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Title

The importance of supplementation of magnesium in pig pregnant condition

By

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Department of Pharmacology
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**This research was supported by the fiscal budget year 1997,
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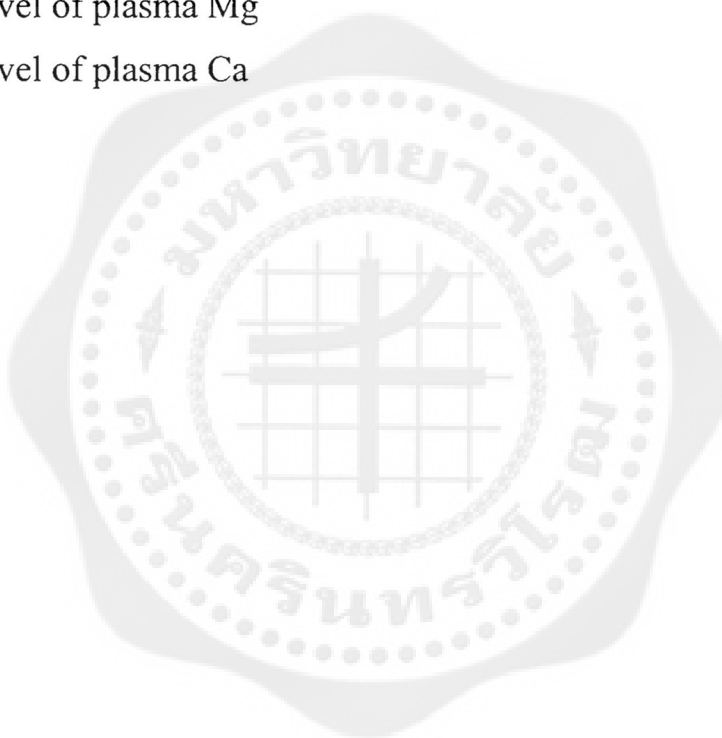
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บทคัดย่อ (Abstract in Thai)

แมกนีเซียมในรูป แมกนีเซียม-แอล-แอสปาเตตไฮโดรคลอไรด์ ขนาด 20 กรัม ต่อตัว ต่อ วันหรือ เทียบเท่าขนาดของ แมกนีเซียม 13 มิลลิกรัม ต่อกิโลกรัม ใช้ป้อนในหมูจำนวน 24 ตัว โดยมีหมูกุ่มควบคุม 24 ตัว (รวมหมูทั้งหมด 48 ตัว ประกอบด้วย พันธุ์แท้ 47 ตัวและพันธุ์ผสม 1 ตัว) น้ำหนักเฉลี่ย 150 กิโลกรัม โดยที่หมูกินอาหารเฉลี่ยต่อวันเป็น 2.4 กิโลกรัม เริ่มให้แมกนีเซียมระหว่าง วันที่ 0 ถึงวันที่ 4 ก่อนการผสมพันธุ์ โดยให้ทุกวันตลอดระยะเวลาการตั้งท้องนาน ประมาณ 117 วันจนถึง 4 วันหลังคลอด ทำการเจาะเลือดจากเส้นเลือดดำข้างลำคอทั้งสิ้น 5 ครั้ง ในสัปดาห์ที่ 0, 4, 8, 12, 16 ของระยะเวลาการทดลอง สัปดาห์ที่ 0 คือระยะเวลาก่อนได้รับแมกนีเซียมและยังไม่ได้ตั้งท้อง สัปดาห์ที่ 4, 8, 12 คือ ช่วงที่หมูตั้งท้อง ส่วนสัปดาห์ที่ 16 คือระยะที่หมูคลอดได้ประมาณ 4 วัน ทำการตรวจวัดพลาสมาแมกนีเซียม และ แคลเซียมโดยใช้เครื่องมือดูดกลืนแสงอะตอมมิก (atomic absorption spectrophotometer) พบว่า ระดับแมกนีเซียมในสัปดาห์ที่ 0, 4, 8, 12, 16 มีค่าเป็น 0.84 ± 0.05 , 0.62 ± 0.1 , 0.65 ± 0.05 , 0.74 ± 0.07 , 0.85 ± 0.12 มิลลิโมล/ ลิตรในกลุ่มควบคุม และมีค่าเป็น 0.87 ± 0.1 , 0.71 ± 0.08 , 0.77 ± 0.17 , 0.81 ± 0.05 , 0.90 ± 0.09 มิลลิโมล/ ลิตรในกลุ่มที่ได้รับแมกนีเซียมตามลำดับ ระหว่างสัปดาห์ที่ 4, 8, 12 ระดับพลาสมาแมกนีเซียมในกลุ่มที่ได้รับการเสริมแมกนีเซียมมีค่าสูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (พี น้อยกว่า 0.01) ขณะที่ระดับพลาสมาแคลเซียมมีค่าลดลง (พี มากกว่า 0.05) ในกลุ่มที่เสริมแมกนีเซียม เมื่อเปรียบเทียบในกลุ่มเดียวกันพบว่าระหว่างการจัดตั้งท้องทั้งพลาสมาแมกนีเซียมและแคลเซียมมีค่าลดลงจากสัปดาห์ที่ 0 อย่างมีนัยสำคัญทางสถิติ (พี น้อยกว่า 0.01) ทั้งกลุ่มที่เสริมแมกนีเซียมและกลุ่มควบคุม แต่หลังจากคลอดระดับพลาสมาแมกนีเซียมเพิ่มขึ้นจนใกล้เคียงกับสัปดาห์ 0 ขณะที่ระดับ พลาสมาแคลเซียมค่อยๆเพิ่มขึ้นระหว่างสัปดาห์ที่ 12 และ 16 แต่ก็ยังคงมีค่าน้อยกว่า สัปดาห์ที่ 0 ทำการตรวจวัดค่าพลาสมากลูโคสซึ่งเก็บรักษาไว้ในซีเดียมฟลูออไรด์ภายใน 24 ชั่วโมงหลังเก็บเลือดด้วย วิธี GOD-PAP method enzymatic colorimetric method พบว่าระดับพลาสมากลูโคสในกลุ่มที่เสริมแมกนีเซียมไม่แตกต่างจากกลุ่มควบคุม (ค่าอยู่ระหว่าง 70-90 มิลลิกรัม/ 100 มิลลิลิตร) เมื่อเปรียบเทียบในกลุ่มเดียวกันพบว่าที่ค่าพลาสมากลูโคสระหว่างตั้งท้องมีค่าต่ำกว่าสัปดาห์ที่ 0 อย่างมีนัยสำคัญทางสถิติ (พี น้อยกว่า 0.01) ทั้งกลุ่มที่เสริมแมกนีเซียมและกลุ่มควบคุม แต่หลังคลอดระดับพลาสมากลูโคสมีค่าสูงขึ้นจนใกล้เคียงกับสัปดาห์แรก ค่าเฉลี่ยระยะการตั้งท้องเป็น 116 ± 3 วันในกลุ่มควบคุม และ มีค่าเป็น 117 ± 2 วันในกลุ่มที่เสริมแมกนีเซียม เปอร์เซนต์การแท้งมีค่าเป็น 8.3 ในกลุ่มควบคุม ขณะที่ มีค่าเป็น 12.5 ในกลุ่มที่เสริมแมกนีเซียม จำนวนลูกหมูที่ได้ทั้งหมดเป็น 184 ตัวในกลุ่มควบคุม ขณะที่ มีค่าเป็น 186 ตัวในกลุ่มที่เสริมแมกนีเซียม เมื่อทดสอบค่าทางสถิติของค่าเฉลี่ยของลูกหมูต่อครอก น้ำหนักลูกหมูแรกคลอด จำนวนลูกหมูที่ผิดปกติ จำนวนลูกหมูที่เป็นมัมมี และ ตายแรกคลอด ไม่แตกต่างจากกลุ่มควบคุม แต่ค่าตัวเลขของจำนวนลูกหมูที่เป็นมัมมี และ ตายแรกคลอดมีค่าน้อยลงอย่างเด่นชัด (พี มากกว่า 0.05) ในกลุ่มที่ได้รับการเสริมด้วยแมกนีเซียม

