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A NEW APPROACH TO THE TREATMENT OF ACUTE INTRAPARTUM FETAL DISTRESS[1]

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Acute intrapartum fetal distress (AIFD) is a condition produced by an acute reduction of the metabolic exchanges between the fetus and mother (*4*). Its main cause is the uterine contractions of labor, which reduce the flow of maternal blood through the intervillous space by compressing the supplying maternal vessels (*3, 22*). Sometimes the contractions may also compress the umbilical vessels and reduce the flow of fetal blood through the chorionic villi (*14*). Both mechanisms lead to reduced feto-maternal exchanges and result in fetal hypoxia, hypercapnia, acidosis, and other homeostatic disturbances (*1, 19*). The measurement of pH, pO_2, and base deficit in fetal blood microsamples (Saling's method) (*25*) makes possible an early diagnosis of AIFD. This diagnosis can also be made by monitoring the appearance of dips II (*11, 19, 20, 21*), typical changes in fetal heart rate (FHR) equivalent to the "late decelerations" described by Hon (*15*).

Once the diagnosis of AIFD is made, the usual therapeutic approach is to administer oxygen (*2*) and glucose to the mother and, if no improvement is obtained, to deliver the fetus as soon as possible, either by cesarean section or by the vaginal route, according to the obstetrical conditions present. The results are not always good; in many instances the newborns are depressed, have a low Apgar score and a marked acidosis, and may require reanimation, tracheal intubation and artificial respiration, intravenous injections of bicarbonate, or TRIS. Many die despite all this treatment or, if they survive, show irreversible damage (*4, 7, 13*) particularly to the central nervous system.

The pathophysiology of the condition (*4, 5, 23*) has led to a new approach to the treatment of AIFD. Preliminary results of its application are reported in this paper. The bases of this new approach are (1) *the inhibition of uterine contractions*, which should augment the flow of blood through the placenta and increase the metabolic exchanges between the fetus and the mother, thus progressively correcting the disturbances in fetal homeostasis; and (2) *the postponement of delivery* until normal homeostasis has been restored, the expectation being that if the fetus has fully recovered *in utero* it will be born in vigorous condition, with a high Apgar score, and will not require resuscitation.

The drug employed for inhibiting uterine contractions is Orciprenaline (*12, 17, 22*);[3] the chemical formula is shown in Figure 1. It is a derivate of epinephrine in which an isopropyl radical has replaced one H of the amino group and the two hydroxyls in the phenyl group are in positions 3 and 5 instead of in positions 3

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[2] Presented by Dr. Caldeyro-Barcia.

[3] Alupent®, manufactured by Bochringer Ingelheim.

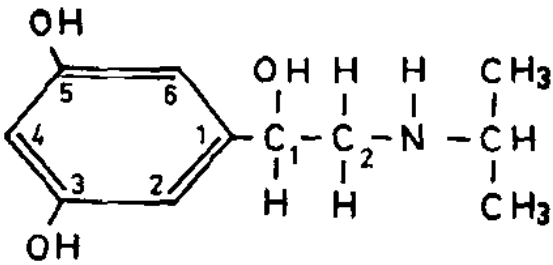

FIGURE 1. Chemical formula of Orciprenaline (Alupent®).

and 4. These structural changes enhance the stimulating effects on the beta adrenergic receptors.

Orciprenaline is administered by continuous intravenous infusion at rates of 20 to 30 μg a minute. Such dosages are usually sufficient to reduce uterine activity markedly in parturient women without producing undesirable side effects like arterial hypotension or severe tachycardia (*17, 24*), which may occur with higher dosages.

