Pupil diameter and light reaction during cardiac arrest and resuscitation

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Objective: Traditionally, both pupil diameter and reaction to light have been examined to confirm the diagnosis of death. In the present study, we investigated quantitative changes in pupil diameter and light reaction for assessing the efficacy of cardiopulmonary resuscitation (CPR) and as a predictor of outcome.

Design: Controlled experimental study.

Setting: Animal research laboratory at a university-affiliated research institute.

Subjects: Fifteen domestic male pigs weighing between 33 and 40 kg.

Interventions: Ventricular fibrillation was induced with an alternating current delivered to the right ventricular endocardium. After 7 mins of untreated ventricular fibrillation, chest compression and mechanical ventilation were initiated and maintained for 6 mins. Restoration of spontaneous circulation then was attempted by electrical defibrillation.

Measurements and Main Results: Spontaneous circulation was reestablished in 9 of 15 animals. Pupils were fully dilated, and pupillary reaction to light was absent in 7 of the 9 resuscitated animals during untreated cardiac arrest. Progressive decreases in pupil diameter were observed together with restoration of light reaction during CPR, in each animal that was successfully resuscitated. When the pupils remained dilated and unreactive after 6 mins of CPR, resuscitation efforts were uniformly unsuccessful. A highly significant linear correlation between coronary perfusion pressure generated during precordial compression and pupil diameter was documented. Both were predictive of outcome.

Conclusions: Dynamic changes of pupil diameter and reactions to light during cardiac arrest and resuscitation were correlated with coronary perfusion pressure, and both predicted the likelihood that spontaneous circulation and cerebral function would be restored.

Key Words: cardiac arrest; cardiopulmonary resuscitation; pupil diameter; light reaction

The widespread implementation of basic life support technique by first responders has significantly improved outcomes of cardiopulmonary resuscitation (CPR) (1). However, we recognize that for both lay and professional providers, there is a paucity of real-time physical signs with which to assess the effectiveness of CPR. Even the traditional “pulse check” largely has been abandoned, not only for confirming the presence of cardiac arrest but also for monitoring the effectiveness of CPR (2, 3).

The Edinger-Westphal nucleus, the visceral nucleus of the third cranial nerve in the pons, and the first thoracic segment of the spinal cord are the dominant sites that regulate pupil diameter and the reaction to light. When light impinges on the retina, the resulting impulses pass first through the optic nerves and then to the pretectal nuclei. From there, impulses pass to the Edinger-Westphal nucleus and finally back through the parasympathetic nerves to constrict the sphincter muscle of the iris. The resulting decrease in diameter represents the pupillary light reflex. When blood flow or the oxygen tension of arterial blood is reduced, the pupils dilate (4). When all blood flow ceases, the pupils dilate widely within an interval of 30–120 secs, and the pupillary reaction to light disappears (5, 6).

Pupil size and its reaction to light historically have been regarded as important predictors of subcortical function and neurologic outcome (7). As such, the pupil serves as an indicator of the effectiveness of cerebral blood flow during chest compression (8, 9). Yet, the prognostic value of dilated and nonreactive pupils in settings of CPR is insecure (10, 11). However, it is well known that the absence of both pupillary reflexes and oculocephalic responses predicts a poor neural outcome (12).

Coronary perfusion pressure (CPP) has been a reliable indicator of the likelihood of successful CPR. CPP is a correlate of myocardial blood flow that is generated during chest compression, and CPP consistently has predicted the likelihood that spontaneous circulation would be restored (13–15). However, the measurement of CPP requires right atrial and aortic catheterization, which strategically is precluded in most settings of cardiac arrest. Because both cerebral and coronary blood flows are correlated with cardiac output generated by precordial compression during cardiac arrest (16, 17), we hypothesized that there would be a close relationship between CPP and pupil reaction. Accordingly, we investigated dynamic changes of pupil diameter and light reaction together with CPP during cardiac resuscitation.

METHODS

Experiments were performed on 15 domestic pigs. All animals received humane care in
compliance with the Guide for the Care and Use of Laboratory Animals (18). The protocols were approved by the Institutional Animal Care and Use Committee of the Institute of Critical Care Medicine. The Institute’s laboratories are fully accredited by the American Association for Accreditation of Laboratory Animal Care.