โดยสรุป ข้อมูลจากการทดลองครั้งนี้พบว่า การเสริมแมกนีเซียมในรูป แมกนีเซียม-แอล-แอสปาเตตไฮโดรคลอไรด์ ขนาด 20 กรัม ต่อตัว ต่อ วันหรือ เทียบเท่าขนาดของแมกนีเซียม 13 มิลลิกรัม ต่อกิโลกรัมต่อวันเป็นเวลานานสามารถตรวจพบการเพิ่มระดับพลาสมาแมกนีเซียมได้ แต่การเพิ่มระดับพลาสมาแมกนีเซียมนี้ไม่มีผลต่อระดับน้ำตาลในเลือด หมูตลอดระยะเวลาการตั้งท้อง และการให้แมกนีเซียมที่ระดับดังกล่าวมีความปลอดภัยไม่ทำให้เกิดการคลอดช้า นอกจากรังสีลดจำนวนของจำนวนลูกหมูที่เป็นมัมมี และ จำนวนลูกหมูตายแรกคลอด ซึ่งนับว่าเป็นผลดีต่อการตั้งครก

คำสำคัญ: การเสริมแมกนีเซียม, หมูตั้งท้อง, พลาสมากลูโคส, มัมมี และ ตายแรกคลอด

Abstract in English

Magnesium (Mg) in the form of magnesium L-aspartate hydrochloride (MAH) 20 g per sow per day equivalent to dose 13 mg of Mg/Kg body weight per sow per day was given to pigs n=24, compared to control group n=24 (totally purebred 47, crossbred 1) body weight amounted to 150 kg and daily food consumption to 2.4 kg, Mg was given at starting 0 to 4 days before mating for all pregnant period ca. 117 days and after delivery for 4 days. Blood collection from jugular vein were done 5 times at weeks 0, 4, 8, 12, 16 of experiment weeks 0 was before pregnant, weeks 4, 8, 12 were during pregnant and week 16 was after parturition 4 days. Plasma magnesium and calcium were measured by atomic absorption spectrophotometer. The level of Mg on weeks 0, 4, 8, 12, 16 were 0.84 ± 0.05 , 0.62 ± 0.1 , 0.65 ± 0.05 , 0.74 ± 0.07 , 0.85 ± 0.12 mmol/l respectively in control group and were 0.87 ± 0.1 , 0.71 ± 0.08 , 0.77 ± 0.17 , 0.81 ± 0.05 , 0.90 ± 0.09 mmol/l respectively in Mg treated group. The level of plasma magnesium in Mg treated group were increased significantly ($p < 0.01$) during week 4, 8, 12 while plasma calcium were slightly decreased ($p > 0.05$) in Mg treated group. During gestation both plasma Mg and plasma Ca in the same group were decreased significantly ($p < 0.01$) from starting week (Week 0), and after parturition plasma Mg was increased to nearly the same level as Week 0 while plasma Ca slightly increased during Week 12 and Week 16 but were still lower than Week 0. Blood glucose preserved in NaF were detected within 24 hrs after blood collection by GOD-PAP method enzymatic colorimetric method. Blood glucose in Mg-treated group was not different from control group (level between 70 to 90 mg/100ml). The pattern of blood sugar during gestation in the same group were also decreased significantly from week 0 ($p < 0.01$) in both control and Mg treated group but after delivery the level of glucose were increased nearly the same level in Week 0. Mean pregnant period were 116 ± 3 days in control group and were 117 ± 2 days in Mg treated group. Percent abortion were 8.3 in control group and were 12.5 in Mg treated group. Totally piglets consume were 184 in control and were 186 in Mg treated group. After statistic analysis, it was found that mean little size, birth weights, abnormality, mummified foetues, and stillbirths were not significant different from control group. But the figures of mean mummified foetues and stillbirths were more prominent better in Mg treated group than control.

In conclusion, these data showed that MAH 20 g/sow/day equivalent to Mg dose 13 mg/Kg per day for long term treatment in pregnant pig can fullfill achieve a significance rise in magnesium levels, but the increased plasma Mg did not change the level of blood glucose in pregnant sow. This supplementation of Mg did not delay parturition and be safe to do on whole pregnant period, some benefit on decrease of mummified foetues and stillbirths were observed .

Key words : Magnesium, Supplementation, Pregnant pigs, Blood glucose, Stillbirths, Mummified foetues

Introduction

Today obstetrics is a field where intravenous pharmacological magnesium therapy is frequently used (1, 2). The main indication of parenteral magnesium in obstetrics is preeclampsia (3). Magnesium salt is important for treatment of preeclampsia on the basis of Mg induced vasodilation on blood vessels (4, 5). Hypomagnesium in pregnant condition is the important factor induced vasoconstriction which the predisposing of preeclampsia (4). Some studies found that Mg depletion occurring during pregnant (6, 7, 8, 9, 10, 11). Classen reported that the rate of abortions in early and late pregnant as well as premature births decreased in pregnant women after administration of Mg due to the inhibing uterine contraction of Mg (12). This is the reason why magnesium can sucessfully in treatment of preeclampsia for long time in human. Another possible indication for giving parenteral magnesium to women in preterm labour has been suggested. A retrospective epidemiological study showed that antenatal exposure of very low birthweight (less than 1500 g) infant to maternal pharmacological magnesium supplementation reduced the incidence of cerebral palsy at age 3 or more. This hypothesis agree with the many reports of a neuroprotective role for magnesium (13, 14, 15).

Table 1 The data of the importance of Mg on pregnancy condition

Groups of experiments	Form of magnesium and administration	The importace for supplement	Groups of researchers
15 early pregnant (13-17 Weeks) 15 late pregnant (28-34 weeks)		Glucose loading in pregnancy by ingestion of glucose 100 g, Mg in RBC was decreased	(16)
10 pregnant (28-32 weeks)	Magnesium pyrrolidone carboxylate	Decrease angiotensin II, leading to decrease risk for hypertension	(17)
No? pregnant women	Magnesium oxide 6 months	Decrease incidence of hypertension in Mg treated group	(18)
40pregnant women (37-42 weeks)	-	Late pregnancy period level of Mg decreased from 0.95 $\pm$ 0.01 mmol/L to	(19)

		0.84± 0.02 mmol/L and during parturition to 0.76± 0.01 mmol/L	
High risk population	Magnesium	Fetal and placenta develop well	(20)
Rat pregnant	Magnesium (MgSO ₄)	Vasodilation of blood vessels	(21)
Pregnant women (n= 51)	-	Level of Mg in umbilical artery and vein were decreased during parturition	(22)
4 month asthma pregnant woman	3 g MgSO ₄ intravenous	Increasing peak expiratory flow rate in acute brochitis compounded by brochospasm	(23)
48 pregnant women (30-32 wees) third trimester	380 mg/day Mg pyrrolidone carboxylate for 4 weeks orally	Oral Mg ²⁺ Supplementation increased platelet function and prevent hypertension	(24)
73 pregnant women related leg cramps	Mg orally for 3 weeks	Oral supplementation decreased leg cramp distress	(25)
1049 pregnant women treated with MgSO ₄ and 1089 pregnant women treated with phenytoin	10-g intramuscular MgSO ₄ loading dose followed by a maintenance dose of 5 g given intramuscular every 4 hrs	MgSO ₄ is superior to phenyltoin for the prevention of eclampsia in hypertensive pregnant women	(26)
42 patient not in labor 31 patient regular labor	-	A low magnesium concentration in the pregnant human myometrium could be a cause of premature labor	(27)

But some authors reported its indications remain controversial. A critical and comprehensive review of Mg as tocolysis agents to stop preterm labour concludes that the only effective are prostaglandine inhibitors. An analysis of randomized placebo-controlled clinical trials showed that parenteral magnesium is no better than placebo (28) even on delaying preterm delivery (29) or in preeclampsia (30). It seems therefore worthy to prove whether Mg is useful for pregnant condition in this experiment.

The other interesting on pregnant condition which found hyperglycemia caused anomaly in fetus. Confirmed by the study which demonstrated the consumption of a diet rich in total sugar (more than 206 g/day) by low income pregnant adolescents was associated with a significant decrease in birth weight and threefold increase in the relative risk of delivering a small-for-gestational-age (SGA) infant (31). In report from Rattanatayarom showed that hypomagnesemia in diabetic condition have higher blood glucose than control group which are diabetic but not hypomagnesemia (32). The role of Mg in blood sugar in pregnancy condition is an interesting point of view, whether Mg-supplementation can change the level of blood sugar in pregnant condition.

Mg is the macronutrient for swine, Bartley reported that the minimum demand level of Mg in pig is 0.03 % to 0.04 % of feed (33).

