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Urinary Excretion of Glycosaminoglycans in Quadriplegia (39963)

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Introduction. Calciuria, osteoporosis, and cutaneous dystrophic changes are of universal occurrence in quadriplegic patients (1, 2). The measurement of urinary collagen degradation products in quadriplegics has demonstrated that one of the first metabolic disturbances detectable after injury is an excessive degradation of skin and bone collagen (3, 4). Since osseous tissue and skin, in addition to collagen, contain glycosaminoglycans (GAG), the present study was performed to investigate whether the urinary excretion of GAG also is altered in quadriplegics. The results show that these patients excrete higher than normal amounts of polymeric GAG and considerably lower amounts of oligosaccharides several weeks after injury, while immediately after injury only the excretion of oligosaccharides is affected.

These findings suggest that the metabolic changes occurring in quadriplegia affect several macromolecular components of connective tissue.

Materials and methods. Cation-exchange resin AG50W-X2 (200-400 mesh, H^+) and anion-exchange resin AGlX-2 (200-400 mesh, Cl^-) were btained from BioRad Laboratories, Richmond, California. Cetylpyridiniumchloride (CPC) was from ICN Pharmaceuticals, Cleveland, Ohio. The five quadriplegic patients (four males and one female) (A, B, C, D, E, respectively; 16, 17, 19, 42, 16 years of age) had sustained spinal cord transections at levels between C-4 and C-6. None had previous significant medical problems. Because of their urinary bladder paralysis, the patients were catheterized. Urine was collected without preservatives as soon as possible after the injury: from the 3rd to the 15th week for A, from the 8th to the 19th week for B, from the 5th to the 17th week for C, from 4 hr to 4 days for E, and on the 7th week for D. As controls, urine specimens were collected from six males and three females (age 16-60). The urine specimens were refrigerated (5°) during collection and stored frozen (−20°) until assayed. All analyses were performed on 24-hr pooled specimens of urine.

Measurement of polymeric GAG and oligosaccharides was performed on 25-ml aliquots of each urine sample (12.5 ml diluted to 25 ml with water when the specific gravity was above 1020) as described previously (5). The results are shown in Fig. 1 and Table I.

Results and discussion. The data summarized in Table I indicate that nine normal individuals excrete on the average 5.74 ± 1.8 mg of polymeric GAG and 52.91 ± 16 mg of oligosaccharides (as hexuronate), with a polymeric GAG/GAG oligosaccharides ratio of 0.113 ± 0.03 (Table I). These values are similar to those reported previously (5).

The urinary excretion of GAG in quadriplegic patients showed considerable variations from day to day and at different times from the occurrence of the lesion. Nevertheless, in Patients A, B, and C, the excretion of polymeric GAG was on the average almost three times higher than that in normal controls, while the excretion of oligosaccharides was about one-half the normal (Table I, Fig. 1). Patient D, from whom only one urine specimen was available, had the same pattern of excretion, while Patient E (studied immediately after the lesion) excreted normal amounts of polymeric GAG and decreased amounts of oligosaccharides.

As a consequence of this pattern of excretion, the ratio polymeric GAG/GAG oligosaccharides was much higher in quadriple-

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gics than in normal controls. This difference became apparent almost immediately after injury and was still apparent 15–19 weeks later.

The ratio of urinary polymeric GAG/GAG oligosaccharides reflects the processes of physiological degradation of GAG (5). In fact, the ratio is very high in patients with various mucopolysaccharidoses (5), because of the well-documented defects in lysosomal enzymes essential for GAG degradation. Vice versa, it is very low in relapsing polychondritis, a condition in which there is excessive mobilization of tissue GAG (N. Di Ferrante, unpublished observations).

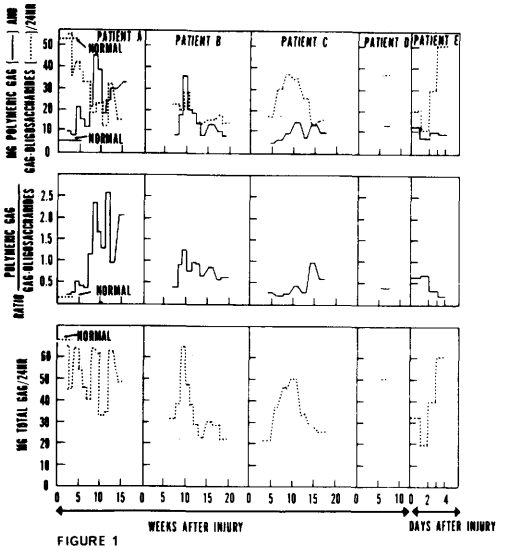

FIGURE 1

FIG. 1. Urinary excretion of glycosaminoglycans (GAG) in normal and quadriplegic individuals. GAG are expressed as milligrams of total hexuronic acid per 24 hr. The indicated horizontal lines represent the normal values. Top: Polymeric GAG and GAG oligosaccharides per 24 hr. Middle: Ratio of polymeric GAG/GAG oligosaccharides. Bottom: Total GAG (polymeric + oligosaccharides) per 24 hr.

In the quadriplegics, the increased excretion of polymeric GAG and the decreased excretion of oligosaccharides observed several weeks after the injury suggest that the documented collagen degradation (3, 4) may cause an excessive mobilization of polymeric GAG from the tissue and their rapid excretion, before the normal processes of degradation, may take place. The essentially normal excretion of polymeric GAG in Patient E suggests that the degradation of collagen must reach a critical level before tissue GAG might be affected.

Summary. Urinary polymeric glycosaminoglycans (GAG) and glycosaminoglycans oligosaccharides were measured in nine normal individuals and in five quadriplegic patients. In the latter, the excretion of polymeric GAG was two- to fourfold higher and the ratio polymeric GAG/oligosaccharide GAG was three- to tenfold higher than the average of normal individuals.

This excessive excretion does not seem to be a consequence of immobilization alone since, in one patient, it was apparent within hours after injury. The previous demonstration that in quadriplegics there is an immediate and excessive degradation of osseous and cutaneous collagen following injury

TABLE I. SUMMARY OF URINARY EXCRETION OF GLYCOSAMINOGLYCANS IN QUADRIPLEGICS AND NONQUADRIPLEGICS.

		GAG (mg of hexuronate/24 hr)			
	Age	Polymeric	Oligosaccharides	Total	Polymeric/oligosaccharides
Nonquadriplegic		5.74 ± 1.8	52.91 ± 16	58.65 ± 16	0.113 ± 0.03
Quadriplegic[a]					
A	16WM	23.02	28.73	51.75	1.123
B	17CM	15.82	19.63	35.45	0.785
C	19WM	9.34	25.29	34.63	0.425
D	42CM	13.40	37.00	50.40	0.362
E	16WM	9.88	28.08	37.95	0.451
Means		14.29 ± 5.55	27.75 ± 6.3	42.04 ± 8.36	0.629 ± 0.321
t Value[b]		3.35	4.17	2.14	3.59
df		4	11	12	4
Significance		<0.05	<0.01	>0.05	>0.05

[a] Values for quadriplegics represent the average of values of a given patient at various times (Fig. 1).
[b] Approximation formula was used for *t* values calculations when groups had significantly different standard deviations.

supports the hypothesis that as the collagen begins to be degraded, polymeric GAG from tissues are also mobilized and excreted in excessive amounts.

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