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The Effect of Sympathectomy on Bone:

—Evaluation with Quantitative Bone Scintigraphy—

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=초　　록=

흰쥐에서 교감신경절제술이 골에 미치는 영향 :

—정량적 골스캔을 이용한 평가—

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근래 골조직에 있어서 자율신경의 기능에 대하여 많은 연구가 이루어지고 있으며, 골내의 자율신경의 해부학적 분포는 많이 알려져 있다. 그러나 임상적으로 반사적 교감신경 이상이나 레이노드 현상 등과 같은 교감신경의 기능이상증에서나, 버거씨병 등의 치료 목적으로 시행되고 있는 교감신경 절제술 후, 자율신경기능의 변화가 사지골의 혈류나 골대사에 미치는 영향에 대하여는 아직도 논란의 여지가 있다. 저자들은 교감신경절제술 후 시간 경과에 따른 골에 미치는 영향을 알아보기 위하여 흰쥐에서 골대사와 혈류상태를 비교적 충실히 반영하는 정량적 골스캔을 시행하였다.

체중 300～400 g의 수컷 흰쥐 10마리에서 복강을 통한 편측 요추부 교감신경절제술을 시행하였고, 수술 전과 후 1일, 3일, 1주, 2주, 3주, 4주에 양측 하지에서 각각 골스캔을 시행하고 교감신경 절제측 하지와 정상 하지에 대칭적으로 관심구역을 정하여 양측의 골스캔상 섭취계수를 비교하였다. 측정부위는 각 하지의 대퇴골간, 경골간 및 중족골로 하였다.

교감신경절제술을 시행한 하지에서는 골스캔 소견상 수술 후 1일 또는 3일부터 동위원소집적이 유의하게 증가되었으며 원위부로 갈수록 더욱 증가되었다. 그러나 3주 이후에는 정상측 수준으로 환원되었다.

교감신경절제술 후 골스캔상 동위원소집적이 증가되는 것은 골자체의 혈류가 증가되기 때문이며 이차적으로 골의 흡수를 유발하여 골밀도가 감소하는 것으로 생각되는데 이러한 변화는 시술 후 1일째부터 관찰되어 사지골이 교감신경 절제에 매우 민감하게 반응하는 것을 알 수 있었다.

Key Words: Sympathectomy, Bone scan

INTRODUCTION

Recently the role of the autonomic nervous system and its effect to the bone has become topic of interest. Several studies have successfully proved the presence of autonomic nerve supply to the bone[1]. However, the functional significance of these nerves in pathophysiology of the disease states such as reflex sympathetic dystrophy, Raynaud phenomenon and Buerger's disease, and of the therapeutic effect of sympathectomy for these disease remaines uncertain. The results of sympathectomy on blood flow of the bone have been controversial[2,3].

The aims of our study were to assess the effect of sympathectomy on bone over time in rats by using quantitative bone scans.

MATERIALS AND METHODS

Ten male rats that weighed three to four hundred grams were studied. Transperitoneal lumbar sympathectomy was performed from the first to the sixth lumbar level under anesthesia with 1-2 milligrams per Kg of intravenous ketamine. The left sympathetic nerves were surgically removed; all excised sympathetic chains were submitted for histological examination to verify that adequate sympathectomy had been performed. 99m Tc-methylene diphosphonate (MDP) bone scan was performed before surgery, at 1 day, 3 days, and one, two, three, and four weeks after a transperitoneal sympathectomy. Control group was non-sympathectomized contralateral legs, and comparison study was done bilaterally. Quantitative bone scintigraphy was obtained 3 hours after intravenous administration of 3mCi of 99m Tc-MDP. The gamma camera used was Siemens Scintiview II (Model ELC 75005) equipped with high resolution collimater. A total of 250 K counts was accumulated over a period of 10 min per view. In order to quantitate the bone scan, regions of interest on each limb were selected. The count of radionuclide uptake was obtained in midshaft of the femur, midshaft of the tibia, and metatarsal bones. Statistical analysis was performed with the assistance of repeated measures ANOVA for three within factors.

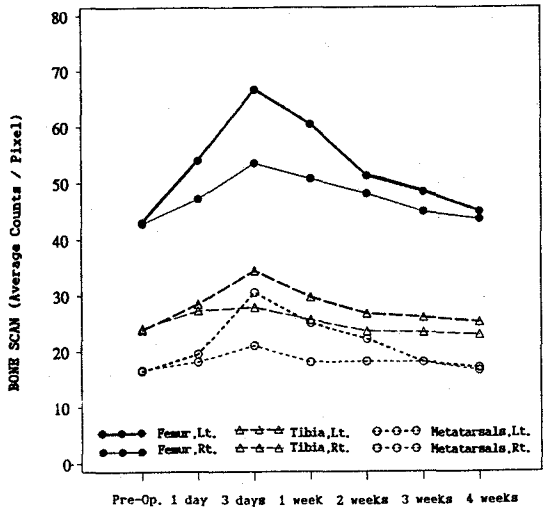

Fig. 1. The quantitated bone scan in the sympathectomized and the non-sympathectomized side.

