ORIGINAL ARTICLES

Use of adrenaline and atropine in neonatal resuscitation

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Abstract

One hundred and five infants treated with adrenaline or atropine, or both, as part of resuscitation on 124 occasions were studied retrospectively. Adrenaline was administered to 98 infants, in 40 of whom it was in combination with atropine, and seven infants received atropine alone. Twenty infants were treated solely on the delivery unit, 81 on the neonatal medical unit, and four in both places. Twelve infants treated on the delivery unit and 13 treated on the neonatal unit survived. Follow up studies showed that 13 infants were handicapped with nine severely handicapped. Extreme prematurity, the need for early or repeated resuscitation using these drugs, particularly for episodes of collapse without a clear precipitating cause, and asystole rather than bradycardia were associated with a worse outcome. Evidence is accumulating to support a view that the use of these drugs for resuscitation at birth and in the first week of life of extremely preterm infants may be inappropriate.

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Active resuscitation of infants is most commonly required at the time of birth, or for intercurrent episodes of collapse during neonatal intensive care. The causes of sufficient collapse to need such intervention are many and varied. Many episodes of deterioration respond quickly to the establishment or re-establishment of adequate ventilator support, external cardiac massage, treatment of the cause of the collapse – for example, drainage of a pneumothorax – administration of alkali, and volume expansion. Adrenaline or atropine, or both, may also be used during resuscitation, and the need for these drugs suggests a more severe and treatment resistant episode of collapse.

Few reports have been published on outcome when adrenaline or atropine, or both, are used in the context of modern neonatal intensive care.^{1 2} A report in 1988 on the outcome of cardiopulmonary resuscitation of infants with birth weights less than 1500 g showed that the overall outcome was poor and suggested that cardiopulmonary resuscitation was a non-validated treatment in the population of infants

studied.¹ Indeed, the subtitle of the paper asked whether such resuscitation was futile.

Against this background we now report our experience in the use of adrenaline or atropine, or both, during resuscitation in the newborn period and the early weeks of life.

Methods

A five year (1987–91) retrospective study has been carried out on those infants who were treated with adrenaline or atropine, or both, either as part of (a) resuscitation at delivery with response enabling admission to the neonatal medical unit or (b) resuscitation during their stay on the neonatal unit, or both.

All patients under the care of one of the authors (DGS) have a clinical abstract completed when they leave the regional neonatal medical unit at this hospital. This abstract, which summarises clinical problems and treatments offered, is routinely completed by that doctor from the notes and charts. Information available from this source has been used to trace the patients and further details obtained from the clinical notes and charts. The data have been analysed by subdivision into four gestational age groups: 28 weeks or less, 29–32 weeks, 33–36 weeks, and 37 weeks or more. Follow up information on the status of survivors has been obtained from consultant paediatricians involved in later care.

Decisions about the use of adrenaline or atropine, or both, during a particular episode of resuscitation were the responsibility of the attending clinician rather than adherence to a set procedure.

Results

During the five year study period 1144 patients were admitted to the care of the consultant firm. One hundred and seventy three (15.1%) were of 28 weeks' gestation or less with 71 deaths (41%), 266 (23.3%) of between 29 and 32 weeks' gestation with 17 deaths (6%), 332 (29%) of between 33 and 36 weeks' gestation with nine deaths (3%), and 373 (32.6%) of 37 weeks' or more with 24 deaths (6%).

Adrenaline was administered as part of resuscitation to 98 patients, in 40 (41%) of whom it was given in combination with atropine. A small group of seven patients received atropine alone, giving a total study

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Table 1 Gestational age, birth weight, and resuscitation details of the 20 infants treated solely on the delivery unit

	Gestational age group (weeks)			
	≤28 (n=5)	29–32 (n=4)	33–36 (n=1)	≥37 (n=10)
Mean (SD) gestational age (weeks)	26.4 (1.8)	30.3 (1.3)	36	39.7 (2.0)
Mean (SD) birth weight (g)	778 (218)*	1418 (132)	2440	3307 (871)
No treated with adrenaline	4	4	1	9
No treated with atropine	1	0	0	1
Apgar scores (min)				
1	0,1,2,2,4	2,2,2,3	5	0,0,0,0,1,1,1,1,2,2
5	2,2,3,4,10	2,3,5,6	Three minutes=0	0,0,1,1,1,2,3,3,4,4
Other treatment given†				
Alkali	5	2	1	10
Albumin	2	1	0	6
Calcium	1	0	0	2
Blood	1	0	0	0

*Hydropic infant of 2369 g at 27 weeks' gestation omitted from analysis.

