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Calcitonin treatment for calcifying tendinitis of the shoulder

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Abstract In an open, uncontrolled trial, the clinical and radiological responses to calcitonin therapy in the treatment of acute calcifying tendinitis of the shoulder were investigated. A total of 35 patients (38 shoulders) were enrolled. Each patient was injected with 10 U synthetic calcitonin intramuscularly twice a week. The mean number of injections was 6.0 (range, 1–16). At the end of the treatment period, 33 shoulders (87%) were pain-free. In 28 shoulders (74%), the localized pain disappeared within 2 weeks of the start of treatment. In 25 shoulders (66%), the clinical results were rated as good, with complete pain relief and sufficient recovery in the activities of daily living (ADL) and active range of shoulder joint motion (ROM). On the contrary, in 4 shoulders (10%) pain persisted, requiring alternative treatment. In 28 shoulders (74%), the pre-existing calcific deposits were remarkably reduced or had disappeared. Radiologically, the shoulders with fluffy-type deposits had greater pain relief and ROM recovery than those with defined-type deposits. However, there was no correlation between the clinical results and localized region or size of deposits. In 19 cases (50%) where the calcified deposits had completely disappeared, the shoulder had become pain-free, and in all of them except two cases there was complete recovery of ROM. No patient developed clinical complications. These results suggest that calcitonin treatment may be useful for calcifying tendinitis of the shoulder, and that this therapy results in both clinical and radiological improvement in this condition.

Key words Calcifying tendinitis • Calcitonin • Rotator cuff • Shoulder

Introduction

Calcific tendinitis of the shoulder is frequently encountered in orthopedic practice. This disease is characterized by the presence of deposits of calcium hydroxyapatite crystals within the rotator cuff, and is one of the most common causes of non-traumatic pain in the shoulder. The natural history of calcifying tendinitis is a process of degeneration of the supraspinatus tendon followed by calcification and eventual rupture into the subacromial bursa [1]. There are various theories on the causation of these calcific deposits. Some Authors think that they are the result of reduced vascularization. However, the etiology remains unclear. Welfing et al. [2] investigated the incidence of radiographically detectable calcific deposits in the rotator cuff in both symptomatic and asymptomatic subjects. They found that when both shoulders were examined radiographically, there was an incidence of 7.5% in 200 asymptomatic shoulders and 6.5% in 925 symptomatic shoulders. In general, this disease is characterized by an acute onset of local pain and tenderness, leading to

restriction of both active and passive movements of the shoulder. Some patients with calcifying tendinitis experience chronic or recurrent pain and disability [3].

Calcitonin is an effective treatment for ectopic calcification in dialysis patients [4]. In dialysis patients with chronic uremia, calcitonin is an established treatment for osteodystrophy and ectopic calcification as a result of secondary hyperparathyroidism [5]. As far as we know, calcitonin therapy for calcifying tendinitis has not yet been reported except when used for ectopic calcification in hemodialysis patients. In the present study, we assessed the therapeutic value of calcitonin in non-hemodialysis patients with calcifying tendinitis of the shoulder.

Materials and methods

We retrospectively studied 35 patients (25 females and 10 males) with calcific tendinitis defined by localized pain, clinical signs of rotator cuff tendinitis and a calcific deposit on radiographs. Prior to this study, we obtained informed consent from all patients who were treated by calcitonin in accordance with the ethical standards of the 1964 Declaration of Helsinki. Among these patients, the right shoulder was affected in 24, the left in 8, and three of the patients had bilateral disease; therefore the total number of affected shoulders was 38. All patients had experienced sudden onset of intractable pain and tenderness in the shoulder region and had a limited range of motion (ROM) as a result of the pain. The mean age of the patients was 51.2 years (range, 31–72 years). Subjects were excluded from this study if they had known degenerative or arthritic problems of the humeroglenoidal or acromioclavicular joint, or rotator cuff tendon failures, as were those with a history of injury or fracture in the shoulder region. In addition, subjects were excluded if they had disorders of calcium metabolism, or if they were being treated with cimetidine or with other drugs that affect calcium metabolism. Patients who had previously been treated with needle aspiration and lavage, or with analgesic or cortisone interventions were also excluded.

Each patient was treated intermittently with synthetic calcitonin: 10 U calcitonin was intramuscularly injected twice a week, and the treatment was continued until the patient was satisfied with the pain relief and recovery of shoulder motion or until the total number of injections reached 16 (treated for 8 weeks).