This project research must prove the important of Mg on pig pregnant condition. Level of Mg, Ca and level of glucose will be measured as main parameter. Clinical examination of delivery and offsprings will be observed.

Purpose of the research

1. to study whether Mg is important in the pregnant condition
2. to study whether Mg can full fill benefit to pregnant condition

Materials and Methods

Total 48 (pure bred 47, crossbred 1) gilts of parity between 2nd to 10th (mean 5.2th ± 2.4) body weight ca 150 kg were randomized divided into 2 groups control and Mg treated group. All were feed with the same standard food amounted to 2.4 kg per day and tape water ad libitum which consisted Mg level in tape water 0.87 mmol/L and Ca level 1.66 mmol/L by analysis. In magnesium treated group used magnesium in the form of magnesium L-aspartate hydrochloride (MAH) dose 20 g of MAH per pig per day equivalent to Mg dose 13 mg/kg BW/day for all pregnant periods and 4 days after parturition, Mg was added once daily in food starting 0-4 days before mating

until parturition. Blood collection from jugular vein were done at week 0 (a day before Mg was given) week 4, week 8, week 12, and after parturition 4 days (week 16), each time during 10 AM-12 AM of experiment. For blood glucose analysis all blood were preserved in NaF tube and were separated plasma immediately 2 hrs after blood collection and measured within 24 hrs. with Peridochrom glucose GOD-PAP method enzymatic colorimetric method from Boehringer. For Mg, Ca measurement, blood collection were collection in heparin and separated plasma immediately 2 hrs after blood collection and preserved in -20° C until analysis with atomic absorption spectrophotometer. On the parturition day, total piglets, little size, little birth weight, stillbirths, mummified foetuses, abnormality , and sex of piglets were observed.

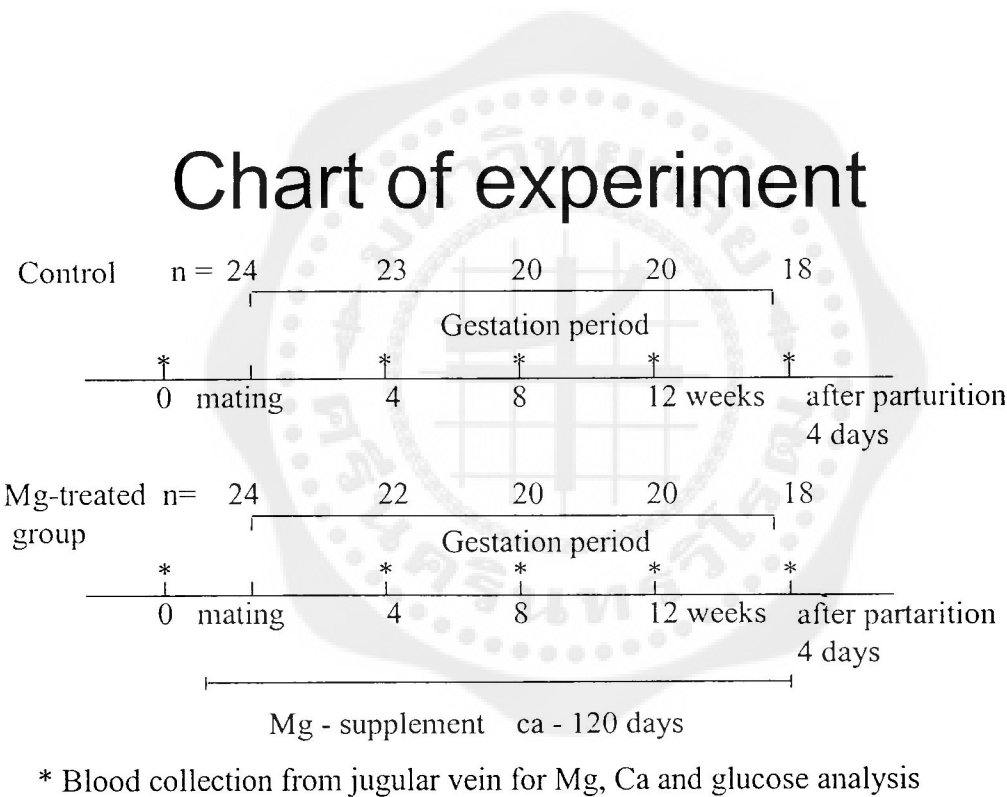
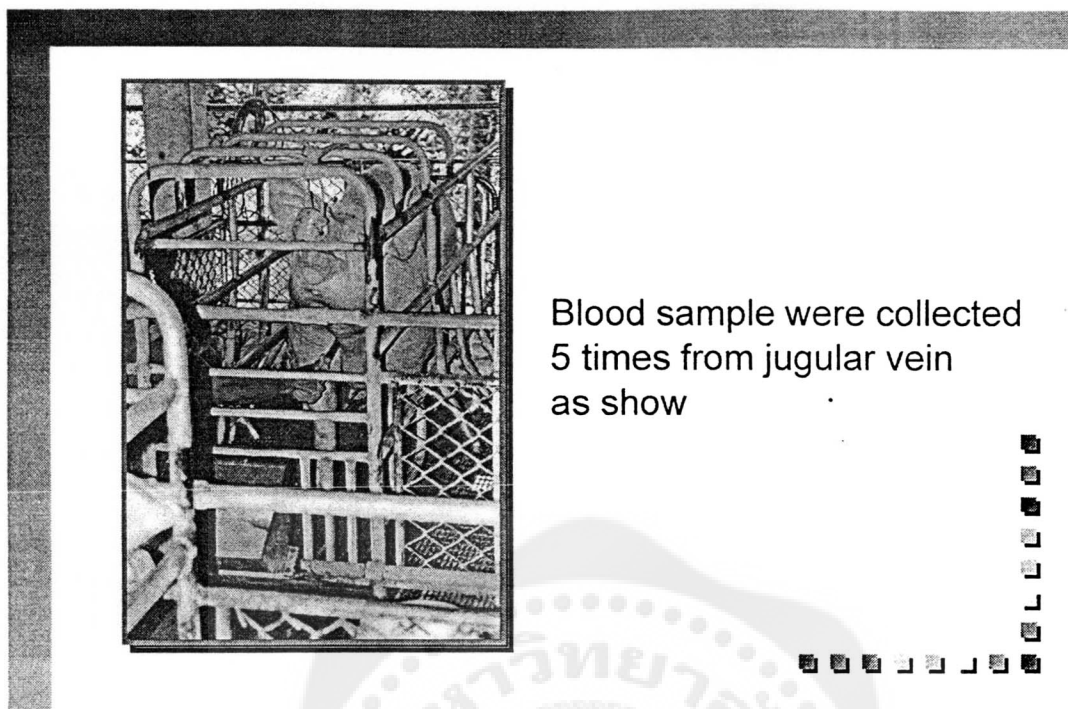


Figure1 Chart of the experiment



Blood sample were collected
5 times from jugular vein
as show

Figure2 Blood collection from jugular vein of pig

Table2 The feed-formulae were used in this experiment

Ingredients	Pregnant perriod	Feeding milk period
Broken rice	840	890
Rice bran	600	480
Rice bran extract	200	0
Soy bean meal	250	215
Soy bean meal extrude	0	265
Fish meal	60	105
Salt	7	7
Dicalcium phosphate	24	27
Shell	10	9
Premix	10	10
Lysine	1.6	305
Choline	1.0	1.0
Methionine	0	0.9
Total	2 ton	2 ton

Structure of MAH

The structural formula of mono-magnesium-L-aspartate-hydrochloride trihydrate has been derived from the chemical and physical properties of the compound (34).