RESULTS

Fig. 1 show the data for the changes of bone scan on the sympathectomized and the non-sympathectomized side over time.

Analysis of bone scans in the sympathectomized limb showed significant increase in radioisotope uptake ($P<0.05$): in the femur, increased uptake was seen ranging from 23.3-54.9% from one day to 1 week: the tibia showed also increased uptake by 24.9-46.7% from 3 days to one week. The largest increases 33.4-91.5% were seen in the matatarsals from 3 days to two weeks after surgery. The values, of radionuclide uptake subsequently returned to control levels by three weeks and the distal part of the lower extremity returned slower than the proximal part.

DISCUSSION

It has been known that the bone has autonomic nerve supply[1]. Most investigators have agreed that the sympathetic nervous system exerts control over blood flow in bone and that this control is to a great extent independent of changes in the systemic circulation[4]. However, the results of sympathectomy on blood flow in bone have been controversial. Some investigators have found no change in bone blood flow after sympathectomy[2], while others have reported a significant increases[3,5]. Davis et al. showed that surgical sympathectomy exerted a significant but transient effect on blood flow in the bone, and the major site of sympathetic tone lies in the distal extremity[3]. The grater increase of blood flow in the distal part of the extremity is physiological evidence to suport the data that the major site of sympathetic tone lies distally in the lower extremity of the dog[6]. In fact, that finding is consistent with the clinical observation that various disorders of the autonomic nervous system, such as reflex sympathetic dystrophy and the Raynaud phenomenon, appear to occur more frequently in a distal distribution.

Increased uptake of a bone seeking radiotracer was described in the bones of paralyzed or sympathectomized limb[7~9]. Indeed, in these conditions it appears that hyperemia seems to be a reasonable mechanism to account for the changes observed. It is not clear, however, whether the effects of sympathectomy to the bone can be accounted for by the change in blood flow or are mediated more directly through the specific neurotrophic agents. Either hyperemia or a direct neural mechanism must be responsible for the bone scan changes. Sudeck's post-traumatic reflex atrophy of the bone is a disease that shows this condition, which is characterized by not only by osteoporosis but also vasomotor changes. The increased uptake is not confined to the periarticular areas as has been previously reported but occurs throughout the affected region. However, the increased uptake is significantly greater in the periarticular area[10].

Recently some researchers showed that sympathetic denervation had effects on bone cell activity. Sandhu et al. (1990) reported increased bone resorption at 1 day and 5 day after sympathectomy[11]; the active resorption surface, number of osteoclast, and osteoclastic volume were significantly increased all together in rat incisor socket. Thus, it certainly appears that the effects of sympathectomy are quite dramatic and complex, and that they occur within hours of interruption of autonomic nerve supply. Our results demonstrated that bone responds to sympathectomy at 1 day. Similar findings were also observed by Davis et al. (1987) that bone blood flow increased 1 day after sympathectomy but flow rates reverted to baseline levels within 3 weeks[3]. There may well be other cell-derived, none vascular mechanisms by which sympathetic innervation affects bone. Kato et al. (1990) have shown the presence of nerve fibers containing VIP as well as CGRP (calcitonin gene related peptide) in the mouse periodontal ligament[12]. Both substance P-and CGRP-immunoreactive nerve fibers are widely distributed in bone[13]. CGRP in bone appears to act like a calcitonin agonist and raises the level of cyclic AMP in osteoblasts[14]. Some vasoactive peptides of sympathetic orgin may modulate osteoclastic activity[15]. Sympathectomy, therefore, may result in the loss of some factors which may function in the neural modulation of bone cell activity. Such a process could account for the cluster of alterations in all aspects of bone metabolism that follows sympathectic denervation.

In our study, sympathectomy significantly increased scintigraphic uptake in bone. Although the mechanisms that influence the bone metabolism may be very complex and irrespective, our results suggest that sympathectomy affects the bone metabolism that eventually leads to demineralization.

CONCLUSION

Our study demonstrated that sympathectomy affects bone for a short period of time (2-3 weeks) after surgery presumably due to increased bone metabolism in the affected regions, thereby significantly increasing the radioisotope uptake. The recognition of change in bone scan after sympathectomy is potentially important in patient management. This study can also be used as postsurgical follow-up tools for assessing the result of sympathectomy.

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