Animal Preparation

Male domestic pigs from a single source breeder, weighing between 33 and 40 kg, were investigated. Animals were fasted overnight except for free access to water. Anesthesia was initiated by intramuscular injection of ketamine (20 mg/kg) followed by ear vein injection of sodium pentobarbital (30 mg/kg). Additional doses of sodium pentobarbital (8 mg/kg) were injected at intervals of approximately 1 hr to maintain anesthesia. After endotracheal intubation, the animals were ventilated mechanically with a tidal volume of 15 ml/kg and a peak flow of 40 L/min of room air with the aid of a volume-controlled ventilator (MA-1; Puritan Bennett, Carlsbad, CA). End-tidal PCO2 was monitored with a mainstream infrared analyzer (01R-7101A; Nihon Kohden Corp., Tokyo, Japan). Respiratory frequency was adjusted to maintain end-tidal PCO2 between 35 and 40 mm Hg. Conventional electrocardiographic scalar limb leads were recorded continuously. The femoral artery was isolated surgically under aseptic conditions. An 8-Fr angiographic catheter (6523; USCI C.R. Bart, Billerica, MA) was advanced through the right femoral artery into the descending thoracic aorta to measure aortic pressure. A pulmonary artery flotation catheter was advanced through the right femoral vein into the pulmonary artery to measure pulmonary artery pressure and right atrial pressure. The appropriate position of the catheter was confirmed by image intensification fluoroscopy.

A 4-Fr pacing wire (EP Technologies, Mountain View, CA) was advanced through a surgically isolated right cephalic vein into the right ventricle, to induce ventricular fibrillation (VF). The tip of the pacing wire was impinged on the apical endocardium during fluoroscopic imaging. A characteristic endocardial injury current confirmed appropriate placement.

Statistical Analyses

Data are presented as mean ± so. Differences in pupillary diameter and in CPP were analyzed with analysis of variance. The presence or absence of light reaction was determined by chi-square test. We regarded p < .05 as statistically significant.

RESULTS

Fifteen animals were studied. Baseline hemodynamic measurement did not differ significantly between the resuscitated and nonresuscitated animals. There were no statistically significant differences of mean pupil diameter before the onset of VF between resuscitated and nonresuscitated animals. The pupils responded briskly to light in each instance.

The reaction to light was lost in 13 of 15 animals within 2 mins after onset of cardiac arrest. In a majority of animals, the pupils were both unreactive and fully dilated after 5 mins of untreated cardiac arrest (Fig. 1). In three animals, the pupil was not fully dilated during the 7 mins of untreated cardiac arrest. The pupil of one animal failed to dilate, and response to light persisted for the entire 7 mins of untreated cardiac arrest. The extent of pupillary reaction after onset of VF was decreased compared to that before arrest (Table 1).

The CPP was consistently greater in resuscitated animals when compared with nonresuscitated animals (26 vs. 10 mm Hg, p < .01; Fig. 2). In each instance, the pupillary reaction to light was restored in animals in which CPP was >20 mm Hg. A highly significant correlation between CPP and pupil diameter was observed (r2 = .59, p = .005; Figs. 3 and 4). In resuscitated animals, CPP was 25.5 ± 5.0 mm Hg during CPR but only 9.6 ± 6.8 mm Hg in animals that failed resuscitation efforts. We coincidentally
observed that one animal which maintained unchanged pupil diameter and light reaction during untreated VF had a spontaneous CPP >20 mm Hg before CPR, in close association with unusually persistent gasping. After successful resuscitation, the pupil diameters over the 4-hr postresuscitation interval ranged from 6.0 to 8.1 mm. Each survivor achieved normal neurologic responsiveness over the ensuring 72 hrs.

DISCUSSION

The early initiation of basic life support provided by first responders largely has improved the outcome of CPR in settings of out-of-hospital cardiac arrest during the last 30 yrs. According to the American Heart Association and European Resuscitation Council Guidelines, both diagnosis of cardiac arrest and monitors indicative of the effectiveness and outcomes of CPR were based on the “pulse check” (20, 21). However, this standard has not withstood tests of objective evaluation (2, 3). As few as 3% of nonprofessional rescuers correctly identified both unconsciousness and the absence of carotid pulse within a time interval of 10 secs and for confirming cardiac arrest within the critical time interval of 10 secs and for monitoring the effectiveness of CPR. Therefore, the possibility presented itself that pupil diameter and light reaction would serve as physical signs for determining the presence of blood flow and for evaluating the effectiveness of CPR.