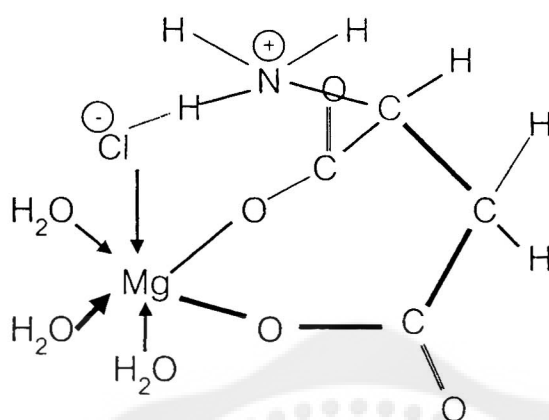


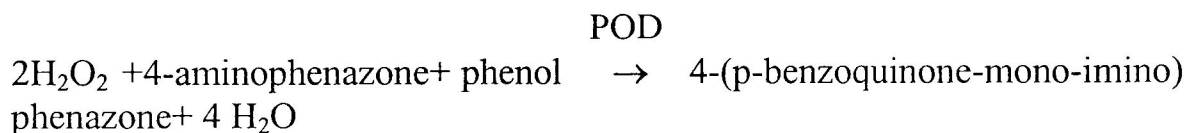
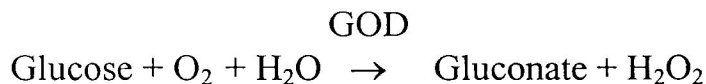
Figure3 Structural formula of mono-magnesium-L-aspartate-hydrochloride trihydrate (MAH). Molecular formula $(C_4H_6ClNO_4)Mg \times 3H_2O$, molecular weight: 245.91

The magnesium ion is bound to the amino acid by the two carboxyl groups of the aspartic acid. The chloride ion and three water molecules are bound to the magnesium ion by coordinate bonds and thus firmly integrated into the complex. The positive charged amino group is folded-back to the negative charged chloride ion due to the electrostatic attraction. By that a polycyclic cage arises, which fixes the halide additionally in its position. The interaction between $-NH_3$ and Cl^- may be an electrostatic one (attraction by ions) or via a weak hydrogen bridge. By that the dissociation in ions is diminished and that is important for the substrate transport in the organism.

Method and principle for glucose analysis

In this experiment glucose analysis was used the method of Peridochrom glucose GOD-PAP enzymatic colorimetric method from Boehringer with the test principle as shown following

Test principle



Procedure for measurement

	Blank	Standard	Sample
Redistrilled water	0.1 ml	-	-
Standard	-	0.1 ml	-
Supernatant	-	-	0.1 ml
Reagent solution	2.0 ml	2.0 ml	2.0 ml

Plasma samples were mixed and incubated at 20 to 25 °C avoid to direct sunlight for 30 to 90 minutes in cuvette 1 cm light path then measured against blank by using spectrophotometer at wavelength 510 nm.

Magnesium and calcium measurement by atomic absorption spectrophotometer

Plasma Mg and Ca were measured by atomic absorption spectrophotometer (AAS) from Shimadzu model 680

Procedure for analysis AAS

1. Prepare SrCl_2 0.25% for dilute plasma and standard solution

$\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$ 0.76 g in 100 ml bidistrilled water

2. Prepare standard solution

: for standard Mg stalk solution was 1000 ppm

pipette Mg stalk solution 10 μl + 50 ml SrCl_2 0.25% for the concentration 0.200 mg/L Mg, absorption read by AAS was ca 0.249

pipette Mg stalk solution 20 μl + 50 ml SrCl_2 0.25% for the concentration 0.400 mg/L Mg, absorption read by AAS was ca 0.473

pipette Mg stalk solution 30 μl + 50 ml SrCl_2 0.25% for the concentration 0.200 mg/L Mg, absorption read by AAS was ca 0.695

: for standard Ca stalk solution was 1000 ppm

pipette Ca stalk solution 25 μl + 50 ml SrCl_2 0.25% for the concentration 0.5 mg/L Mg, absorption read by AAS was ca 0.026

pipette Ca stalk solution 50 μ l + 50 ml SrCl_2 0.25% for the concentration 1.0 mg/L Mg, absorption read by AAS was ca 0.052

pipette Ca stalk solution 75 μ l + 50 ml SrCl_2 0.25% for the concentration 1.5 mg/L Mg, absorption read by AAS was ca 0.084

3. Prepare plasma samples as follow

pipette plasma 250 μ l + 25 ml of SrCl_2 0.25%

All dilutions were prepare in volumetric flask.

Statistic analysis

All parameters were analyzed on statistic computer program SPSS window version 6.1, first were analyzed for normal distribution (Komogorov-Smirnov-test) and homogeneity of variances (Levene's test) . For parametric test used t-test independent sample setting the level of significance at $p < 0.05$ and 0.01, there were gestation period, little size, little birth weight, stillbirths, mummified fetuses, and abnormality for t-test. Plasma glucose used one way ANOVA and Scheffe test. For non parametric used Kruskal Wallis 1-way ANOVA, the differences pair by Mann whitney U-Wilcoxon Rank Sum W test. There were parity, plasma Mg, Ca for non parametric test.

Results

Table3 The number of pigs starting and final in the experiment

Starting number of pigs	Anestrus	Return anestrus	Infertility	Abortion	Dead after parturition	Final number of pigs
Control N=24	N=2 8.3%	N=0 0%	N=1 4.2%	N=2 8.3%	N=1 4.2%	N=18
Mg - treated group N=24	N=1 4.2%	N=1 4.2%	N=1 4.2%	N=3 12.5%	N=0 0%	N=18

On the beginning of this experiment the number of starting pigs were $n=24$ in control group. There were some pigs excluded during experiment by the reason of anestrus, infertility, abortion and dead after parturition as shown in the table 3. The abortion of 2 pregnant pigs in control group occurred on both date 29th of gestation. And one sow died after delivery 1 day, this might be uterus rupture after parturition. The final number of control pigs on the end of this experiment were 18 pigs which were equal to Mg treated group.

While on the beginning of this experiment the number of starting pigs were $n=24$ in Mg treated group. There were some pigs also excluded during experiment by the reason of anestrus, infertility, abortion as shown in the same table. The abortion of 3 pregnant pigs in this group occurred on date 23rd, 93rd, 103rd of gestation. The final number of Mg treated pigs on the end of this experiment were 18 pigs which were equal to control group.

Table4 The effect of Mg-supplementation in pregnant sows and offsprings (piglets).

Sows and piglets	Control (n=18)	Mg treated gr (n=18)
Parity	5 th $\pm$ 3	5 th $\pm$ 2
Gestation period (days)	116 $\pm$ 3	117 $\pm$ 2
Little size (piglets)	10.2 $\pm$ 2.2	10.3 $\pm$ 2.1
Little birth weights (Kg)	1.5 $\pm$ 0.2	1.6 $\pm$ 0.3
Male : female of piglets	5 : 5	6 : 4
Total piglets consume	184	186
Stillbirths (%)	5.4%	4.8%
Mummified foetuses (%)	3.3%	1.6%
Abnormality (%)	1.1%	1.1%

Mean gestation period was 116.3 ± 2.5 days in control group and was 117.05 ± 1.8 in Mg-treated group, mean little size was 10.2 ± 2.2 in control group and was 10.3 ± 2.1 in Mg-treated group, the mean little birth weights were 1.52 ± 0.21 kg in control group and 1.62 ± 0.28 kg in Mg-treated group, mean stillbirths were 10 piglets from total 184 piglets consume or 0.55 ± 1.09 (5.4%) in control group and were 9 piglets from total 186 piglets consume or 0.5 ± 0.7 (4.8%) in Mg treated group, mean mummified foetuses were 6 piglets from total 184 piglets consume or 0.33 ± 0.76 (3.3%) in control group and were 3 piglets from total 186 piglets consume or 0.166 ± 0.52 (1.6%) in Mg treated group, mean abnormality were 2 piglets from total 184 piglets consume or were 2 piglets from total 186 piglets consume or 0.11 ± 0.3 (1.1%) the same as magnesium treated group, sex of piglets in control group male to female were 4.5 ± 1.7 to 4.7 ± 1.9 and 5.6 ± 1.9 to 3.88 ± 1.13 in Mg treated group. There was no significant difference between control and Mg treated group on gestation period, little size, little birth weights, stillbirths, mummified foetuses, and abnormality. Nevertheless, the figures of Mg treated group seemed to be more benefit on stillbirths and mummified foetuses.