In all patients, a subjective evaluation was performed with a questionnaire (Table 1), completed by the patients, that assessed the degree of pain perception (40 points) and the ability to perform normal tasks of daily living in both activity and position-related terms (20 points). Moreover, active shoulder ROM was objectively assessed before and at the end of treatment, using tests (Table 1) of active range of shoulder motion (40 points). The grades of shoulder function were defined: on the basis of both the total score (maximun, 100 points) and the pain score as follows: *good*, the total score is more than 80 points and the pain score is ≥40 points; *fair*, the total score is 60–79 points and the pain score ≥30 points; *poor*, the total score is <60 points or the pain score is <30 points.

Radiographic examination was performed in all patients before and after the treatment. Anteroposterior views in internal and external rotation were routinely taken. In each case, we assessed the localization, size and shape of the calcific deposit. The area (maximum length and width in millimeters) of each calcific deposit was estimated. When more than 2 calcific deposits were present, the size of this cluster (mm^2) was measured and the cluster was then counted as a single calcification.

Table 1 Outline of the scoring system for the questionnaire completed by the patients. The maximum score is 100 points and comprises 40 points for pain score, 20 points for 5 activities of daily living, 20 points for abduction and 20 points for flexion

Factor (maximum score)	Score	Definition
Pain (40 points)	40	No pain
	30	Slight pain
	20	Moderate pain
	10	Marked pain
	0	Severe pain with sleep disturbance
ADL limitation in 5 different activities (total, 20 points)[a]	4	No limitation
	3	Slight limitation
	2	Moderate limitation
	1	Marked limitation
	0	Complete disability
Active ROM in abduction and flexion (20 points for each movement)	20	ROM >120°
	10	ROM 90°–120°
	0	ROM <90°

ADL, activities of daily living; *ROM*, range of motion

[a]Combing hair, dressing, reaching behind back, using arm above shoulder level, and using back pocket

The appearance of the calcific deposit was categorized into the following two types: *fluffy type*, which had cloudy limitations and varying density, and was scattered throughout the structure; and *defined type*, which was densely structured, sharply outlined and homogeneous. In those patients who consented, the contralateral shoulder was also examined radiologically in order to assess the degree of calcification in the non-symptomatic shoulder. All radiographs were interpreted by an independent radiologist with no knowledge of the calcitonin treatment used.

The values of each parameter were compared between before and after the treatment. For group comparisons of changes, we used the *t* test for independent samples or the Welch test, as appropriate. A value of $p<0.05$ was considered significant.

Results

We assessed 38 consecutive cases of calcifying tendinitis of the shoulder in 35 patients. The mean duration of the symptoms was 4.1 days (range, 1–28 days). In all except 6 cases, the first consultation was performed within 1 week of the onset of symptoms. At the first consultation, all patients had severe pain in the shoulder with marked limitation of joint movement. In 36 cases (94%), the patients had experienced nocturnal discomfort resulting in sleep disturbance. At clinical evaluation (Table 2) mean pain score was 4.2 points (range, 0–10 points), and the mean ADL limitation score was 4.5 points (range, 0–9 points). Four of these patients had cervical spondylosis. There was no correlation between the dominant hand and the affected side. At the first consultation, physical examination showed that the mean active ROM was 54.9° (range, 20–120°) in flexion and 50.3° (range, 20–130°) in abduction. The mean ROM score was 2.6 points (range, 0–40 points). Radiographic examination showed that the deposits were localized in supraspinatus area in 26 cases (69%), and the remaining 12 cases (31%) were in the infraspinatus or teres minor area. In 31 shoulders (82%), multiple deposits were present. The mean area (maximum length x width, mm^2) of the calcific deposits was 92.2 mm^2 (range, 9–390 mm^2). The size of the calcific deposits did not appear to correlate with the subjective and objective parameters (data not shown). In 24 cases (63%), the deposits were fluffy in type, and in 14 cases (37%) they were of the defined type. The size of the deposits of the fluffy type was significantly greater than that of the defined type ($p<0.01$). However, there were no significant differences in subjective and objective parameters before calcitonin treatment between these groups.

