# Correction of defective magnesium absorption after parathyroidectomy by portacaval shunt*)

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**Zusammenfassung**

Durch einen portocavalen Shunt (PCS) kann die nach Parathyroidectomie (PTX) hervorgerufene verminderte Ca-Absorption mit Hypocalcämie korrigiert werden (Al-Jurf, 1979). Da Ca und Mg möglicherweise gleiche Absorptionswege besitzen, wurde angenommen, daß PCS ähnliche Effekte auf die Mg-Absorption haben würde. Es wurde die Mg-Absorption in Segmenten aus dem Jejunum und Ileum bei Ratten in vivo nach PTX bzw. PCS mit der Wiederdurchströmungstechnik untersucht; außerdem wurde bei ähnlich behandelten Tieren im Serum Mg, Ca und $PO_4$ gemessen.

| | Kontrolle | PTX | PTX + PCS |
|---|---|---|---|
| Serum-Mg (mg %) | 0,85 ± 0,01 | 0,68 ± 0,02 | 0,90 ± 0,03 |
| Serum-Ca | 2,33 ± 0,08 | 1,45 ± 0,10 | 2,30 ± 0,03 |
| Serum-$PO_4$ | 9,5 ± 1,03 | 10,3 ± 1,83 | 7,13 ± 0,95 |
| Mg-Absorption: Jenunum (µmol/g Trokkengewicht) | 4,3 ± 0,9 | −12,2 ± 4,4 | 5,5 ± 1,7 |
| Mg-Absorption: Ileum | 7,1 ± 1,5 | −12,1 ± 4,7 | 7,3 ± 3,7 |

Die Mg-Absorption war vermindert nach PTX und normal nach PTX + PCS. Serum-Mg und Serum-Ca waren erniedrigt nach PTX und normal nach PTX + PCS. Ratten entwickelten nach PTX + PCS eine Hypophosphatämie (H). Es wird angenommen, daß die H nach PCS das Serum-Mg und Serum-Ca sowie die Mg-Absorption korrigierten, möglicherweise über eine entsprechende Stimulation der 1,25 Dihydroxycholecalciferol-Produktion.

**Summary**

Portacaval shunt (PCS) corrected defective Ca-absorption and hypocalcemia resulting from parathyroidectomy (PTX) (Al-Jurf, 1979). Because Ca and Mg absorption may share common pathways, we suspected that PCS may have similar effect on Mg absorption. We studied Mg absorption in jejunal and ileal segments in the rat after PTX and PCS by in vivo recirculation technique. We also studied changes in serum magnesium, calcium and phosphate in similarly treated rats. Results are shown in table below.

| | Control | PTX | PTX + PCS |
|---|---|---|---|
| Serum-magnesium (Mg) mg/100 ml | 0.85 ± 0.01 | 0.68 ± 0.02 | 0.90 ± 0.03 |
| Serum calcium (Ca) | 2.33 ± 0.08 | 1.45 ± 0.10 | 2.30 ± 0.03 |
| Serum phosphate ($PO_4$) | 9.5 ± 1.03 | 10.3 ± 1.83 | 7.13 ± 0.95 |
| Mg absorption, jejunum µmole/gm dry wt | 4.3 ± 0.9 | −12.2 ± 4.4 | 5.5 ± 1.7 |
| Mg absorption, ileum | 7.1 ± 1.5 | −12.1 ± 4.7 | 7.3 ± 3.7 |

Mg absorption was significantly reduced after PTX and normal in PTX + PCS. Serum Mg and Ca were reduced after PTX and normal after PTX + PCS. PTX + PCS rats developed significant hypophosphatemia. We believe that the hypophosphatemia produced by PCS may have corrected serum Mg and Ca and intestinal Mg absorption through its alleged stimulating effect on 1,25-dihydroxy-cholecalciferol production.

