ORIGINAL ARTICLE

Effects of Remifentanil Anesthesia on Cardiac Electrophysiologic Properties in Children Undergoing Catheter Ablation of Supraventricular Tachycardia

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Abstract Remifentanil is commonly used during anesthesia in pediatric electrophysiologic studies (EPS). The purpose of this study is to determine the effects of remifentanil on the cardiac electrophysiologic properties of children undergoing ablation of supraventricular tachycardia (SVT). A prospective study was performed in patients undergoing EPS before ablation of SVT. Each patient received two different anesthetic protocols: protocol 1 = propofol (200 mcg/kg/min) and protocol 2 = propofol (120 mcg/kg/min) plus remifentanil (0.3 mcg/kg/min). EPS data were measured during the steady state of each protocol. Paired Student t test was performed for analysis of continuous data. All p values <0.05 were considered statistically significant. Fifteen patients were enrolled between April 2005 and January 2006. The mean age was 13.3 ± 2.9 years (range 6.7 to 17.7). Seven patients had atrioventricular (AV) nodal re-entry tachycardia; 5 patients had Wolff-Parkinson-White syndrome; 2 patients had a concealed accessory pathway; and 1 patient was not inducible. Of the 14 patients who underwent ablation, 13 (93%) achieved successful. The baseline sinus cycle length extended from 884 ± 141 ms during protocol 1 to 980 ± 165 ms during protocol 2 ($p = 0.01$), and the Wenckebach cycle length lengthened from 377 ± 96 ms to 406 ± 109 ms ($p = 0.01$). No other variables measured (atrial-His (AH) and His-ventricular (HV) interval, atrioventricular node (AVN), and atrial, ventricular, and accessory pathway effective refractory periods) changed significantly between the two different protocols. In pediatric patients undergoing EPS before ablation of SVT, remifentanil appears to slow both sinus and AV nodal function. These effects should be taken into consideration when performing EPS.

Keywords Remifentanil · SVT · Ablation

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Introduction

Electrophysiologic studies (EPS) with ablation of the arrhythmia substrate have become standard treatment for pediatric patients with supraventricular tachycardia (SVT) [6]. Presently, general anesthesia is often used during pediatric cardiac EPS to provide comfort, avoid pain, and provide immobility at critical moments of the procedure, such as the Brockenbrough transeptal puncture and during delivery of radiofrequency energy [10]. Various anesthetic agents (both gaseous and intravenous) have been used successfully for this purpose [3, 8, 9, 11].

Remifentanil is a potent synthetic opioid with μ-agonist action that has recently become more commonly used as an anesthetic agent in children. Although the drug retains the widely familiar characteristics of opioids, including parasympathomimetic effects, it is unique by virtue of its

pharmacokinetics. It has a fast onset of action and peak effect, with a rapid distribution half life of 1 min. The effective biologic half-life and its elimination half-life are both approximately 3 to 10 min, respectively [7]. Absence of postanesthesia nausea and vomiting is thought to be due to the lack of accumulation of the drug even after prolonged administration. For all of these reasons, remifentanil is used increasingly as an anesthetic agent during EPS and other interventions in children [5, 13]. It is known that remifentanil can cause hypotension and bradycardia [5]. However, data describing its impact on the cardiac electrophysiologic system are limited.

The purpose of this study was to determine the effects of remifentanil on the cardiac electrophysiologic properties of children undergoing catheter ablation of SVT to better understand its potential suitability for this procedure.

Materials and Methods

Patients

This study was performed at a single tertiary care center. After Institutional Review Board approval was obtained, a prospective study was performed. Patients undergoing EPS for possible ablation of SVT were offered enrollment in the study. Parental consent and assent of minors were obtained. The inclusion criterion was patients younger than 21 years of age with structurally normal hearts undergoing EPS for possible ablation of SVT. Exclusion criteria were contraindication to the use of propofol or remifentanil, depressed ventricular systolic function by echocardiography, and incessant tachycardia (requiring rapid procedural evaluation and ablation and thus precluding precise measurements).