Figure 2 shows records of uterine contractions and FHR obtained in one case of very severe AIFD that was treated according to the approach described. The patient was a primigravida with 43 weeks of amenorrhea. Labor started spontaneously at hour 00:00. At hour 3:30, when cervical dilatation was 5 cm and the fetal head was in station –2, the membranes were artificially ruptured. At hour 3:55 a typical AIFD syndrome (*9, 10, 11*) developed in the FHR tracing, which showed a dip II following each uterine contraction. The pH of the fetal blood measured at hour 4:20 was 7.03—a very low value indicating severe fetal acidosis. The diagnosis of very severe AIFD was thus confirmed by two methods of assessing fetal condition. It should be noted that meconium was absent from the amniotic fluid, which shows the unreliability of this sign for the diagnosis of AIFD.

At hour 4:34 (Figure 2A) the intravenous infusion of Alupent was started, at the rate of 20 μg a minute; it was continued at the same rate for one hour. The uterine contractions were markedly inhibited; their average intensity, which had been 45 mm Hg before the infusion,

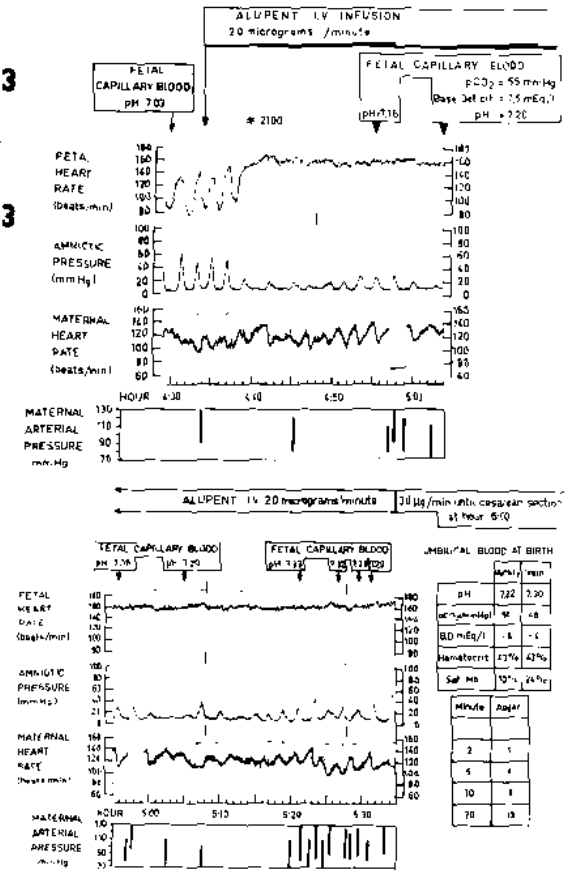

FIGURE 2. Records obtained in case of extremely severe AIFD, with marked acidosis (pH = 7.03) and dips II in FHR tracing. A (top): infusion of Alupent to mother inhibited uterine contractions and improved fetal conditions. B (bottom): Infusion was continued until cesarean section. Fetal pH recovered progressively to normal values. Records were discontinued at hour 5:35, to move patient to operating room. At right, umbilical-vessel blood samples obtained at birth and serial Apgar scores.

was reduced to 10 mm Hg during the first 30 minutes of administration of the drug. In the following 30 minutes uterine activity increased very gradually, indicating that the myometrium was partially escaping from the inhibitory influence of the drug (Figure 2B), but it remained well below the pre-infusion values at all times during the infusion.

Dips II disappeared from the FHR tracing as soon as the contractions became too weak to hinder maternal blood flow through the placenta.

The baseline FHR became slightly tachycardic (155–160 beats/min) during the first 30 minutes of the infusion and rose slowly to 165 beats/min during the next 30 minutes. This mild tachycardia is interpreted as a direct effect of Alupent on the fetal heart.

The pH of the fetal blood (Figures 2 and 3) increased progressively. It was 7.16 at hour 4:55, 20 minutes after the onset of the infusion, and 10 minutes later (hour 5:05) it had reached 7.20, which is the lowest limit of the normal range. It continued to rise, and in 20 minutes more (hour 5:25) had reached perfectly normal values (7.27 to 7.32), which were confirmed in three samples obtained between hours 5:25 and 5:32. Although no more samples were obtained between hour 5:32 and delivery at hour 6:00, it apparently remained within the normal range, since the blood sampled at birth from the umbilical artery and vein had normal pH values.