†Values are number of patients.

Table 2 Main illnesses and treatments of the 20 infants resuscitated at birth. Values are number of infants

Clinical details	Gestational age group (weeks)			
	≤28 (n=5)	29–32 (n=4)	33–36 (n=1)	≥37 (n=10)
Main illness				
Surfactant deficient lung disease	3	2	–	–
Pulmonary interstitial emphysema	1	–	–	–
Acquired pneumonia	2	2	–	–
Septicaemia	2	–	–	–
Bowel perforation	1	–	–	–
Patent ductus arteriosus	1	–	–	–
Disseminated intravascular coagulation	1	–	–	–
Bronchopulmonary dysplasia	1	1	–	–
Rhesus disease	1	–	–	–
Pneumothorax	–	1	–	–
Transient tachypnoea	–	2	–	–
Hydrocephalus	–	1	–	–
Neuromuscular disorder with reduced movement and joint deformities	–	–	1	–
Hypoxic-ischaemic encephalopathy	–	–	–	9
Non-rhesus hydrops	–	–	–	1
Convulsions	–	–	–	10
Main treatment				
IPPV/CPAP*	5	3	1	10
Dopamine/dobutamine	1	0	0	3
Tolazoline	0	0	0	0
Indomethacin	1	0	0	0
Anticonvulsant drugs	0	0	0	10

*IPPV/CPAP=intermittent positive pressure ventilation/continuous positive airway pressure.

population of 105 infants. Twenty eight infants (27%) resulted from multiple pregnancies. Twenty three infants (22%) were born after antenatal transfer of the mother to this hospital, and 48 (46%) were transferred in after birth.

Twenty (19%) infants were treated with adrenaline or atropine solely on the delivery unit, 81 (77%) only on the neonatal medical unit, and four (4%) in both places. Overall 25 infants (24%) survived, 12 (60%) of those

treated only on the delivery unit, 13 (16%) of those treated only on the neonatal medical unit, and none of those treated in both places. At follow up 13 (52%) of the survivors were handicapped – seven (58%) of the survivors treated on the delivery unit and six (46%) of those treated only on the neonatal unit. Little or no follow up data were available on three children.

GROUP TREATED ONLY ON DELIVERY UNIT (20 INFANTS)

Eighteen infants received adrenaline alone and two received atropine alone as part of birth resuscitation. The gestational age range was 24–42 weeks (mean (SD) 34.3 (6.2)) and the birth weight range was 530–5300 g (2335 (1244)). Table 1 gives the clinical details by gestational age groups. These infants had all been intubated by 5 minutes after birth. The route of administration of adrenaline was noted in 16 patients and was variously given by the intravenous (six), intracardiac (five), or endotracheal tube (10) route, three infants receiving it by two routes and one by three routes. A prompt response was noted in eight infants. Atropine was only given intravenously. The cause of the poor condition at birth was variable in the two more preterm groups and included antepartum haemorrhage, rhesus hydrops, loss of the fetal heart before delivery, and unexpectedly poor condition at birth. The infant at 33–36 weeks' gestation had a myopathy, and the infants at 37 weeks or more all had fetal bradycardias, most with meconium staining, one with loss of the fetal heart