The mean number of injections given was 6.0 (range 1–16). In 24 cases (55%), the local pain remarkably decreased within 1 week. At the end of the treatment period, the shoulder was pain-free in 33 of 38 cases (87%). Regarding the remaining 5 cases, in four there was improvement in the degree of pain, although there was some residual impairment in ADL. In one case, there was no beneficial effect on the pain. After treatment, subjective parameters were remarkably improved, the mean pain and ADL scores were 37.4 points (range, 10–40 points) and 16.1 points (range, 4–20 points), respectively. Each parameter recovered with significant differences compared to the pretreated condition. Additionally, shoulder ROM markedly improved after treatment. There was complete recovery of the active ROM for abduction in 28

Table 2 Clinical and radiological results before and after calcitonin treatment in 38 shoulders. Values are mean (SD) unless otherwise indicated

	Before treatment	After treatment	*p* value
Clinical parameter			
Pain score	4.2 (5.0)	37.4 (7.2)	<0.01
Pain-free case, *n* (%)	0 (0)	33 (87)	
ADL score	4.5 (2.2)	16.1 (4.0)	<0.01
Flexion (°)	54.9 (23.6)	160.0 (24.2)	<0.01
Abduction (°)	50.3 (21.6)	154.2 (26.5)	<0.01
ROM score	2.6 (7.9)	37.4 (6.9)	<0.01
Total score	11.3 (12.3)	90.7 (17.3)	<0.01
Clinical results, *n* (%)			
Good	0 (0)	25 (66)	
Fair	0 (0)	9 (24)	
Poor	38 (100)	4 (10)	
Radiographical results			
Deposit size, mm^2	92.2 (63.5)	37.1 (50.5)	<0.01

cases (74%). The ROM score exhibited remarkable improvement with significant differences between before and after the treatment (Table 2).

On radiographic evaluation, 28 of 38 cases (*responder group*) had significant reduction in the calcific deposits, with complete disappearance in 19 out of them. In the remaining 10 cases (*non-responder group*), the sizes of deposits decreased by less than 30%. Therefore, we investigated the differences in clinical results between responder and non-responder groups. We found that the non-responder group was significantly worse in all clinical parameters compared with the responder group (Table 3). On the contrary, in all cases where the calcified deposits had completely disappeared, the shoulder had become pain-free, and in all except two cases there was complete recovery of active ROM. Therefore, we examined whether the localization of the deposit had influenced the effect of calcitonin therapy or not, but we did not find an association between the place of deposit and the success of therapy (data not shown). In addition, there was no correlation between the effect of calcitonin therapy and the radiological size of these deposits prior to treatment (data not shown). Next, we investigated a correlation between the shape of the deposit and the effects of calcitonin. We found that patients with fluffy-type deposit were significantly better in pain relief and ROM recovery than those with defined-type deposits (Table 4).

Next, we divided the patients into two groups on the basis of dosage of calcitonin given: *low dose group*, calcitonin injections were required for up to 6 times; *high dose group*, the injections were required for 7 times or more. We found that the low dose group had significantly smaller calcific deposits before treatment, but there were no other significant differences in clinical parameters between these groups before treatment. On the other hand, the low dose group was significantly better than the high dose group in all clinical parameters after the treatment (Table 5).

Table 3 Clinical results before and after the treatment in responder and non-responder groups. Values are mean (SD)

	Responder (n=28)	Non-responder (n=10)	p value
Pre-treated condition			
Pain score	5.0 (5.1)	2.8 (4.5)	NS
ADL score	4.8 (2.1)	3.8 (2.5)	NS
ROM score	3.1 (8.8)	1.9 (5.8)	NS
Total score	12.9 (12.8)	8.0 (10.9)	NS
Deposit size, mm^2	94.2 (72.0)	87.8 (41.9)	NS
Post-treated condition			
Pain score	39.2 (3.9)	33.3 (10.7)	<0.05
ADL score	17.2 (2.3)	13.6 (5.6)	<0.01
ROM score	39.2 (3.9)	33.3 (9.8)	<0.01
Total score	95.6 (9.4)	80.3 (25.1)	<0.01

NS, not significant

Table 4 Clinical and radiological results in fluffy-type and defined-type groups. Values are mean (SD)