The remarkable improvement obtained in the pH of fetal blood is graphically illustrated in Figure 3. To the author's best knowledge, this is the first case reported of a complete recovery

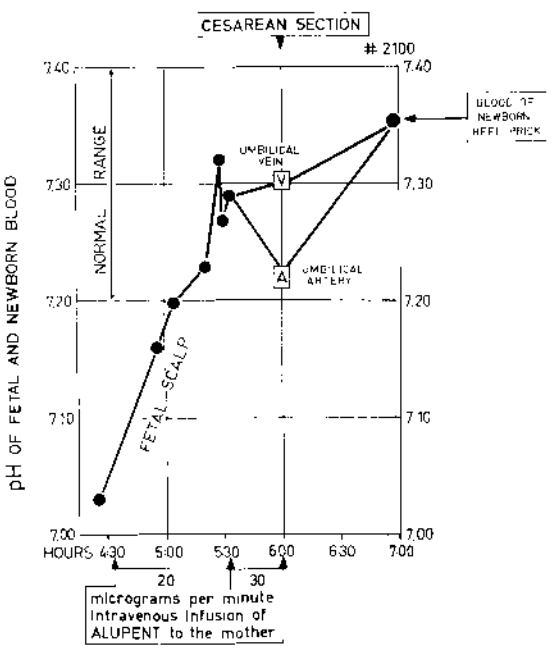

FIGURE 3. Values of fetal blood pH in same case illustrated in Figure 2. Initial extreme fetal acidosis was corrected by administration of Alupent to mother.

to a normal pH obtained *in utero* in a human fetus affected by severe acidosis during labor.

The infusion of Alupent at the rate of 20 μg a minute produced no significant changes in maternal arterial pressure, but it did cause a rise in maternal heart rate to 120 beats/min (Figure 2); this tachycardia caused no subjective symptoms in the mother, and the maternal ECG showed no other abnormal changes.

At hour 5:35 the recording of uterine contractions and of fetal and maternal heart rates was discontinued and the patient was transferred to another room for cesarean section. Alupent infusion was continued at the rate of 30 micrograms per minute until the moment of sectioning the uterus.[1] The infant was delivered at hour 6:00 in good condition, as is shown by the serial Apgar scores (7, 8, 9, and 10 at the second, fifth, tenth, and twentieth minutes of life) and by the composition of the blood obtained from the umbilical vessels clamped at the time of delivery.

The newborn weight was 3,400 grams and the crown-heel length 50 cm. The infant was thoroughly examined at birth and also at the first, third, and thirtieth days of life. EEGs were obtained at one, eight, and thirty days of life. All the examinations and EEGs were normal. The excellent outcome of this labor is much better than could have been expected if the classical approach had been employed for the treatment.

From previous work (*6, 8*) it can be predicted that if the conditions existing between hours 4:00 and 4:35 (dips II and severe fetal acidosis) had persisted uncorrected for more than 60 minutes, the fetus would have died *in utero*, from acute intrapartum asphyxia. If delivered alive, the newborn would have been severely depressed, requiring tracheal intubation and artificial respiration and intravenous injection of bicarbonate and glucose. If it had survived,

[1] Because of uterine relaxation and vasodilation caused by Alupent, severe maternal hemorrhage may occur after separation of the placenta. To prevent this complication the infusion should be discontinued before the uterus is sectioned and a potent oxytocic drug should be administered immediately after delivery of the fetus.

the likelihood of permanent brain damage and pulmonary complication would have been very high (*8*, 9, 13). Had an emergency cesarean section been performed, for example at hour 4:35, the infant would still have been severely depressed, although the damage would have been less because of the shorter period of intrauterine asphyxia.