Table 3 Eventual outcome of 20 infants treated at birth

	Gestational age group (weeks)			
	≤28 (n=5)	29–32 (n=4)	33–36 (n=1)	≥37 (n=10)
Deaths	3	0	1	4
Age at death	2 hours, 29 hours, 8 days	–	33 days	6 days, 60 days, 68 days, 152 days
Survivors	2	4	0	6
Normal	0	One aged 2 years	–	One aged 11 months
Handicapped	2	1	–	4
Details of handicap	Fits, microcephaly, cerebral palsy, left hemiplegia, blind in one eye and severe visual disability in the other eye	Developmental delay, GQ 59 at 25 months walked 27 months, no words at 30 months	–	Permanent disability from Erb's palsy Mild spastic diplegia High tone deafness at 15 months needing hearing aids Spastic quadriplegia at 42 months, GQ=21
Microcephaly, cerebral palsy with left hemiplegia, no speech at 23 months				
Short/no follow up	–	2 Lost to follow up after eight weeks Normal at 7 months	–	1 No follow up at all, mother schizophrenic

Table 4 Gestational age, birth weight, main illness and treatment of 81 infants treated on the neonatal medical unit only. Values are number of infants

Clinical details	Gestational age group (weeks)			
	≤28 (n=47)	29–32 (n=15)	33–36 (n=7)	≥37 (n=12)
Mean (SD) gestational age (weeks)	25.6 (1.5)	30.5 (1.1)	33.6 (0.5)	38.6 (1.6)
Mean (SD) birth weight (g)	851 (223)	1394 (367)	2140 (411)	2841 (707)
Main illness				
Surfactant deficient lung disease	44	13	5	–
Pneumothorax	20	6	2	4
Pulmonary interstitial emphysema	20	5	2	–
Acquired pneumonia	17	5	–	3
Patent ductus arteriosus	15	–	–	–
Septicaemia	15	8	–	3
Convulsions	14	6	–	5
Bronchopulmonary dysplasia	12	–	–	–
Pulmonary haemorrhage	–	6	–	–
Disseminated intravascular coagulation	–	5	3	–
Ascites	–	5	–	–
Congenital malformation	–	3	–	6
Pulmonary oedema	–	3	–	–
Rhesus incompatibility	–	–	3	–
Congenital pneumonia	–	–	2	–
Main treatment				
IPPV/CPAP*	47	15	7	12
Dopamine/dobutamine	23	11	5	6
Tolazoline	11	6	2	3
Indomethacin	11	2	0	0
Anticonvulsant drugs	5	2	0	6

*IPPV/CPAP=intermittent positive pressure ventilation/continuous positive airway pressure.

before delivery, and one with shoulder dystocia.

Table 2 gives details of the illnesses present after transfer to the neonatal unit, together with specific treatments offered across the four gestational age groups.

Table 3 documents the eventual outcome for the four gestational age groups and gives details of handicaps and follow up. There were 12 survivors. The eventual outcome for the small group of infants of 28 weeks' gestation or less was particularly poor, with all five dying or being severely handicapped.

Seven of the eight infants who eventually died survived longer than 12 hours from the time of their resuscitation at birth. The range of survival was one to 152 days with a total survival of 328 days. Only one of the five still-born infants survived and that infant was handicapped.

GROUP TREATED ONLY ON THE NEONATAL MEDICAL UNIT (81 INFANTS)

Table 4 gives details of the gestational age, birth weight, main illnesses suffered by 20% or more of these infants, and the main treatments offered. As expected, as problems due to

surfactant deficient lung disease and extreme prematurity decreased, so those due to congenital malformations increased with rising maturity. The congenital abnormalities included five infants with complex congenital heart disease, one with a simple atrial septal defect, one with an absent pituitary gland and adrenal hypoplasia, and one with the rib gap syndrome.

Table 5 gives the age at which the infants had their first major collapse requiring treatment with adrenaline or atropine, or both, together with the main causes of collapse. It also shows the number of infants who responded to such resuscitation by surviving for at least 12 hours but who ultimately died, and the number and condition of those who were long term survivors. The total periods of survival from resuscitation to death in those infants who survived at least 12 hours from resuscitation were: ≤28 weeks, 143 days; 29–32 weeks, 13 days; and ≥37 weeks, 84 days. The main causes of the episodes of collapse necessitating intense resuscitation are given. The miscellaneous group includes infants who collapsed with intraventricular haemorrhage associated with increased fontanelle tension and convulsions, those who

Table 5 Details of the age of first collapse, response to treatment, and cause of collapse in the 81 infants treated only on the neonatal medical unit