**Résumé**

Le shunt porto-cave (SPC) a corrigé l'absorption déficitaire du Ca et l'hypocalcémie résultant de la parathyroïdectomie (Al-Jurf, Surg. Forum, 1979). Du fait que le Ca et le Mg peuvent partager des voies communes, nous avons supposé que le SPC peut présenter un effet similaire sur l'absorption du magnésium. Nous avons étudié l'absorption du Mg dans les segments de l'iléon et du jéjunum chez le rat après la parathyroïdectomie (PTX) et le SPC par la technique de recirculation in vivo. Nous avons étudié aussi les modifications dans le Mg, le Ca, et les $PO_4$ chez des rats de façon semblable. Les résultats sont présentés dans le tableau cidessous.

| | Contrôle | PTX | PTX + SPC |
|---|---|---|---|
| Mg sérique (en mg/100 ml) | 0,85 ± 0,01 | 0,68 ± 0,02 | 0,90 ± 0,03 |
| Ca sérique | 2,33 ± 0,08 | 1,45 ± 0,10 | 2,30 ± 0,03 |
| phosphate sérique ($PO_4$) | 9,5 ± 1,03 | 10,3 ± 1,83 | 7,13 ± 0,95 |
| absorption du Mg, jejunum | 4,3 ± 0,9 | −12,2 ± 4,4 | 5,5 ± 1,7 |
| absorption du Mg, iléon | 7,1 ± 1,5 | −12,1 ± 4,7 | 7,3 ± 3,7 |

L'absorption du Mg a été significativement réduite après la parathyroïdectomie et elle a été normal dans le groupe PTX +

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SPC. Le Mg et le Ca sérique ont été abaissés la PTX et ont été normaux après PTX + SPC. Les rats PTX + SPC ont présenté une hypophosphatémie. Nous croyons que l'hypophosphatémie produite per le SPC peut avoir corrigé le Mg et le Ca sérique et l'absorption intestinale du Mg par l'intermédiaire de son effet stimulant allégé sur la production de dihydroxy-1,25 cholécalciférol.

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## Introduction

Portacaval shunt was recently shown to correct or prevent the development of hypocalcemia after parathyroidectomy [1], and to normalize intestinal calcium absorption in the parathyroidectomized rat [2]. The exact mechanism(s) responsible for these effects of portacaval shunt remain unclear. Parathyroidectomy is also followed by hypomagnesemia [3] and decreased magnesium absorption from the intestine [4]. Because the metabolisms of calcium and magnesium may share common pathways [5, 6, 7], the mechanisms that control calcium homeostasis after parathyroidectomy and portacaval shunt could be expected to be also operative in magnesium homeostasis. The present experiment was undertaken to study the possibility that portacaval shunt construction could prevent the development of hypomagnesemia and correct the defective intestinal magnesium absorption in parathyroidectomized rats.

## Material and methods

Male Sprague Dawley rats (Biolabs, St. Paul, MN) averaging 200 g in body weight were divided into three groups of 6—7 rats each. In one group (PTX), the parathyroid glands were excised with the superior pole of each thyroid lobe; the rest of the thyroid gland was left undisturbed. In the second group (PTX + PCS), after parathyroidectomy an end-to-side portacaval shunt was constructed. The third group underwent a sham laparotomy and served as controls (C). The rats were raised under usual laboratory conditions and fed laboratory rat chow (Teklad Company, Winfield, Iowa) which contained 1.2 g of calcium, 0.2 g of magnesium, 0.9 g of phosphate and 1 000 UI of vitamin D per 100 g dry weight. The chow and tap water were allowed ad libitum for three weeks before the final studies were performed.