Anesthesia

All patients underwent anesthesia induction with propofol and endotracheal intubation. Propofol has been studied in the electrophysiology laboratory and has been found to have either electrically neutral or clinically insignificant effects [3, 9]. This agent was also chosen for safety reasons because the incidence of rigidity due to remifentanil was decreased with previous propofol administration [16]. Each enrolled patient received two different anesthetic maintenance combination protocols in a randomly determined order. Protocol 1 consisted of an infusion of propofol (200 mcg/kg/min) with an air/oxygen mixture maintaining fractional inspired oxygen at 30%. Protocol 2 included propofol (120 mcg/kg/min) plus remifentanil (0.3 mcg/kg/min) in an air/oxygen mixture maintaining fractional inspired oxygen at 30%. All patients received 20 min of each protocol with a washout period of 20 min between both protocols. Propofol

infusion rates were maintained according to published recommended ranges for pediatric patients undergoing general anesthesia [10]. Electrophysiologic data were measured during the steady state of each protocol. The pediatric electrophysiologist obtaining the data was blinded to the order in which the protocols were administered. The measurements were obtained during EPS before the ablation.

EPS

Venous access was obtained through bilateral femoral veins and the right internal jugular vein. Transvenous electrode catheters were introduced and positioned in the right atrial appendage, right ventricular apex, and bundle of His and inside the coronary sinus. Surface ECG and intracardiac electrograms were recorded on a multichannel recording system (EP MedSystem, EP Medical System Inc, West Berlin, NJ). The baseline cycle length and intracardiac intervals were recorded in each state. Burst atrial pacing was performed to determine the Wenckebach cycle length (WBCL). Overdrive atrial pacing was used to measure the corrected sinus node recovery time. Atrial and ventricular extrastimulus testing was performed to determine the atrioventricular (AV) nodal effective refractory period (ERP; accessory pathway ERP, atrial ERP, retrograde ventriculoatrial ERP, and ventricular ERP. If tachycardia was induced, the mechanism and the cycle length of tachycardia were recorded. Patients with Wolff-Parkinson-White syndrome underwent a modified protocol. Testing for accessory pathway refractoriness was performed before any ablative procedures, and the two protocols were repeated after the ablation for evaluation of AV nodal function. In patients without evidence of accessory pathway conduction and suspected AV nodal re-entry tachycardia (AVNRT), an isoproterenol infusion was used after the two protocols if tachycardia was not inducible in the baseline state.

Statistical Analysis

Data was analyzed using STATA 9.2 statistical software (STATA, StataCorp, College Station, TX). Catagoric and dichotomous variables were expressed as percentages, and continuous variables were expressed as means ± SDs. Paired Student t test was used for analysis of continuous data. All p-values <0.05 were considered statistically significant.

Results

Patients

Fifteen patients consented for the study between April 2005 and January 2006. The mean age was 13.3 ± 2.9 years

Table 1 Summary of electrophysiologic data (all data in ms)

Parameter	Baseline (protocol 1)	Remifentanil (protocol 2)	p
Cycle length	884 ± 141	980 ± 165	0.01
AH interval	86 ± 28	77 ± 25	NS
HV interval	35 ± 25	30 ± 28	NS
cSNRT	343 ± 175	331 ± 158	NS
WB CL	377 ± 96	406 ± 109	0.01
AVNERP	281 ± 52	305 ± 77	NS
APERP ($n = 5$)	354 ± 121	372 ± 122	NS
AERP	220 ± 26	222 ± 34	NS
VAERP	304 ± 64	310 ± 51	NS
VERP	268 ± 64	256 ± 25	NS

cSNRT corrected sinus node recovery time, *AVNERP* atrioventricular node effective refractory period, *APERP* accessory pathway effective refractory period, *AERP* atrial effective refractory period, *VAERP* ventriculoatrial effective refractory period, *VERP* ventricular effective refractory period, *AH* atrial-His, *HV* His-ventricular, *ms* milliseconds

(range 6.7 to 17.7). Nine patients (60%) were female. Seven patients had AVNRT; 5 patients had WPW syndrome; 2 patients had a concealed accessory pathway; and 1 patient with history of documented tachycardia and was not inducible. Of the 14 patients who underwent an ablation, 13 (93%) achieved success. One patient with atypical AVNRT could not be successfully ablated.

