/min}$ in 20 children undergoing indicated cardiac electrophysiologic testing.²⁰ This study also found that the esmolol dosage required to control hypertension was higher than that used in adults. Esmolol doses used to control hypertension after cardiac operations in adults are generally 100 to $300 \mu\text{g/kg/min}$.⁹ The higher doses used in this study are likely related to the degree of hypertension in these patients (mean 13.3% above the 95th percentile for age). Percent change in SBP was the only hemodynamic parameter associated with esmolol dose. Further reduction in SBP to progressively higher esmolol blood concentrations and doses has been reported in adults.^{11,27} The hemodynamic measurements obtained immediately after esmolol infusion represent how rapidly the offset of HR and blood pressure responses to esmolol begin to occur in most patients.

The pharmacokinetics of esmolol have been reported in children during cardiac catheterization,

where the elimination $t_{1/2}$ was shorter (2 to 4 minutes)^{19,21} and the dose requirements to produce β -blockade were higher²⁰ than those observed in adults. The extremely short $t_{1/2}$ of esmolol in children (mean 2.7 minutes) was also observed in this study. TBC of esmolol was higher in patients who underwent repair of aortic coarctation than patients undergoing repair of other congenital heart defects. Esmolol is rapidly metabolized by red blood cell esterases to an acid metabolite (ASL-8123) and methanol.¹¹ This would imply that red blood cell esterase activity is enhanced in patients with aortic coarctation. This enhanced TBC may explain the observation that steady-state esmolol blood concentrations were not significantly different between the coarctation and congenital heart defect groups. Studies in adults and children have not consistently reported an association between esmolol dose and blood concentration at steady state.^{24,19} This investigation found an association between dose and concentration that supports a previous observation in adults.⁸

In the pediatric intensive care setting, a cardioselective β -blocker that is easily titratable with a rapid onset and offset of action would be ideal, particularly in patients at high risk for adverse effects. Esmolol met these criteria in 19 of 20 children with

significant to severe hypertension after cardiac operations. This preliminary investigation demonstrated that esmolol was a safe and effective agent for the management of postoperative hypertension in the population studied. As with any β -blocker, caution should be used in patients with bradycardia, poor left ventricular performance, high-degree heart block, congenital heart defects with right-to-left shunting, chronic airway disease (e.g., asthma), diabetes, or other peripheral vascular diseases.

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