Table5 The level of plasma glucose, A=before MAH was given, B= MAH has been given, a significant differences from b at the same column at $p<0.01$

Time of the experiments	Plasma glucose(mg/100ml) Mean $\pm$ SD	
	Control	Mg treated group
Beginning time ^A (0 week)	82.9 $\pm$ 7.8 ^b n=23	81.0 $\pm$ 8.8 ^b n=24
4 weeks gestation ^B	68.7 $\pm$ 7.6 ^a n=23	67.5 $\pm$ 9.9 ^a n=22
8 weeks gestation ^B	68.7 $\pm$ 9.3 ^a n=20	68.8 $\pm$ 8.2 ^a n=20
12 weeks gestation ^B	65.5 $\pm$ 8.5 ^a n=20	66.9 $\pm$ 8.3 ^a n=20
After parturition 4 days ^B (16 weeks)	83.2 $\pm$ 10.3 ^b n=18	89.9 $\pm$ 13.6 ^b n=18

Blood sugar analysis on week 0,4,8,12, and after 4 days parturition were 82.9 $\pm$ 7.8, 68.7 $\pm$ 7.6 , 68.7 $\pm$ 9.3 , 65.5 $\pm$ 8.5 , 83.2 $\pm$ 10.3 mg/100ml, respectively in control group and were 81.0 $\pm$ 8.8 , 67.5 $\pm$ 9.9 , 68.8 $\pm$ 8.2 , 66.9 $\pm$ 8.3 , 89.9 $\pm$ 13.6 mg/100ml respectively on Mg-treated group. There was no significant difference between Mg treated group and control group in all periods of experiments. Blood sugar decreased significantly ($P<0.01$) during gestation both of control and Mg treated group compared to starting week (week0) and after parturition blood sugar increased to the same level as beginning time.

Table6 The level of plasma Mg, A=before MAH was given, B= MAH has been given, * significant differences from control group at the same row at $p<0.01$, a significant differences from b at the same column at $p<0.01$

Time of the experiments	Plasma magnesium(mmol/L) Mean $\pm$ SD	
	Control	Mg treated group
Beginning time ^A (0 week)	0.84 $\pm$ 0.05 ^b n=22	0.87 $\pm$ 0.09 ^b n=23
4 weeks gestation ^B	0.62 $\pm$ 0.10 ^a n=23	0.71 $\pm$ 0.08* ^a n=21
8 weeks gestation ^B	0.65 $\pm$ 0.05 ^a n=19	0.77 $\pm$ 0.17* ^a n=21
12 weeks gestation ^B	0.74 $\pm$ 0.07 ^a n=19	0.81 $\pm$ 0.05* ^a n=20
After parturition 4 days ^B (16 weeks)	0.85 $\pm$ 0.12 ^b n=18	0.90 $\pm$ 0.09 ^b n=18

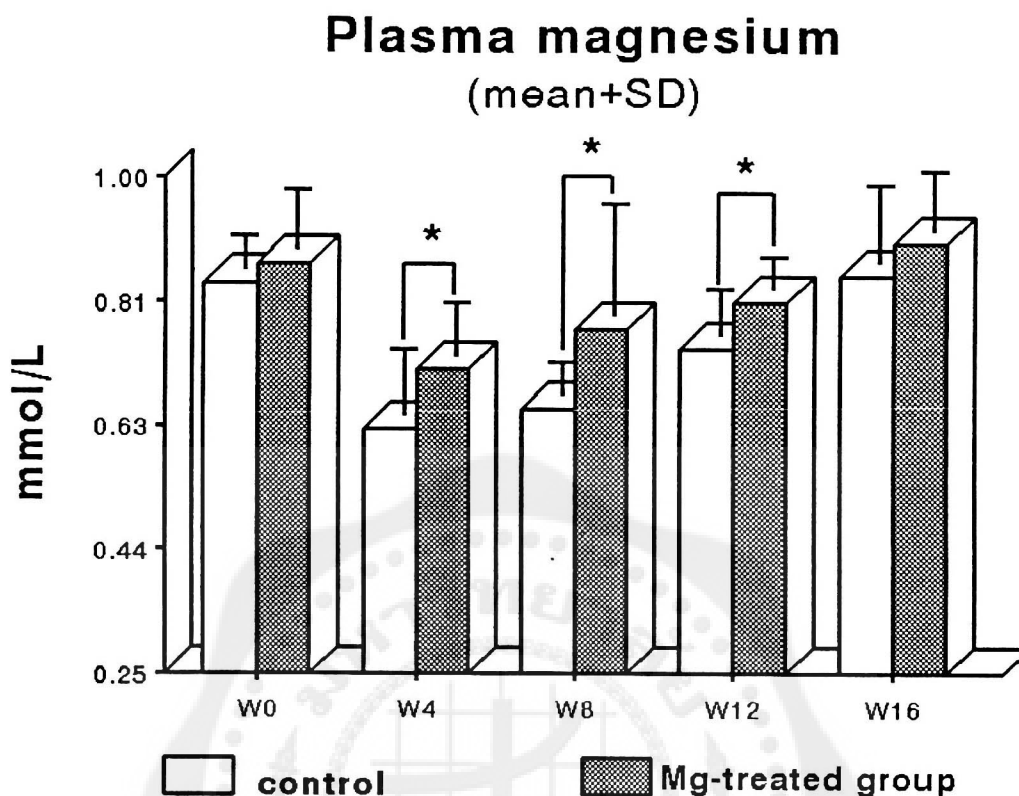


Figure 4 The level of plasma Mg in sows. W0 =before MAH was given ,W1, W8, W12, W16 = MAH has been given, * significant difference at $p < 0.01$

Plasma Mg were measured by atomic absorption on week 0, 4, 8, 12, and after parturition 4 days were 0.84 ± 0.05 , 0.62 ± 0.1 , 0.65 ± 0.05 , 0.74 ± 0.07 , 0.85 ± 0.12 mmol/L respectively in control group and were 0.87 ± 0.09 , 0.71 ± 0.08 , 0.77 ± 0.17 , 0.81 ± 0.05 , 0.90 ± 0.09 mmol/L in Mg-treated groups. On starting week and after parturition there was no significant differences between control and Mg treated group. During gestation (week 4, week 8, week 12) the level of plasma Mg decreased significantly at p less than 0.01 in both two groups compared with starting week in the same group, the lowest level observed on week 4. And the level of plasma Mg in Mg treated groups during gestation (week 4, week 8, week 12) were higher significantly from control group at p less than 0.01. It meant that dose of MAH 20 g/sow/day can be achieved a significance rise in magnesium levels in this experiment.

Table7 The level of plasma Ca. A=before MAH was given, B= MAH has been given, a significant differences from b at the same column at $p<0.01$, c significant differences from d at the same column at $p<0.01$

Time of the experiments	Plasma calcium(mmol/L) Mean $\pm$ SD	
	Control	Mg treated group
Beginning time ^A (0 week)	2.80 $\pm$ 0.22 ^{b, d} n=18	2.78 $\pm$ 0.20 ^{b, d} n=21
4 weeks gestation ^B	2.28 $\pm$ 0.15 ^{a, c} n=21	2.26 $\pm$ 0.14 ^{a, c} n=19
8 weeks gestation ^B	2.22 $\pm$ 0.15 ^{a, c} n=18	2.17 $\pm$ 0.10 ^{a, c} n=19
12 weeks gestation ^B	2.48 $\pm$ 0.19 ^a n=16	2.39 $\pm$ 0.13 ^a n=17
After parturition 4 days ^B (16 weeks)	2.46 $\pm$ 0.19 ^{a, d} n=18	2.45 $\pm$ 0.13 ^{a, d} n=18

Plasma Ca were measured by atomic absorption on week 0, 4, 8, 12, and after parturition 4 days were 2.80 $\pm$ 0.22, 2.28 $\pm$ 0.15, 2.22 $\pm$ 0.15, 2.48 $\pm$ 0.19, 2.46 $\pm$ 0.19 mmol/L respectively in control group and were 2.78 $\pm$ 0.20, 2.26 $\pm$ 0.14, 2.17 $\pm$ 0.10, 2.39 $\pm$ 0.13, 2.45 $\pm$ 0.13 mmol/L in Mg-treated groups. The level of plasma calcium decreased slightly ($p>0.05$) in Mg treated group from control group as the same period of experiment. But the level of plasma Ca decreased significantly ($P<0.01$) during gestation and after parturition in both of control and Mg treated group compared to starting week in the same group, the lowest level observed on week 8.

