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Aluminium effect on serum calcium concentration

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RESUMEN

Efecto de la hiperaluminemia sobre niveles de calcio sérico.
En estudios en ratas se comprueba que la infusión intravenosa de aluminio aumenta el calcio sérico total, al mismo tiempo que disminuye de un modo proporcional la concentración de calcio iónico. La paratiroidectomía no modifica dichos resultados. El aluminio induciría aumentos del calcio ligado a proteínas, a la vez que disminuiría proporcionalmente el calcio libre.

SUMMARY

Aluminium effect on serum calcium concentration.
In rats, intravenous infusion of aluminium increased total plasma calcium; however, the level of ionised serum calcium decreased. Parathyroidectomy did not affect the aluminium-induced changes in serum calcium. Aluminium overload might increase the fraction of bound calcium which in turn, would lower the fraction of ionised calcium.

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Aluminium effect on serum calcium concentration

Hypercalcemia is a frequent finding in dialysis osteomalacia [1]. Since both a relative deficiency of parathyroid hormone (PTH) and decreased PTH secretory capacity are often present in dialysis osteomalacia [1, 2], PTH is unlikely to be the cause of the observed hypercalcemia. The most frequent explanation for the hypercalcemia is that movement of calcium into bone is impeded and with end stage renal disease, excretion of calcium by the kidney is impaired. Thus, any stimulus producing a positive calcium balance such as treatment with vitamin D or its metabolites, or increased calcium transfer via the dialysate may produce hypercalcemia [3, 4].

Aluminium is highly protein bound [5] and has a strong affinity for inorganic compounds, such as hydroxyl groups, fluoride, and phosphate, and organic compounds including proteins [6, 7]. Since albumin and phosphates bind calcium in blood [8], it is possible that aluminium may alter calcium binding in the plasma, leading to a disequilibrium between bound and ionized calcium.

The purpose of the present study is to evaluate the effect of an intravenous aluminium infusion on the plasma level of total and ionized calcium.

Male Wistar rats weighing 450 to 650 grams were divided into 5 groups. In groups I and II both receiving a calcium free peritoneal dialysis, the effect of intravenous aluminium administration on plasma calcium concentration (group II) was compared to a control (group I). In groups III-V, further studies were performed to delineate the mechanism by which intravenous aluminium administration may affect the plasma calcium level.

The 5 groups included in this study are: Group I, controls, received a 2 hour peritoneal dialysis with a calcium free dialysate. Group II, received peritoneal dialysis as in group I simultaneous with an intravenous infusion containing 0.4 mg of aluminium per 100 grams of body weight. Since hypercalcemia was observed in group II, 2 additional groups (III and IV), in which both total and ionized calcium measurements were obtained, were studied without peritoneal dialysis to delineate the cause of hypercalcemia. Group II, received a 2 hour intravenous infusion containing o.2 mg of aluminium per 100 grams of body weight. In order to learn if an intravenous aluminium infusion affected the measurement of calcium in the absence of PTH, parathyroidectomy was performed in group V, which subsequently received a 2 hour intravenous infusion containing 0.4 mg of aluminium per 100 grams of body weight.

In group I, the plasma calcium decreased from baseline after 30 ($P < 0.005$) and 120 ($P < 0.005$) minutes of a calcium free peritoneal dialysis. In group II, the plasma calcium concentration was elevated during the aluminium infusion despite a calcium free peritoneal dialysis. The elevated plasma calcium concentration in group II at the initiation of peritoneal dialysis may be explained by the fact that the aluminium infusion was begun 20 minutes before baseline plasma calcium levels were obtained. Despite an elevated total calcium level at 120 minutes, the ionized calcium concentration was decreased.

The efficacy of calcium removal with peritoneal dialysis is similar and progressive in both groups I and II. The amount of calcium removed at the end of 120 minutes of peritoneal dialysis was comparable in the two groups.