	Gestational age group (weeks)															
	≤28 (n=47)				29–32 (n=15)				33–36 (n=7)				≥37 (n=12)			
	≤48 hours	3–7 days	8–21 days	≥22 days	≤48 hours	3–7 days	8–21 days	≥22 days	≤48 hours	3–7 days	8–21 days	≥22 days	≤48 hours	3–7 days	8–21 days	≥22 days
No of affected	24	6	7	10	7	3	4	1	7	0	0	0	7	2	0	3
No surviving >12 hours from resuscitation	5	1	1	3	1	1	2	0	0	–	–	–	1	1	–	1
Range of survival time in infants surviving >12 hours (days)	2–13	25	10	2–63	3	1.5	1–7	–	–	–	–	–	1	10	–	73
No of ultimate survivors	1	1	2	4	1	1	0	0	2	–	–	–	1	0	–	0
Main cause of collapse (No of infants)*																
Pneumothorax	9 (H)	3 (H)	1	1 (N)	2 (H)	1 (N)	1	–	1	–	–	–	1 (N)	–	–	–
Overall decline in condition	8	–	2 (H)	1	4	–	2	1	3 (H)	–	–	–	2	1	–	2
Pulmonary haemorrhage	–	1	3	–	–	–	–	–	–	–	–	–	–	–	–	–
Blocked tube/reintubation	2	1	1 (N)	3 (NNH)	–	–	1	–	1	–	–	–	1	–	–	1
During other procedure	–	–	–	1	–	1	–	–	2 (N)	–	–	–	1	–	–	–
Miscellaneous	5	1	–	4	1	1	–	–	–	–	–	–	2	1	–	–

*N=normal survivor; H=handicapped survivor.

deteriorated because of renal failure with hyperkalaemia and hypoglycaemia, collapse associated with subglottic stenosis, collapse after intravenous phenytoin treatment, and collapse with abdominal distension and anaemia in an infant who already had significant bronchopulmonary dysplasia.

Fifty seven infants had at least one cranial ultrasound scan during their stay on the neonatal medical unit. Thirty (53%) had their only scans before or about at the time of their episode of major collapse, nine (16%) had their only scan after the episode of collapse, and 18 (32%) had scans before and after the collapse. Within the group who only had scans before the collapse 16 (53%) showed normal appearances or subependymal haemorrhage only, seven (23%) intraventricular haemorrhage, three (10%) intraventricular haemorrhage with ventriculomegaly, three (10%) isolated ventriculomegaly, and one (3%) periventricular leukomalacia.

Two of the group of nine infants (22%) who had ultrasound scans only after their collapse had a normal appearance, one (11%) intraventricular haemorrhage, two (22%) intraventricular haemorrhage with ventriculomegaly (plus periventricular leukomalacia in one), two (22%) intracortical blood (one with later periventricular leukomalacia and cerebral atrophy), one ventriculomegaly, and one bright thalami.

In the group who had scans both before and after their collapse four (22%) were normal before, one (6%) showed subependymal haemorrhage, two (11%) intraventricular haemorrhage (one with periventricular leukomalacia), five (28%) showed intraventricular haemorrhage with ventriculomegaly (one with periventricular leukomalacia), three (17%) showed intracortical blood (one with periventricular leukomalacia), one (6%) showed periventricular leukomalacia alone, one bright thalami, and one ventriculomegaly with atrophy. Scans after the collapse in this group showed no change in six and deterioration in 12 infants.

Ultrasound scans at the end of the hospital stay of the seven normal survivors showed normal appearances in two, enlarged lateral ventricles in four (one with periventricular brightness), and slight cerebral atrophy in one. Scans at the same time in the six handicapped survivors showed isolated enlargement of the lateral ventricles in one, cystic periventricular leukomalacia in one, porencephalic cysts with enlarged lateral ventricles or cerebral atrophy in two, cysts in the caudate nucleus in one, and thalamic brightness in one.

Twenty five infants from multiple pregnancies were treated only on the neonatal medical unit. Twenty (80%) died, three (12%) were normal, and two (8%) were handicapped.