Discussion

For the number of pigs which were excluded in this experiment by abortion in control and in Mg treated group, there were two pigs from 24 pregnant pigs from control group aborted both on 29th days of gestation while there were three pigs from 24 pregnant pigs from Mg treated group aborted during day 23rd, 93rd, and 103rd. In summary there was one pig abortion in Mg treated group more than control group. The abortion time in control group occurred in seemly early pregnant period, while the Mg treated group occurred more in late of pregnancy period. This was interesting to investigate why mg treated group had more percentage abortion more than control group. In the future experiment the number of pigs should also more than 24 sothat the the number of abortion could be compared more clearly. In the same as the number of pig which was died after parturition in control group owing to the

rupture of uterus during parturition while there was no occurred in Mg treated group whether Mg was important in the stage of uterine contraction and blood supply in uterus during parturition. The next further experiment with more samples might be useful for answer this question.

For supplement with Mg to the pregnant pig during the whole period of pregnancy was confirm by a double blind study was performed in the 568 cases of pregnancy women Mg was given 15 mmol Mg in form of magnesium aspartate hydrochloride or 300 mg aspartic acid (placebo) per day . There were significant differences in higher birth weights in Mg treated group than the placebo , babies of mothers supplemented with magnesium also showed better Apgar scores, the results of this study strongly recommend a supplementation of Mg during the whole period of pregnancy (35) as done in this experiment, however the number of samples in this experiment were less than reported by Spaetling in 1988 (35). Nevertheless the figures of little size, little birth weight, total piglets consume and especially stillbirths and mummified fetuses were more better in Mg treated group than control group. Gordon in 1997 (36) reported that farrowings of long duration and increased time-intervals between piglets at birth are associated with a greater incidence of intrapartal stillbirths, more than 80% of these stillbirths are believed to occur in the last third of the litter sothat this might be the reason that why in Mg treated group had less incidence of stillbirths. Mg supplementation may improve the duration or decreased time-intervals during parturition.

For plasma glucose there was no change in the level of Mg treated group and control group. The level of glucose in both two group during pregnancy were decreased, because of the restricted feed energy intake during pregnancy by the routine farm management by deceased amount of food intake per day. In this experiment there was no pregnant sow which developed diabetic during pregnancy sothat for studying the diabetic condition in pregnant pig should be study in more sample than 48 sows.

Magnesium aspartate hydrochloride is described as the most readily absorbed magnesium salt. Magnesium may cause diarrhoea. Thus, only limited amounts can be given by mouth. About 0.37 mmol per kg BW are required to achieve a significant rise in serum magnesium levels (37). In this experiment 20 g of MAH per pig per day equivalent to Mg dose 13 mg per kg BW per day or 0.53 mmol per kg BW for all pregnant periods and 4 days after parturition, there was no pregnant pigs got diarrhoea whole time of this experiment. The level of Mg in plasma were also increased significantly ($p < 0.01$) during weeks 4 to weeks 12 of gestation, it confirmed that the Mg level up to 0.37 mmol per kg BW could achieve a significant rise in plasma level as shown in this experiment. During gestation here Mg were decreased

significantly ($p < 0.01$) in the same group in both control and Mg treated group compared to starting week which was agreed with the reported of some authors (6, 7, 8, 9, 10, 11) reported that normal pregnancy, circulating Mg concentrations have been drop significantly.

For plasma calcium there was slightly decreased ($p > 0.05$) in Ca level in Mg treated group compared to control group during week 4 to week 16 of the experiment. This was found the same as long term treatment with $MgSO_4$, serum concentration of Ca decreased, but the mechanism in a decline in serum Ca concentration is unclear, the urinary losses of Ca are a great concern (38). When compared to the same group the level of plasma Ca decreased significantly ($P < 0.01$) from starting week during gestation and after parturition in both of control and Mg treated group, the lowest level observed on week 8. This decreased Ca level parallel to the decreased Mg level during gestation, and started to be slightly increased during weeks 12 the same as Mg level.

Conclusion. These data showed that MAH 20 g/sow/day equivalent to Mg dose 13 mg/Kg per day for long term treatment in pregnant pig can fullfill achieve a significance rise in magnesium levels, but the increased plasma Mg did not change the level of blood glucose in pregnant sow. This supplementation of Mg did not delay parturition and be safe to do on whole pregnant period, some benefit on decrease of mummified fetuses and stillbirths were observed.

Acknowledgement

I wish to thank for Verla Pharm, Tuzing, Germany for MAH supporting, and to Asst. Prof. Kumpee Kortheerakul, regional swine expert for his guidance in pig farm management and blood collection.

Appendix

Raw data

Abbreviations and the units (in parentheses) for raw data

Gr =group

no.p =number of pregnant

dayp =days of pregnant

lit.s =little size

sti.b =stillbirths

mum =mummified foetuses

abno =abnormality

fema =female

lit.w =little weight (kilogram)

to.lit.w=total little weight (kilogram)

Gr	no.p	dayp	lit.s	sti.b	Mum	Abno	male	fema	lit.w	to.lit.w
1	4	115	12	0	0	0	5	7	1.45	17.5
1	8	119	11	0	0	0	6	5	1.77	19.5
1	6	117	12	0	0	0	3	9	1.70	20.5
1	2	110	7	0	0	0	3	4	1.35	9.5
1	2	116	13	2	0	0	6	5	1.45	16.0
1	2	118	13	0	1	1	4	7	1.27	14.0
1	3	115	10	2	0	0	4	4	1.18	9.5
1	8	116	13	4	0	0	5	4	1.27	11.5
1	6	117	10	0	0	0	4	6	1.65	16.5
1	8	118	12	0	3	0	6	3	1.44	13.0
1	7	118	8	0	0	0	3	5	1.50	12.0
1	3	116	6	0	0	1	3	2	2.00	10.0
1	1	117	11	1	1	0	8	1	1.66	15.0
1	1	111	7	0	0	0	3	4	1.50	10.5
1	1	115	10	0	0	0	5	5	1.55	15.5
1	5	118	11	0	1	0	5	5	1.45	14.5
1	1	120	8	1	0	0	1	6	1.42	10.0
1	6	118	10	0	0	0	7	3	1.75	17.5
2	4	117	11	1	0	1	5	4	1.60	14.5
2	4	114	12	0	0	0	7	5	1.45	17.5
2	6	117	5	1	0	0	1	3	2.25	9.0
2	8	118	12	1	0	0	7	4	1.30	14.5
2	7	117	11	0	0	0	8	3	1.50	16.5
2	2	117	10	0	0	0	8	2	1.90	19.0
2	5	119	9	0	0	0	6	3	1.38	12.5
2	4	113	10	2	0	0	5	3	1.50	12.0
2	5	118	11	0	0	1	5	5	1.65	16.5
2	7	116	9	0	0	0	6	3	1.27	11.5
2	7	119	12	0	1	0	7	4	1.59	17.5
2	4	120	7	0	0	0	2	5	2.07	14.5
2	4	118	11	1	2	0	5	3	1.68	13.5
2	3	118	10	1	0	0	5	4	1.77	16.0
2	2	117	9	0	0	0	5	4	2.05	18.5
2	6	114	15	0	0	0	9	6	1.43	21.5
2	4	116	10	2	0	0	5	3	1.25	10.0
2	1	119	12	0	0	0	6	6	1.62	19.5

Gr	Weeks	Glucose (mg/100ml)	Mg (mmol/L)	Ca (mmol/L)
1	0	73.07	.76	2.51
1	0	73.20	.79	.
1	0	79.61	.93	.
1	0	90.61	.77	.
1	0	82.02	.88	2.74
1	0	93.80	.86	2.89
1	0	88.42	.82	2.71
1	0	76.78	.88	2.86
1	0	83.49	.86	2.45
1	0	70.17	.89	3.00
1	0	79.93	.83	3.18
1	0	88.71	.84	.
1	0	70.65	.81	2.79
1	0	83.55	.91	3.05
1	0	78.32	.	.
1	0	97.68	.83	2.70
1	0	84.72	.86	3.13
1	0	88.28	.79	2.67
1	0	85.75	.84	2.77
1	0	96.90	.78	2.65
1	0	74.72	.77	2.97
1	0	80.96	.92	3.03
1	0	84.35	.79	2.45
1	0	.	.	.
2	0	79.93	.90	2.96
2	0	85.16	.97	.
2	0	89.45	.81	2.83
2	0	86.88	.90	2.76
2	0	75.69	1.00	2.90
2	0	65.80	.84	3.11
2	0	84.16	.85	2.55
2	0	80.52	.77	2.67
2	0	89.30	.92	2.97
2	0	89.15	.74	2.92
2	0	84.65	.76	2.86
2	0	84.85	.97	2.69
2	0	79.88	.86	2.81
2	0	89.75	.80	2.71
2	0	79.24	.83	2.78
2	0	80.46	.80	2.61
2	0	77.66	.84	2.86
2	0	79.14	.95	2.84
2	0	89.68	.	.
2	0	81.40	1.08	2.26
2	0	52.42	.95	3.07
2	0	70.02	.81	.
2	0	90.52	.73	2.47
2	0	77.32	1.01	2.82
1	4	61.20	.62	2.57
1	4	58.17	.72	2.28
1	4	65.17	.67	2.49
1	4	61.20	.62	2.49
1	4	68.17	.77	2.31
1	4	68.51	.58	2.31
1	4	67.85	.59	2.31
1	4	76.88	.52	2.07
1	4	85.09	.87	2.05
1	4	60.40	.60	2.25
1	4	.	.	.
1	4	65.66	.62	2.32
1	4	77.76	.67	2.39
1	4	69.37	.59	2.27