In groups III and IV, in addition to measurement of total calcium, ionized calcium is measured simultaneously. In group III, rats receiving 0.4 mg of intravenous aluminium per 100 grams of body weight, the total plasma calcium increased ($P < 0.02$) and the ionized calcium decreased ($P < 0.001$) during the 2 hour infusion. In group IV, rats receiving 0.2 mg of intravenous aluminium per 100 grams of body weight, the total plasma calcium increased ($P < 0.02$) and the ionized calcium increased ($P < 0.02$) during the 2 hour aluminium infusion. In group II, receiving a similar dose of intravenous aluminium as group III but also receiving calcium free peritoneal dialysis, the total calcium is less but not significantly different at the end of 2 hours. In both groups II and III, the ionized calcium is less than group IV ($P < 0.001$) at 2 hours.

In groups III and IV, the baseline ionized calcium is slightly greater than 50 % of the total calcium. The percentage falls progressively and by 120 minutes the percent ionized calcium is less in group III than in group IV ($P < 0.001$). Similarly in group II, the percent ionized calcium is less than group IV ($P < 0.001$).

In group V, the plasma calcium decreased 3 days after parathyroidectomy. After 120 minutes of intravenous aluminium administred at a dose of 0.4 mg per 100 grams of body weight, the plasma calcium increased ($P < 0.05$).

Discussion

Despite a 2 hours calcium free peritoneal dialysis, an intravenous infusion of aluminium results in hypercalcemia. This finding occurs despite the removal of calcium during peritoneal dialysis. Even though total plasma calcium concentration is increased, the level of ionized calcium is decreased. Subsequent studies in groups III and IV clearly demonstrate that the administration of intravenous aluminium produces hypercalcemia and yet the ionized calcium concentration decreases. The absence of PTH has no effect on the capacity of intravenous

aluminium administration to elevate plasma calcium levels.

In this study, it is shown that a peritoneal dialysis with a calcium free dialysate lowers the plasma calcium level in the rat. However, when intravenous aluminium is administered simultaneously, hypercalcemia is observed. It, also clearly demonstrated that an effective exchange of calcium occurs in group II and that total calcium removal is comparable to group I. Thus, a failure to remove calcium via peritoneal dialysis does not contribute to the differences observed between group I and group II.

The finding that calcium removal with peritoneal dialysis is comparable in groups I and II is also important because with hypercalcemia a proportional increase of peritoneal ultrafilterable calcium is expected. This does not occur in group II presumably because the ionized calcium concentration does not increase, but actually decreases. Thus, an increased calcium content in the dialysate is not observed. In addition, the finding that the calcium concentration of the dialysate does not increase also indicates that the aluminium induced calcium binding in plasma produces a complex of sufficient size that it is not readily filtered during peritoneal dialysis.

The intravenous administration of aluminium produces hypercalcemia in the absence of peritoneal dialysis. The extent of hipercalcemia appears to be dose dependent, being greater with the higher dose. In addition, despite the presence of hypercalcemia, ionized calcium levels are decreased. At neither the higher (group III) nor the lower (group IV) dose of aluminium is a normal level of ionized calcium present at the end of a 120 minutes infusion. The higher dose of intravenous aluminium produces both the more marked hypercalcemia and the lower level of ionized calcium.

The finding that parathyroidectomy does not affect the aluminium induced changes in plasma calcium, indicates that PTH is not necessary for the hypercalcemic effect of aluminium. The presence of high concentration of aluminium in the blood clearly affects calcium homeostasis. From this study, it appears that aluminium increases the fraction of bound calcium in the plasma which, in turn, lowers the fraction of ionized calcium. This may result in movement of ionized calcium from bone and interstitial space to the blood. Thus, the total plasma calcium level increases because of movement of calcium into the plasma. As ionized calcium moved into the vascular space, more is bound increasing the total calcium content and maintaining a decreased fraction of ionized calcium. This, in turn, produces additional recruitment of bone and interstitial calcium until a new equilibrium is established.

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