Net magnesium absorption studies were done in the rats after anesthesia was induced by intraperitoneal injection of a mixture of ethylurea (K & K Laboratiories, Plainview, New York) and sodium phenobarbital (6:1), using an in vivo perfusion technique in 30—40 cm long segments of jejunum and ileum. The net magnesium transport per unit length or weight in these segments was judged and used to represent absorption. The details of the method were described in previous publications [8, 9]. The jejunal segments began at a point 1 cm below the ligament of *Treitz*, and the ileal segments extended to within 1—2 cm of the ileocecal valve. Each segment was flushed clean with saline and air prior to the perfusion studies. The lumen of each segment was perfused with a solution containing 145 mmoles of sodium chloride, 50 mg of phenol red (as a non-absorbable marker for volume change) and 2.5 mmoles of magnesium chloride per liter. The osmolality of the solution was adjusted by the addition of mannitol to approximately 300 mOsm/kg. The perfusion solution was recirculated through each segment for 105 minutes at a rate of 0.6 ml/min from reservoirs containing 10 ml of perfusion fluid. The first 45 minutes of perfusion were allowed in order to attain steady state conditions. At the end of this 45 minute period, an 0.5 ml aliquot of the reservoir was obtained to determine the concentrations of magnesium and phenol red (initial values). A similar aliquot was obtained at the end of the experiment to determine the final concentrations of magnesium and phenol red (final values). At the end of the perfusion period blood was obtained from the aorta. The perfused segments were stripped from the mesentery and after gently expressing the remaining fluid their length and wet weight were measured. The tissues were then dried in a vacuum oven at 90° for 24 hours and reweighed.

Serum magnesium and calcium as well as magnesium concentration in aliquots of the perfusion solutions were determined using an atomic absorption spectrometer (Model 303, Perkin Elmer, Norwalk Connecticut). Serum phosphate was measured by a modification of the method of Fiske [11]. Phenol red was determined as described by *Schedl* and *Clifton* [10].

The net transport of water was determined from the change in concentration of phenol red during perfusion. The transport of magnesium was calculated using the following equation:

$$\text{Net magnesium transport } (\mu\text{moles/hr}) = V_i([Mg]_i - [Mg]_f \cdot \frac{PR_i}{PR_f})$$

where V represents the volume of the perfusion solution in ml in the reservoir. Subscripts i (initial) and f (final) denote the

values of the solutions sampled at 45 and 105 minutes respectively after the start of the perfusion period. [Mg] represents the concentration of magnesium in the perfusion solution in μ moles/ml. PR is the phenol red concentrations in μg/ml in the perfusion fluid.

Positive values were considered to indicate net movement of magnesium out of the lumen into the body (net absorption), and negative values to indicate net movement of magnesium into the intestinal lumen (net secretion).

The normalized unpaired Student's t test was used for statistical comparison of differences between corresponding mean values obtained for the different groups of rats. A P value of less than 0.05 was considered to indicate a statistically significant difference between two mean values.

## Results

The intestinal segments' wet weight and water content and weight per unit length ratio were essentially the same in all three groups. The concentration of magnesium, calcium and the phosphate in the serum of the three groups of rats are depicted in Table 1. In the PTX rats, concentrations of both magnesium and calcium were significantly lower than in C rats ($p < 0.05$). In the PTX + PCS rats, serum magnesium and calcium levels were similar to the normal controls. Serum phosphate was lower in the group with PTX + PCS, but the values did not reach statistical significance.

Tab. 1: Mean ± SE serum magnesium, calcium and phosphate in the three groups at the end of the intestinal perfusion (mmole/L).

| | C | PTX | PTX + PCS |
|---|---|---|---|
| Magnesium | 0.85 ± 0.01 | 0.68 ± 0.02* | 0.90 ± 0.03 |
| Calcium | 2.33 ± 0.08 | 1.45 ± 0.10* | 2.30 ± 0.03 |
| Phosphate | 9.5 ± 1.03 | 10.3 ± 1.87 | 7.13 ± 0.95 |

* Significantly different from the corresponding control values ($p < 0.05$—0.005).

Net transport of magnesium and water in the perfused segments are shown in Table 2. In the PTX rats negative net magnesium transport was found in both the jejunal and ileal segments. In the PTX + PCS and C rats, positive net magnesium transport was noted in both segments. The rates of magnesium transport were not significantly different in the jejunal and ileal segments in any individual group.

There was a negative net water transport in both intestinal segments in the PTX rats. In the PTX + PCS and C rats there was positive net transport in both segments and mean values were significantly different from those of the PTX rats ($p < 0.05$).