Asystole occurred at the time of the event requiring resuscitation in 15 (19%) of the 81 infants. Nine (60%) died within six hours, four (27%) between 36 hours and 2.25 months and two (13%) survived, both handicapped. Bradycardia occurred at the time of collapse in 66 (81%) infants. Thirty nine (59%) died

within six hours, 16 (24%) between seven hours and 73 days (median 51 hours) after treatment, and 11 (17%) survived, seven (11%) being normal and four (6%) handicapped.

Fifty two (64%) infants were clearly documented in the notes as receiving external cardiac massage. Retrospective review suggests that in seven to nine infants the use of adrenaline or atropine, or both, without external cardiac massage was a gesture at resuscitation, as in the case of an infant dying of complex congenital cyanotic heart disease. The consultant cardiologist, when telephoned about the infant's deterioration, stated nothing further could be done. This comment was recorded in the casenotes yet the resident clinician still gave adrenaline. Other infants in this group were treated when in terminal metabolic derangement with congenital septicaemia or when they already had sclerema or massive intraventricular haemorrhage with convulsions. In other casenotes there were references to 'full CPR' (cardiopulmonary resuscitation), or it was clear that aggressive resuscitation was taking place with the siting of intravenous lines, insertion of chest drains or pericardial drains, reintubation, ordering blood transfusions, and at times carrying on resuscitation for up to one hour. Three infants not clearly documented as having external cardiac massage went on to become normal survivors and three were handicapped survivors.

The route of administration of adrenaline was clearly documented in 50 (66%) of the 76 infants who received it. The most commonly used route was intravenous: 39 (51%) patients (23 (30%) only by this route), followed by 19 (25%) who received it via endotracheal tube (seven (9%) only by this route), and 13 (17%) who received it by intracardiac injection, none receiving it only by that route. Thirty three (43%) infants only received adrenaline via one route, 13 (17%) via two routes, and four (5%) via all three routes.

In most of the remainder who received adrenaline it has to be assumed that the intravenous route was used in 22 instances, as the drug is documented among several other agents given intravenously, and via the endotracheal tube in one. Only in three instances was there no clue to the route of administration. Atropine was given to 44 patients and in 29 (66%) the route was clearly documented, being intravenous in 27 (61%), intracardiac in one (2%), and via the endotracheal tube in one. In 12 instances the route of administration was assumed to be intravenous for reasons given above and in three instances there was no clear indication of the route used.

Fifteen (19%) infants required repeat resuscitation with adrenaline or atropine, or both, during their stay on the neonatal unit. Eleven of these episodes occurred within 24 hours of the initial collapse and four infants required repeat treatment with adrenaline or atropine, or both, between 2.5 and 25 days after such initial treatment. Only one infant, who had first been treated at the age of 73 days, survived. Table 6 gives details of the

Table 6 Treatment given during 96 episodes of collapse in 81 infants with number of survivors

Drug treatment	Gestational age group (weeks)							
	≤28 (55 episodes)		29–33 (19 episodes)		33–36 (8 episodes)		≥37 (14 episodes)	
	No of treated episodes	No (%) surviving	No of treated episodes	No (%) surviving	No of treated episodes	No (%) surviving	No of treated episodes	No (%) surviving
Adrenaline	25	5 (20)	11	1 (9)	3	1 (33)	8	1 (13)
Adrenaline and atropine	25	2 (8)	8	1 (13)	5	1 (20)	6	0
Atropine	5	1 (20)	0	–	0	–	0	–
Bicarbonate	32	4 (13)	16	2 (13)	6	2 (33)	12	1 (8)
Albumin	26	7 (27)	8	2 (25)	4	1 (25)	5	0
Calcium	19	2 (11)	12	1 (8)	7	1 (14)	5	0
Reintubation/intubation	18	5 (28)	3	1 (33)	1	0	7	1 (14)
Chest drain insertion	14	3 (21)	4	2 (50)	1	0	2	1 (50)
Blood transfusion	4	0	1	0	4	2 (50)	1	0
TRIS	4	0	4	0	3	1 (33)	0	–
Frusemide	2	0	1	0	0	–	1	0

treatments given for the 96 episodes of collapse and the overall outcome.