Pupil diameter and the reaction to light previously have been investigated as indicators of cerebral blood flow (8). Because cardiac resuscitation is intended to provide adequate myocardial and cerebral perfusion (9, 24, 25), we anticipated and found a link with CPP. Earlier workers had confirmed that pupil diameter and reaction to light during CPR predicted long-term survival (26). In the present experimental study, which used a well-established porcine model of cardiac arrest and resuscitation, pupils of all but three animals were maximally dilated and failed to react to light after 7 mins of untreated VF. During CPR, pupil diameter decreased and the pupil reaction to light was present in each animal in which spontaneous circulation was subsequently restored. Among animals that maintained maximally dilated pupils which failed to react to light within 6 mins after start of CPR, no animal was successfully resuscitated.

Paralysis of the efferent iridoconstrictor pathway accounts for dilation of the pupil (4). Such paralysis follows critical reductions in oxygen tension of the oculomotor nucleus. After cardiac arrest, oxygen supply to peripheral tissues is reduced critically within 15 secs after cessation of circulation (27). According to Messer (5), pupil dilation begins approximately 45 secs after cessation of cerebral blood flow and is complete at approximately 1 min and 45 secs. However, under conditions in which forward blood flow is maintained, and especially in concert with spontaneous gasping during untreated VF, there may be substantial delay. In three animals in the present study, this was the case. We had previously documented that gasping predicts greater resuscitability in experimental animals and therefore prognosticates a favorable outcome (12, 28).

CPP is predictive of myocardial blood flow generated during CPR and therefore predicts the success of resuscitation (13). If cardiac output is increased to levels between 25% and 30% of normal during CPR, the pupil diameter is reduced and light reaction is likely to be restored (4). These levels of cardiac output and the associated increases in peripheral resistance account for increases in CPP to levels that predict successful resuscitation (29). However, when CPP is <10 mm Hg, all animals manifested dilated and fixed pupils. When CPP was >20 mm

Table 1. Pupil diameters before and after 1 and 2 mins of ventricular fibrillation (VF)

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>Stimulation</th>
<th>Reduction</th>
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<tr>
<td>Before VF</td>
<td>7.2 ± 0.9</td>
<td>5.8 ± 1.1</td>
<td>19.4</td>
</tr>
<tr>
<td>VF 1 min</td>
<td>8.8 ± 1.0</td>
<td>8.2 ± 1.0</td>
<td>6.8*</td>
</tr>
<tr>
<td>VF 2 mins</td>
<td>9.7 ± 0.9</td>
<td>9.6 ± 0.9</td>
<td>1*</td>
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*p < .001 vs. before VF.

Figure 2. The differences in coronary perfusion pressure (CPP) and pupil diameter during cardiopulmonary resuscitation between resuscitated and nonresuscitated animals. The numbers indicate the number of surviving animals at noted time intervals. *p < .05 vs. nonresuscitated animals.

Figure 3. The differences in light reaction during cardiopulmonary resuscitation between resuscitated and nonresuscitated animals. *p < .05 vs. nonresuscitated animals’ coronary perfusion pressure (CPP).

Figure 4. Correlation between coronary perfusion pressure and pupil diameter.
Hg during CPR, the pupil diameter was reduced, reaction to light was restored, and all of the animals were resuscitated. Accordingly, a highly significant linear correlation was confirmed between the CPP generated during precordial compression and pupil diameter.

Because effective resuscitation improved blood flow not only to the heart but to the brain, it would presumably restore oxygen tension to the oculomotor centers of the brain stem. A limitation of the present study is that cerebral perfusion pressure and cerebral blood flows were not measured. However, dynamic changes of pupil diameter and light reaction correlated with the outcome of coronary perfusion and cardiac resuscitation including cerebral recovery. Eye signs, therefore, served as a noninvasive, real-time indicator of the effectiveness of CPR and predicted the likelihood of successful resuscitation.

REFERENCES