Tab. 2: Mean ± SE magnesium and water transport in the jejunum and ileum of the three groups.

| Rats | PTX | PTX + PCS | C |
|---|---|---|---|
| Transport of magnesium per hour in: | | | |
| Jejunum | | | |
| μmoles/cm | −0.17 ± 0.06* | 0.08 ± 0.02 | 0.06 ± 0.01 |
| μmoles/g wet wt | −2.50 ± 0.8 * | 1.20 ± 0.3 | 0.90 ± 0.2 |
| μmoles/g dry wt | −12.2 ± 4.4 * | 5.50 ± 1.7 | 4.30 ± 0.9 |
| Ileum | | | |
| μmoles/cm | −0.17 ± 0.06* | 0.09 ± 0.03 | 0.09 ± 0.02 |
| μmoles/g wet wt | −2.50 ± 0.8 * | 1.20 ± 0.1 | 1.40 ± 0.3 |
| μmoles/g dry wt | −12.1 ± 4.7 * | 7.30 ± 3.7 | 7.10 ± 1.5 |
| Transport of water per hour in: | | | |
| Jejunum | | | |
| ml/g wet wt | −0.30 ± 0.28* | 0.54 ± 0.10 | 0.38 ± 0.12 |
| Ileum | | | |
| ml/g wet wt | −0.52 ± 0.35* | 0.35 ± 0.10 | 0.21 ± 0.09 |

* Significantly different from the corresponding control values ($p < 0.05$—0.005).

## Discussion

The results of this study confirm previous experimental work that showed hypomagnesemia and decreased magnesium absorption after parathyroidectomy. They also demonstrate that these effects (hypomagnesemia and a diminished rate of magnesium absorption) of parathyroidectomy can be prevented by portacaval shunt. A similar effect of parathyroidectomy and portacaval shunt on serum calcium [1, 2, 12] and intestinal calcium absorption [2] was observed in previous experiments. Because portacaval shunt alone did not produce significant changes from the control in our previous experiments [2, 13] or in the experiments of others [1, 12], a group with portacaval shunt alone was not used in this study.

Parathyroid hormone appears to influence magnesium absorption from the intestine. An increase in magnesium absorption has been observed in hyperparathyroidism [4] and after the administration of parathyroid hormone [14], and a decrease has been observed after parathyroidectomy [4]. The effect of parathyroid hormone on magnesium absorption may be similar to its effect

on calcium absorption and, although a direct effect of parathyroid hormone on its absorption has been suggested [15], it is commonly believed that the hormone influences the absorption through the activation of 1,25-$(OH)_2D_3$ formation in the kidney [16, 17, 18, 19].

The major mode of magnesium transport across the intestinal epithelium was thought to be through a diffusive process because it correlated very closely with net water movement [20]. Other investigations [21, 22] suggested that both carrier mediated and diffusive processes are involved. The data in this experiment suggest that magnesium transport is mostly diffusive because its net movement correlated with the net movement of water.

The possibility that the regulation of calcium and magnesium is dependent on the same factors, and that the two cations share a common absorptive system in the intestine has been suggested in many studies [5, 6, 7]. Several other investigations have also suggested common mechanisms or pathways in the metabolism of the two divalent cations, based on studies of their reabsorption in the renal tubule [23, 24] and their concentrations in bone after parathyroidectomy [25, 26].

In our previous studies, significant hypophosphatemia was observed with portacaval shunt [13]. Similarly, significant hypophosphatemia has also been observed in other studies in animals treated with portacaval shunt and parathyroidectomy [12]. This hypophosphatemia may be the factor producing the increase in the intestinal absorption of magnesium similar to the effect of phosphate depletion recorded in other experiments [27]. Contrary to our findings, however, overall hypomagnesemia was observed in that other study [27]. On the other hand, the two processes observed in our experiment (hypophosphatemia and normomagnesemia) may be independent of each other and dependent on unknown other factors.

*Lee* et al [12] postulated that the portal blood may carry a factor active in the metabolism of calcium. Normally, such a factor will be conjugated or deactivated in the liver. With portacaval shunt, the factor will escape conjugation and reach the systemic circulation in effective concentrations to produce normocalcemia. Such a factor (if it exists) may also be expected to possess properties that influence magnesium metabolism.

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