There were 13 survivors among those treated only on the neonatal medical unit. At or below 28 weeks' gestation eight of 47 infants (17%) survived, between 29 and 32 weeks' two of 15 (13%) survived, between 33 and 36 weeks' two of seven (29%) survived, and at 37 weeks' gestation and beyond one of 12 (8%) survived. These 13 survivors were treated with adrenaline or atropine, or both, on a total of 15 occasions. In eight episodes the response to adrenaline was prompt, and in two episodes slow. In four the response to adrenaline and atropine was prompt and in the remaining case the response to atropine alone was also prompt. The 68 infants who died were treated on 81 occasions. The response was prompt in eight episodes treated with adrenaline alone, seven treated with adrenaline and atropine, and one treated with atropine alone. Survival from the time of resuscitation lasted beyond 72 hours in six episodes where the response was prompt (seven days to nine weeks). The response was slow in seven episodes treated with adrenaline alone, seven treated with adrenaline and atropine, and two treated with atropine alone. One infant survived from the time of resuscitation beyond three days for 73 days. All other infants treated with adrenaline or atropine, or both, showed no response and died within 4.5 hours of treatment.

Table 7 Survival and follow up data on the infants treated only on the neonatal medical unit

Age treated	Condition on follow up
≤28 weeks' gestation	
26 hours	Aged 28 months. Not thriving; developmental delay at 5 months level; spastic diplegia
5 days	Aged 18 months. Hydrocephalus – shunt; visual delay from cortical damage; severe developmental delay; spastic diplegia; cerebellar atrophy
14 days	Normal except few words at 28 months; asthma
15 days	Aged 27 months. Blind due to retinopathy of prematurity; limited attention span
38 days	Aged 19 months. Blind in one eye and little vision in other due to retinopathy of prematurity; developmental delay; diplegia; tracheostomy
61 days	Normal aged 3 years. GQ 99
64 days	Normal aged 34 months. Asthma/eczema
73 and 98 days	Aged 20 months. Normal except for speech; tracheostomy
29–32 weeks' gestation	
<24 hours	Aged 4 years. Cortical blindness; severe developmental delay; diplegia; failure to thrive
6 days	Aged 13 months. Normal
33–36 weeks' gestation	
<24 hours and 2 days	Aged 5 years. Moderate hemiplegic cerebral palsy
<24 hours	Aged 14 months. Normal
>37 weeks' gestation	
<24 hours	Aged 12 months. Normal

Table 7 documents the age at which survivors were treated with adrenaline or atropine, or both, together with their condition at follow up. Treatment of 24 infants of ≤28 weeks' gestation before the age of 48 hours was associated with the survival of one infant (4%) who was severely handicapped. The 30 infants treated within this group before the age of 168 hours gave rise to two survivors (7%), both severely handicapped. One of the seven infants in the 29–32 weeks' gestation group (14%) who were treated before the age of 48 hours survived – again with severe handicap. Although later use of adrenaline or atropine, or both, in the most preterm infants could be associated with a normal eventual outcome, it was only in the groups of 33 weeks' gestation or more that normal survival was seen in association with the use of adrenaline or atropine, or both, before the age of 48 hours.

GROUP TREATED ON DELIVERY UNIT AND NEONATAL UNIT (FOUR INFANTS)

Three infants with gestational ages of 25–27 weeks and birth weights of 700–770 g, together with an infant with non-rhesus hydrops with a birth weight of 2320 g at 31 weeks' gestation formed this group, who all received adrenaline at birth. In addition, all had been resuscitated at delivery with endotracheal intubation, and three had received treatment with alkali.

The three extremely preterm infants all had surfactant deficient lung disease. All four in this group received ventilator support. The episode of collapse requiring repeat treatment (adrenaline in four and atropine in one) occurred between the ages of 1.75 and 34 hours of life. The length of survival after resuscitation was at most eight hours and all had died by the age of 42 hours.

Discussion

The indications for, doses of, and best route of administration of adrenaline and atropine during resuscitation in very early life remain unclear. For example, one standard British textbook of neonatology gives, in different sections of the book, different doses of the two drugs for resuscitation purposes.³

Intravenous or intracardiac administration have been accepted routes in the past.