1	4	58.43	.54	2.18
1	4	81.12	.51	.
1	4	67.08	.70	2.33
1	4	77.27	.50	2.23
1	4	63.84	.72	2.27
1	4	78.27	.69	2.08
1	4	70.21	.52	2.01
1	4	60.92	.47	2.22
1	4	64.66	.70	2.45
1	4	73.00	.53	.
2	4	70.49	.79	2.05
2	4	63.74	.84	.
2	4	70.61	.77	2.13
2	4	70.93	.69	2.01
2	4	34.05	.74	2.28
2	4	55.36	.72	2.38
2	4	74.63	.65	2.24
2	4	73.46	.59	2.31
2	4	66.10	.70	2.16
2	4	87.71	.68	2.16
2	4	62.98	.67	2.38
2	4	63.22	.68	2.31
2	4	65.60	.70	2.48
2	4	.	.	.
2	4	62.95	.75	2.32
2	4	64.69	.65	2.39
2	4	72.43	.	.
2	4	74.58	.88	2.55
2	4	74.08	.53	2.16
2	4	72.52	.72	2.23
2	4	68.21	.73	.
2	4	.	.	.
2	4	72.63	.70	2.27
2	4	63.90	.74	2.13
1	8	67.77	.60	2.16
1	8	.	.	.
1	8	77.86	.70	2.21
1	8	61.01	.60	2.21
1	8	79.24	.62	2.04
1	8	71.66	.69	2.47
1	8	69.10	.63	2.45
1	8	51.89	.66	2.26
1	8	.	.	.
1	8	79.30	.69	2.16
1	8	.	.	.
1	8	51.03	.73	2.34
1	8	.	.	.
1	8	58.11	.64	2.28
1	8	78.98	.64	1.86
1	8	81.01	.59	2.21
1	8	71.82	.70	2.24
1	8	75.22	.63	2.10
1	8	58.94	.64	2.23
1	8	69.33	.74	2.47
1	8	73.60	.73	.
1	8	66.00	.56	2.16
1	8	63.99	.62	2.19
1	8	.	.	.
2	8	64.57	.77	2.44
2	8	.	.	.
2	8	75.04	.68	2.20
2	8	62.24	.66	2.15
2	8	73.99	.81	2.00
2	8	80.21	.71	2.32

Gr	Weeks	Glucose (mg/100ml)	Mg (mmol/L)	Ca (mmol/L)
2	8	66.79	.77	2.03
2	8	62.74	.79	2.19
2	8	71.38	.72	2.11
2	8	57.51	.69	2.16
2	8	83.25	.61	2.09
2	8	66.79	.65	2.16
2	8	70.25	.78	2.20
2	8	.	.	.
2	8	79.40	.71	2.16
2	8	71.57	.71	2.26
2	8	63.56	.73	.
2	8	58.77	.83	2.08
2	8	77.61	.80	2.26
2	8	75.08	.92	2.12
2	8	50.55	.72	2.18
2	8	.	.	.
2	8	67.34	.65	2.20
2	8	66.10	1.44	.
1	12	61.75	.71	2.67
1	12	.	.	.
1	12	37.82	.84	2.83
1	12	60.10	.81	2.69
1	12	70.85	.77	2.44
1	12	70.86	.69	.
1	12	63.28	.68	.
1	12	68.36	.62	.
1	12	.	.	.
1	12	58.11	.83	2.37
1	12	.	.	.
1	12	74.58	.71	2.41
1	12	.	.	.
1	12	64.43	.77	2.53
1	12	61.90	.81	2.43
1	12	67.28	.65	2.29
1	12	74.13	.74	2.34
1	12	76.64	.75	2.24
1	12	66.18	.81	2.57
1	12	73.90	.85	2.49
1	12	63.76	.75	2.47
1	12	66.24	.61	2.15
1	12	63.44	.70	2.80
1	12	.	.	.
2	12	55.15	.84	2.55
2	12	.	.	.
2	12	73.07	.86	2.54
2	12	57.26	.76	2.22
2	12	61.18	.81	2.32
2	12	60.07	.79	2.51
2	12	.	.	.
2	12	71.41	.80	2.45
2	12	79.88	.81	2.51
2	12	70.33	.81	2.31
2	12	63.78	.72	.
2	12	65.54	.89	2.53
2	12	60.21	.86	2.39
2	12	.	.	.
2	12	53.12	.77	2.35
2	12	64.18	.83	2.18
2	12	61.56	.75	.

2	12	72.07	.86	2.53
2	12	84.40	.67	2.18
2	12	65.84	.81	.
2	12	72.77	.89	2.42
2	12	.	.	.
2	12	69.25	.84	2.32
2	12	76.25	.79	2.29
1	16	80.03	.95	2.57
1	16	.	.	.
1	16	100.53	.75	2.75
1	16	87.64	.82	2.32
1	16	94.95	1.08	2.69
1	16	89.45	.87	2.20
1	16	85.42	.78	2.32
1	16	64.95	.74	2.31
1	16	.	.81	2.54
1	16	89.39	.93	2.42
1	16	.	.	.
1	16	89.24	.72	2.58
1	16	.	.	.
1	16	95.13	.86	2.35
1	16	65.07	.	.
1	16	72.48	.76	2.08
1	16	88.86	.72	2.53
1	16	.	.	.
1	16	73.60	.85	2.42
1	16	76.59	1.16	2.28
1	16	74.63	.94	2.50
1	16	80.21	.75	2.65
1	16	90.07	.80	2.69
1	16	.	.	.
2	16	83.91	.85	2.52
2	16	.	.	.
2	16	73.30	1.09	2.47
2	16	97.58	.78	2.33
2	16	95.86	.93	2.46
2	16	62.77	.92	2.56
2	16	.	.	.
2	16	125.92	.99	2.70
2	16	106.45	.90	2.54
2	16	92.04	.84	2.50
2	16	91.56	.75	2.42
2	16	87.64	1.07	2.34
2	16	101.85	.77	2.49
2	16	.	.	.
2	16	85.68	.91	2.48
2	16	77.81	.83	2.52
2	16	80.41	.93	2.13
2	16	86.48	.91	2.55
2	16	.	.	.
2	16	.	.	.
2	16	90.37	.83	.
2	16	.	.	.
2	16	90.76	.93	.
2	16	87.50	.96	.