Electrophysiologic Data

Table 1 lists the electrophysiologic data. The baseline sinus cycle length measured 884 ± 141 ms during protocol 1.
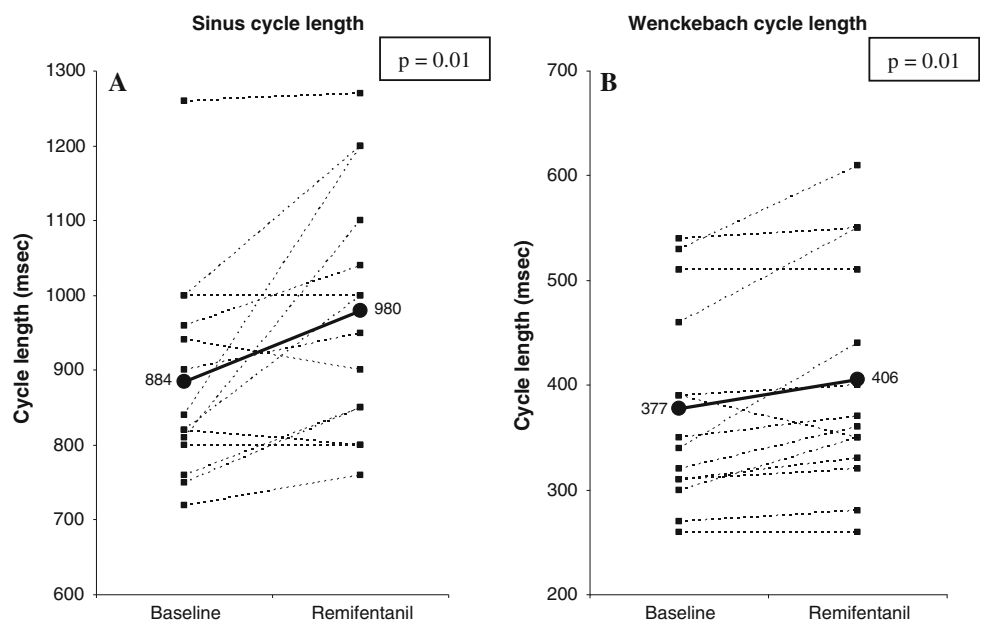
The sinus cycle length increased to 980 ± 165 ms during protocol 2 ($p = 0.01$) (Fig. 1a). Similarly, the WBCL measured 377 ± 96 ms during protocol 1 and increased to 406 ± 109 ms during protocol 2 ($p = 0.01$) (Fig. 1b). No other variables measured showed a significant change during infusion between the two protocols. Tachycardia was inducible in the baseline state in 3 of the 7 patients with AVNRT. An infusion of isoproterenol was necessary to induce tachycardia in 4 patients with AVNRT. There were no complications related to the procedure or the anesthesia.

Discussion

Since the initial reports of the ablation procedure in pediatric patients [14, 15], general anesthesia has been used routinely during these studies [6]. Anesthesia is frequently used to ensure comfort to the child and assure immobility, thus facilitating accurate mapping and subsequent ablation of the arrhythmia substrate. A short-acting agent is ideal in these studies to facilitate titration and manipulate anesthetic effects to obtain pertinent study data. Remifentanil has been used more frequently during anesthesia in pediatric patients in different settings [2, 12].

Remifentanil is known to cause hypotension and bradycardia [1]. These cardiovascular effects are thought to be related to an increase in parasympathetic tone provoked by the drug. Fattorini et al. [4] demonstrated that bradycardia caused by remifentanil was reversed by the administration of atropine. Parasympathetic effects on the heart result in slowing of sinus node activity and decreased AV nodal conduction. In our study, the main findings were consistent

Fig. 1 Change in sinus and WBCL

with this notion; specifically, the baseline sinus cycle length was prolonged by a mean of almost 100 ms, indicating a significant effect on the sinus node. Considering previous observational data, this behavior of remifentanil was somewhat expected. Similarly, the WBCL was longer during remifentanil infusion, suggesting an effect on the AVN. Although there was mild prolongation of the AVN effective refractory period with the remifentanil protocol, the difference was not statistically significant.

Although the data in this work clearly benefit from the prospective nature of the study design and the blinded data collection, the limitation of this study is the small number of subjects enrolled. Enrollment in this study required additional time for general anesthesia, and many parents and guardians were concerned about the risks despite the absence of any complications encountered during the study period. For this reason, enrollment was challenging. Another limitation of the study is that patients in the remifentanil protocol received a lower dose of propofol; however, previous studies demonstrated no significant effect of propofol on the cardiac conduction system in children undergoing ablation for tachyarrhythmias [9].

In conclusion, in pediatric patients undergoing EPS before ablation of SVT, remifentanil appears to slow both sinus and AV nodal function. These effects should be taken into consideration when performing EPS. Although it has many important anesthetic benefits, remifentanil may not be an optimal agent for certain cases in the electrophysiologic laboratory, particularly where AV nodal function must be preserved and closely monitored. Further data collection on its effects on the electrophysiologic properties of the heart is indicated.

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