PLACENTAL TRANSPORT OF CHELATED IRON

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INTRODUCTION

The placenta anatomically separates the circulatory systems of the mother from her fetuses. As the sole purveyor of fetal nutrients, it is both active and selective in modifying molecules of maternal origin and then transferring the new molecular structures to the fetuses.

One such modification involves the movement of maternal plasma iron through the placenta to the fetus. It was originally believed that the iron received by the fetus was in the form of intact hemoglobin which was liberated from maternal erythrocytes[1]. Later research has shown that maternal iron is actually plasma iron[2]. It is transferred from maternal blood through the chorionic villi of the areolae bound to specific protein molecules which have been synthesized by the placenta to specifically transport the iron from the mother to the fetus[3,5].

Structurally it appears that the microvilli formed by the placenta are similar to those found in the intestinal lumen. Consequently, the mineral transport role of certain placenta-formed proteins[3] may be identical to the role of carrier proteins in the intestinal absorption of iron[4], since both intestinal and placental absorption of iron appear to require chelation with specific molecular configurations of protein[4,5].

In the intestine there are two mineral absorptive mechanisms[4]. One is for the uptake of ions. The other is designed to absorb bivalent minerals, such as iron, that have been chelated with amino acids. These double heterocyclic ring molecules have the molecular weight of a dipeptide with a mineral (<1000) and are electrically neutral. Double labeled radioisotope studies with ^{59}Fe and ^{14}C have indicated that this iron chelate is frequently absorbed from the mucosa to the serosa as an intact molecule[4]. This phenomenon results in significantly higher body deposition of iron from the chelate compared to equivalent dosages of ferrous salts[6-9].

A similar type of increased iron deposition in the fetus has been noted when these same iron amino acid chelates have been fed to gestating pigs. At farrowing, piglets from sows and/or gilts receiving iron amino acid chelates have had increases in liver iron of between 34%[10] and 91%[8], spleen iron of 8.6%[10], muscle iron of 3%[10], plasma iron of between 9.8%[10] and 682%[9], and hemoglobin of between 12.2%[10] and 12.9%[9]. The mothers received 0.5 g[8], 0.6 g[9], or 0.85 g[10] of iron as the amino acid chelate daily starting 4 weeks prior to expected parturition. With these data in mind, the question was asked: Since iron amino acid chelate probably arrives in the blood intact[4], is it also transported to the fetus intact via the placenta bypassing the normal maternal carrier degredation and placental restructuring[3] before entering fetal plasma?

METHOD

Since U. S. federal laws discourage the use of radioisotopes in large animals, 12 Sprague-Dawley female rats that had been synchronously impregnated were divided into groups of 3. (There are obvious anatomical differences in the placentas of rats and pigs; consequently, the results can only be compared qualitatively not quantitatively[11].)

Each female received 4.4 μ.c.i. of ^{59}Fe, either as iron amino acid chelate or $FeCl_3$ with and without a cholinesterase inhibitor, 3 days prior to sacrifice. Necropsy occurred 1 day before calculated parturition. The iron was combined with 25 μl of water and each dose administered by automatic pipette to the rat after it was partially anesthetized with ether.

Necropsy was by cervical dislocation. Radioassay was carried out with a Nuclear-Chicago 2851 Gamma Counter with a two-inch NaI crystal.

RESULTS

The results are shown in Table 1. The fetal uptake of iron from the amino acid chelate was much greater than from $FeCl_3$. The 2, 2-dichlorovinyl dimethyl phosphate resulted in greater absorption for both the chloride and chelate groups, but the increase for the chloride was only 23.0% compared to 131.1% for the chelates.

TABLE 1

Treatment	cc/m/fetus	
	Mean	S.D.
$^{59}FeCl_3$	90.3	±28.6
^{59}Fe A.A. Chelate	127.0	±79.6
$^{59}FeCl_3$ + 2, 2-dichlorovinyl dimethyl phosphate	111.1	±26.2
^{59}Fe A.A. Chelate + 2, 2-dichlorovinyl dimethyl phosphate	293.5	±157.7

CONCLUSION

If fetal uptake of iron from maternal plasma was due solely to placentally-produced carrier proteins, then the iron from both the chelate and the chloride groups would have had equal affinity for the carrier for iron uptake regardless of the form of iron administered. In this case, increased uptake from the chelate group would have been due solely to increased maternal intestinal absorption of that form of iron; but when the results of the chelate and chloride groups are compared and the vasodilator added, the increased fetal uptake of iron is not proportional. If these comparisons were proportional, a similar placental pathway for both forms of iron, dependent upon the same number of carrier proteins, would be indicated. The dissimilarity suggests a secondary, more efficient iron absorptive placental pathway when amino acid chelates of iron are consumed. This rationale explains the increased iron levels in piglet tissues as a function of time as described above.

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