Figure 4 illustrates another case of AIFD treated with Alupent. The records were obtained in a multipara with a prolonged pregnancy (43 weeks of amenorrhea), in whom labor started spontaneously at hour 00:00. Membranes were ruptured at hour 3:05. At hour 3:25 cervical dilatation was 7 cm and the station of the fetal head was −2. All uterine contractions in which the amniotic pressure at the peak was higher than 60 mm Hg produced dips II, indicating the presence of AIFD. A severe fetal bradycardia (80–90 beats/min) started at hour 3:49 and lasted four minutes. Treatment with an intravenous infusion of Alupent at the rate of 20 μg a minute was started at hour 3:52. The contractions were markedly inhibited, the full effect being obtained three minutes after the start of the infusion. The dips II disappeared as soon as the intensity of the contractions diminished. The baseline FHR, which was tachycardic (160 beats/min) before treatment, slowly descended toward normal levels and in 12 minutes was 140 beats/min. At hour 4:05 the recording of FHR, uterine contractions, and maternal arterial pressure was discontinued so that the patient could be transferred to the operating room. The administration of Alupent was continued.

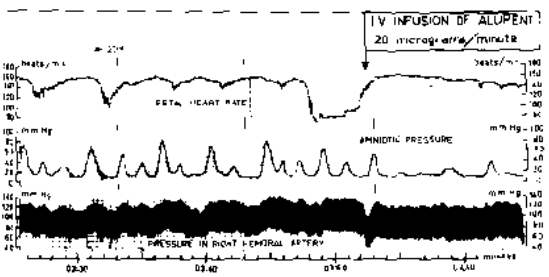

FIGURE 4. Records obtained in case of severe AIFD diagnosed by dips II and prolonged bradycardia at hours 3:48 to 3:52. Administration of Alupent to mother inhibited uterine contractions and FHR recovered normal pattern. Recording was discontinued at hour 4:05, to move patient to operating room. Alupent administration was continued until sectioning of uterus. Fetus was delivered at hour 4:42 in good condition.

The infant was delivered by cesarean section at hour 4:42 with Apgar scores of 9, 10, and 10 at the first, fifth, and tenth minutes of life. The newborn weight was 3,900 grams and the crown-heel length 52 cm. Thorough examination of the infant during the first 18 months of life showed no abnormalities whatsoever.

Discussion

From previous work (*6*, *8*, *18*) it is known that newborns are usually depressed and have a low Apgar score when signs of AIFD (dips II in the FHR tracing, pH of fetal blood below 7.20) have consistently been found during the hour preceding delivery. Both fetuses reported here, if delivered at the time when these signs were present, would most probably have been severely depressed. On the other hand, prolonging the period of AIFD without effective treatment leads to aggravation of the condition and eventually to intrapartum death.

In both cases reported here the excellent condition of the newborns was attributed to the recovery period of 50 to 80 minutes during which the uterine contractility was inhibited and the fetuses were able to restore normal homeostasis.

This approach to the treatment of AIFD has some advantages over other current therapeutic methods:

1. It suppresses a known factor in fetal asphyxia—the uterine contractions—and does so very rapidly, in two or three minutes after the Alupent infusion is started.

2. Normal homeostasis is restored by increasing feto-maternal metabolic exchanges through the placenta, which is the organ best suited to the purpose. In contrast, artificial pulmonary ventilation of a depressed newborn is very effective in correcting hypoxia and hypercapnia but is unable to modify, for example, metabolic acidosis or exhaustion of carbohydrate reserves. To correct such disturbances the newborn needs an

intravenous infusion of glucose, bicarbonate, or THAM or other treatment.

3. The other procedures—tracheal intubation of the newborn, positive pressure pulmonary ventilation, catheterization of the umbilical vein, injection of glucose and bicarbonate—all require skilled personnel and are not entirely innocuous (*16*).

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