Endotracheal tube administration of adrenaline during resuscitation at birth has been suggested as the most rapidly effective route,⁴ and the same route for atropine has been shown to be as effective as the intravenous route in older children.⁵ As our data show, all or some of these routes may be used during a single attempt at resuscitation.

A review paper on resuscitation of newborn infants refers to the use of adrenaline without reference to long term outcome.⁶ There is no specific reference to the use or value of adrenaline or atropine in the section on resuscitation of preterm infants. Two large review papers on cardiopulmonary resuscitation of low Apgar score newborn⁷ or stillborn infants⁸ do not refer to the frequency with which adrenaline or atropine had been used in resuscitation, nor their relation with eventual outcome.

As the expertise and treatments used in the care of sick neonates improve and the gestational age of viability decreases, it is important that treatments, including those that have been available for a long time, undergo detailed evaluations. The availability of a particular treatment does not imply its efficacy or appropriateness in ever changing situations. Cardiopulmonary resuscitation, which includes the use of adrenaline or atropine is one such treatment and Lantos *et al*, in their study of very low birthweight infants, suggested that it was a non-validated treatment which might be considered futile.¹ Our study covers a wider population than that of Lantos *et al* and although it is not possible to conclude that the use of adrenaline or atropine as part of resuscitation is non-validated in all situations, it is clear that there are groups of patients and situations where its use should be questioned.

It may be difficult to withhold a readily administered treatment and it might be argued that nothing is lost by giving such a treatment in situations where there is little or no hope. To some extent this is true. In our study of 105 infants, 55 (52%) of those receiving cardiopulmonary resuscitation, including adrenaline or atropine, or both, died immediately after or within 12 hours of treatment, the outcome being therefore largely the same whether such treatment was given or withheld. Of the remaining 50 infants, 25 survived more than 12 hours but ultimately died, with an average survival time of 23 days after resuscitation. The average survival time of those treated on the central delivery unit (eight infants) was 41 days, and for those treated on the neonatal medical unit (17 infants) it was 14 days. Overall 13 of the 25 infants who survived were handicapped (nine severely), with a further three having little follow up information available. These figures raise ethical issues and also have service implications. It might indeed be argued that far from 'losing nothing' by instituting resuscitation with adrenaline or atropine we are increasing the number of severely handicapped survivors, and by prolonging the process of dying depriving other infants of the benefits of admission for neonatal intensive care.

With the above in mind it would be helpful to be able to predict those infants where the use of adrenaline or atropine might be considered inappropriate.

Twenty infants, five stillborn and 15 on the neonatal unit, were asystolic. Three of these survived and all were handicapped.

In infants treated only on the neonatal medical unit there were eight survivors in the group of ≤ 28 weeks' gestation and of these four were handicapped, which includes all of those treated at the age of less than one week. In the 29–32 weeks' gestation group there were only two survivors and the infant treated before the age of 48 hours is handicapped. Our finding of a poor overall outcome for the most preterm and smallest infants who require such resuscitation early in life agrees with the few other published reports.^{1,2}

Ten (77%) of the 13 survivors in the neonatally treated group had a correctable precipitating cause – that is, pneumothorax or blocked tube – and of these infants six are normal on follow up and four handicapped (two of the latter were ≤ 28 weeks' gestation and treated within one week of birth, and one 29–32 weeks' gestation and treated within 48 hours). Two of the other three survivors required resuscitation due to an overall decline in condition – both of these were handicapped – and one required resuscitation after collapse during a clinical procedure (now normal).

Therefore the failure of very preterm infants who collapse in the earliest days of life to respond promptly to correction of the cause of their collapse – that is, drainage of a pneumothorax or re-establishment of a secure airway with use of alkali and volume expansion as appropriate – could be considered an indication to withdraw care. This may also be appropriate management for the very preterm infant aged several weeks or months who has a major deterioration when still affected by another significant life threatening disease. At gestational ages of 33 weeks or more, however, the use of adrenaline or atropine may result in a normal infant even when used in the first days of life.