Bibliography

1. Durlach, J.; Durlach, V.; Bac, P.; Bra, M.; Guet-Bara, A.: Magnesium and therapeutics. *Magnes. Res.* **7** (1994) 313-328.
2. Bennett, P.; Edwards, D.: Use of magnesium in obstetrics. *Lancet.* **350** (1997) 1491.
3. Durch, J.; Bac, P.; Bara, M., Guet-Bara, A.: Is the Pharmacological use of intravenous magnesium before preterm cerebroprotective or deleterious for premature infants? Possible importance of the use of magnesium sulphate. *Magnes. Res.* **11** (1998) 323-325.
4. Altura, B.M.; Altura, B.T.; Carella, A.: Magnesium-deficiency spasms of umbilical vessels : relation to preeclampsia, hypertension, growth retardation. *Science.* **221** (1993) 376-378.
5. Kisters, K.; Spieker, C.; Niedner, W.; Faera, I.; Rahn, K.H.; Zidek, W.: Magnesium metabolism in pregnancy and preeclampsia. In : Gof, S.; Dralle, D.; Vecchiet, L (eds). *Magnesium 1993*,. John Libby London, Paris, Rom. 1994, pp 401-3.
6. Hall, D.G.: Serum magnesium in pregnancy. *Obstet. Gynecol.* **9** (1957) 158-162.
7. Wilbell, L.; Gebre-Medhin, M.; Lindmark, G.: Magnesium and zinc in diabetic pregnancy. *Acta. Paediatr. Scand.* [Suppl] **320** (1985) 100-106.
8. DeJorge, F.B.; Delascio, D.; Cintra, A.B.U.; Antunes, M.L.: Magnesium concentrations in the blood serum of normal pregnant women. *Obstet Gynecol.* **25** (1965) 253-254.
9. Sheldon, W.L.; Aspillaga, M.O.; Smith, P.A.; Lind, T.: The effect of oral iron supplementation on zinc and magnesium levels during pregnancy. *Br. J. Obstet. Gynecol.* **92** (1985) 892-898.
10. Moser, P.B.; Issa, C.F.; Reynolds, R.D.: Dietary magnesium intake and the concentration of Magnesium in plasma and erythrocyte of postpartum women. *J. Am. Coll. Nutr.* **4** (1983) 387-396.
11. Stanton, M.F.; Lowenstein, F.W.: Serum magnesium in women during pregnancy, while taking contraceptives and after menopause. *J. Am. Coll. Nutr.* **6** (1987) 313-319.

12. Classen, H.G.; Helbig, J.: Magnesium therapy in pregnancy pharmacologic and toxicologic aspects of magnesium supplementation and use in preclampsia and threatened premature labor. *Fortchr-Med.* **102** (1984) 841-844.
13. Nelson, K.B.; Grether, J.K.: Can MgSO₄ reduce the risk of cerebral palsy in very low birth-weight infants? *Pediatrics.* **95** (1995) 263-269.
14. Bac, P.; Herrenknecht, C.; Pages, N.; Dupont, C.; Durlach, J.: Retroversible model of magnesium depletion induced by systemic kainic acid in jection in magnesium deficient rats.I. Comparative studied of various magnesium salts. *Magnes. Res.* **9** (1996) 281-291.
15. Muir, K.W.: New experimental and clinical data on the efficacy of pharmacological infusions in cerebral infarct. *Magnes.Res.* **11** (1998) 43-56.
16. Smith, M.A.; Nagey, D.A.; Moser – Veillon, P.B.: Plasma and erythrocyte magnesium changes following a glucose challenge during pregnancy. *Am Coll Nutr.* **11** (1992) 426 – 431.
17. Tranquilli, A.L.; Mariani, M.L.; Mazzanti, L.; Valensise, H.; Garzetti, G.G.; Romanini, C.: Magnesium pyrrolidone Carboxylate infusion reduces angiotensin II pressor response in pregnant women at risk for hypertension. *Am. J. Obstet. Gynecol.* **167** (1992) 885 – 888.
18. D’Almeida, A.; Carter, J.P.; Anatol, A.; Prost, C.: Effects of a combination of evening primrose oil (gamma linolenic acid) and fish oil (eicosapentaenoic + docahexaenoic acid) versus magnesium, and versus placebo in preventing pre - eclampsia. *Women Health.* **19** (1992) 117 – 131.
19. Weissberg, N.; Schwartz, G.; Shemesh, O.; Brooks, B.A.; Algur, N.; Eylath, U.; Abraham, A.S.: Serum and Mononuclear cell Potassium, magnesium, Sodium and Calcium in pregnancy and labour and their relation to uterine muscle contraction. *Magnes. Res.* **5** (1992) 173 - 177.
20. Favier, M.; Faure, P.: [Supplements during pregnancy : ifad or necessity?]. *Revue Francaise de Gynecologie et d Obstetrique.* **89** (1994) 210 – 215.

21. Aloamaka, C.P.; Ezimokhai, M.; Morrison, J.; Cherian, T.; Effect of pregnancy on relaxation of rat aorta to magnesium. *Cardiovasc. Res.* **27** (1993) 1629 – 1633.
22. Handwerker, S.M.; Altura, B.T.; Royo, B.; Altura, B.M.: Ionized magnesium and calcium levels in umbilical cord serum of pregnant women with transient hypertension during labor. *Am. J. hypertens.* **6** (1993) 542 – 545.
23. Skobeloff, E.M.; Kim, D.; Spivey, W.H.: Magnesium sulfate for the treatment of bronchospasm complicating acute bronchitis in a four-months' - pregnant woman. *Ann. Emerg. Med.* **22** (1993) 1365 – 1367.
24. Tranquilli, A.L.; Mazzanti, L.; Staffolani, R.; Salvolini, E.; Garzetti, G.G.; Romanini, C.: Functional platelet modifications induced by oral magnesium supplementation in normotensive and hypertensive pregnancy. *Boll. Soc. Ital. Biol. Sper.* **70** (1994) 249 – 256.
25. Dahle, L.O.; Berg, G.; Hammar, M.; Hurtig, M.; Larsson, L.: The effect of oral magnesium substitution on pregnancy induced leg cramps. *Am. J. obstet. Gynecol.* **173** (1995) 175 – 80.
26. Lucas, M.J.; Leveno, K.J.; Cunningham, F.G.: A comparison of magnesium sulfate with phenytoin for the prevention of eclampsia. *N. Engl. J. Med.* **333** (1995) 201 – 205.
27. Cunze, T.; Rath, W.; Osmers, R.; Martin, M.; Warneke, G.; Kuhn, W.: Magnesium and Calcium concentration in the pregnant and non-pregnant myometrium. *Int. J. Gynecol. obstet.* **48** (1995) 9 – 13.
28. Higbig, K.; Xenakis, E.M.J.; Pauerstein, C.J.: Do tocolytic agents stop preterm labor? A critical and comprehensive review of efficacy and safety. *Am. J. Obstet. Gynecol.* **168**(1993) 1247-1259.
29. Bennett, P.; Edwards, D.: Use of magnesium in obstetrics. *Lancet.* **350** (1997) 1491.
30. Witlin, A.G.; Friedman, S.A.; Sibai, B.M.: The effect of MgSO₄ therapy on duration of labor in women with pre-eclampsia at term : a randomised double blind placebo controlled trial. *Am. J. Obstet. Gynecol.* **176** (1997) 623-627.

31. Lender, C.M.; Hediger, M.L.; Scholl, T.O.; Khoo, C.S.; Slap, G.B.; Stallings, V.A.: Effect of high-sugar intake by low- income pregnant adolescents on infant birth weight. *J. Adolesc.Health*. **15** (1994) 596-602.
32. Rattanatayaron, W.; Classen, H.G.; Schimatshek, H.F.; Jensen, U.; Drescher, B.; Guenther, T.: Increase of streptozocin toxicity by magnesium deficiency in the diabetic rat model. *Arzneimittel-Forschung/Drug Research* **44** (1994) 1237-1241.
33. Bartley, J.C. (1961) Cited in Crenshaw TD : Chapter 11 Sodium, potassium, magnesium, and chloride in swine nutrition. In : Miller ER, Ullrey DE, Lewis AJ(eds) : Swine nutrition. Boston, London, Singapore, Sydney, Toronto, Wellington 1991 pp 183-191.
34. Fischer, F.; Helbig, J.; Rieder, H.: Forschungs- und Entwicklungsabteilung der Firma Verla-Pharm, Tutzing and Jaeger, E.: Max-Planck-Institut fuer Biochemie, Abteilung Peptidchemie Muechen. Unveroeffentlicht, 1977.
35. Spaetling, L.; Spaetling, G.: Magnesium supplementation in pregnancy: A double blind study. *British Journal of obstetrics and Gynaecology* **95** (1988) 120-125.
36. Gordon, I.: Piglet mortality, chapter 5: Control of farrowing In : Controlled reproduction in pigs. Vol. 3 Cab international , London, New york. 1997 pp 125.
37. Classen, H.G.; Spaeth, M.: Resorption and storage of magnesium after te administration of $MgCl_2$, $MgSO_4$ and of Mg- Aspartate as base or as its halogen hydrogen acid compounds. *Naunyn, Schmiedeberg's Arch. Pharmacol. Suppl. to vol* **277** (1973) R 10.
- 38 Smith, L.G.Jr.; Burns, P.A.RN.; Schanler, R.J.: Calcium homeostasis in pregnant women receiving long-term magnesium sulfate therapy for preterm labor. *Am. J. Obstet. Gynecol.* **167** (1992) 45-51.

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