The use of adrenaline or atropine on the delivery unit is a more difficult issue as there is little time and often little information on which to base a decision to begin or withhold full resuscitation. The use of adrenaline or atropine at the time of birth was not found to be associated with a generally good overall outcome, although by the definitions of our study the episode of resuscitation had been successful and the infant admitted alive to the neonatal medical unit. There was then a 40% death rate and a 58% handicap rate in survivors. Although on the evidence available to us 42% of the survivors were normal, three of five infants affected only had short periods of follow up. The outcome once again for the group with a gestational age of 28 weeks or less was particularly poor. It is appropriate to question the value of adrenaline or atropine as part of resuscitation at the time of birth in extremely preterm infants.

In conclusion, the following factors have been found to be associated with a poor outcome: extreme prematurity; early need for or repeated resuscitation with adrenaline or atropine, or both; the absence of clear precipitating factors causing the collapse needing resuscitation; and asystole rather than bradycardia. In the presence of any, and especially combinations, of these factors the attending clinician can reasonably question whether or not the use of adrenaline or atropine, or both, is justified. Evidence is now accumulating to support a view that the use of adrenaline or atropine, or both, for resuscitation in the first week of life in extremely preterm infants may be inappropriate and if an infant does not respond to the correction of an easily treated underlying problem, this can be considered to be an indication to withdraw support. A detailed and helpful review of the ethical aspects of cardiopulmonary resuscitation in paediatric practice has now been published.⁹

We are grateful for the secretarial help of Maureen Jones.

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Commentary

This paper is a useful reminder that the outlook is very poor when there is cardiopulmonary collapse of such severity as to require resuscitation by cardiac stimulants (rather than by simply achieving adequate oxygenation), especially with very premature infants <33 weeks' gestation. It would be dangerous to interpret these observations as meaning that such resuscitation should never be attempted. Rather this paper should serve as a reminder that the pursuance of intensive support at all costs is not always appropriate.

This is a clinical paper, but there are also moral and legal arguments to take into account when faced with dilemmas of this sort. It is useful to be able to turn to first principles. The interests of the child are paramount, a concept with which paediatricians are comfortable. From this we can establish a hierarchy of responsibilities and recognise that the interests of parents, though undoubtedly important, are secondary. The interests of society, and here the financial implications of intensive support may be included, take third place.

But what are the best interests of the child? To answer this we must first establish as precise a prognosis as possible. Sims *et al* have helped us with this: the overall outcome in the group described was very poor. The use of cranial ultrasound may have allowed the prognosis to be even more precisely defined for the individual.

The problem with the authors' recommendation that 'the failure of very preterm infants who collapse in the earliest days of life to respond promptly to correction of the cause of their collapse . . . could be considered an indication to withdraw care' is that it is often the most junior and inexperienced member of the team who has to decide to institute resuscitation.

The withdrawal of intensive support is not a decision to be made by a relatively inexperienced doctor on his or her own in the middle of the night. It is a decision that requires the full participation of the medical team, the nurses who are involved with the care of the baby, and the parents. The parents' views are most important: the baby cannot tell us what he or she wants, and generally it is the parents who are considered to be the people who have the best interests of their child most at heart, provided they have been informed as fully as possible of the prognosis by their baby's medical attendants. The process has been well described by Whitelaw *et al*.¹ If any of the discussants take the line that it would not be appropriate to stop intensive support, full support is continued, although discussions about its appropriateness should also continue.

What is the position of the law? There are at least two fairly recent cases relating to neonates. In the first (baby C)² the court allowed intensive support to be withdrawn from a baby whose outlook was considered to be extremely poor, and in the second (baby J)³ a decision by the High Court judge was made for it not to be instituted. Both judgments were upheld by the Court of Appeal. In both cases it was evident that a clear idea of the prognosis, as established by the use of scientific techniques and clinical experience, was essential in deciding how best to proceed.

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Commentary

I suspect that, over the years, most of us have built up *ad hoc* resuscitation policies. These may no longer be good enough as many purchasers and trust boards insert into quality requirements written protocols on who should and should not be resuscitated. Designed