	Fluffy-type (n=24)	Defined-type (n=14)	p value
Pre-treated condition			
Pain score	4.2 (5.0)	4.3 (5.1)	NS
ADL score	4.4 (2.5)	4.6 (1.7)	NS
ROM score	3.3 (9.2)	1.8 (5.3)	NS
Total score	11.9 (13.7)	10.4 (9.7)	NS
Deposit size, mm^2	99.6 (75.1)	79.6 (35.0)	<0.01
Post-treated condition			
Pain score	38.3 (5.6)	35.7 (9.4)	<0.05
ADL score	16.5 (3.5)	15.3 (4.7)	NS
ROM score	38.3 (5.6)	34.7(8.5)	<0.05
Total score	93.1 (14.1)	86.7 (21.8)	NS
Deposit size, mm^2	37.5 (55.0)	36.4 (43.8)	NS

NS, not significant

Table 5 Clinical and radiological results in low-dose and high-dose injection groups. Values are mean (SD)

	Low-dose group (n=28)	High-dose group (n=10)	p value
Pre-treated condition			
Pain score	5.0 (5.1)	2.0 (4.2)	NS
ADL score	5.2 (1.9)	2.5 (1.8)	NS
ROM score	2.9 (9.1)	2.0 (6.3)	NS
Total score	13.8 (13.2)	8.5 (9.2)	NS
Deposit size, mm^2	79.9 (31.7)	126.8 (108.5)	<0.01
Post-treated condition			
Pain score	39.6 (1.9)	31.0 (12.0)	<0.01
ADL score	17.7 (2.2)	11.4 (4.2)	<0.05
ROM score	39.3 (3.8)	32.0 (10.3)	<0.01
Total score	96.6 (7.0)	74.4 (26.1)	<0.01
Deposit size, mm^2	28.4 (44.4)	61.4 (60.7)	NS

NS, not significant

Overall, in 25 of 38 cases (66%), shoulder function was rated as good after treatment. These patients gained complete pain relief, and they sufficiently recovered in ADL and shoulder ROM. In 9 cases (24%), shoulder function was rated as fair, with occasional episodes of pain and mild limitations in active ROM and ADL. There was persistent pain requiring alternative treatment in only 4 cases (10%). There were no clinical complications in our cases during the treatment.

Discussion

Calcifying tendinitis was first described more than 100 years ago, and the shoulder is a common site for calcific deposits [6]. In addition, calcifying tendinitis is considered to be a frequent cause of shoulder pain and disability [6]. Bosworth reported a radiographic survey of 6 061 adult white-collar workers [7]; where there was radiographic evidence of calcific deposits in the shoulder, 35% of these patients had previously been symptomatic. Calcifying tendinitis seems to be more common in women and most of the patients are between 30 and 60 years of age [7, 8]. The patient demographics in our study show similar patterns. Although the diagnosis can be fairly straightforward, conservative treatment of primary calcifying tendinitis is often difficult, since the cause is unknown.

In the majority of patients, the treatment of symptomatic calcifying tendinitis is nonoperative [1, 3, 6]. Initially, this consists of a trial of anti-inflammatory medication, analgesia, and a gentle program of exercises through the full ROM in order to prevent a frozen shoulder. If this treatment is unsuccessful, it can be supplemented by needle aspiration and lavage or by steroid injections [1, 6, 9]. Extracorporeal shock wave treatment [10] and ultrasound therapy [11] have also been reported as useful in the treatment of calcifying tendinitis of the shoulder. In general, most Authors agree that operative treatment should only be considered when nonoperative treatment has been unsuccessful over a long period of time [1, 3, 6].

Cimetidine is useful in the treatment of periarticular calcium-deposit disease in patients who are being treated with hemodialysis [12]. Cimetidine is an H_2-blocker and has been reported to improve calcium metabolism and periarticular calcium deposits in patients on hemodialysis [12], although the mechanism of action is unknown. Cimetidine is considered to be a useful treatment for calcifying tendinitis, although it has the potential for interaction with other medications such as phenytoin, theophylline and warfarin.

It is well recognized that calcitonin is effective in the treatment of ectopic calcification in hemodialysis patients [5, 13]. Calcitonin was originally discovered in 1962 and is well known as hypocalcemic hormone [13, 14]. The hypocalcemic action is principally due to a potent inhibitory action on osteoclast-mediated bone resorption. In addition, a significant decrease in osteoclastic hyperactivity results in osteolytic pain relief [5]. The clinical use of calcitonin is widespread in the treatment of bone disorders, including Paget's disease, osteoporosis, and hypercalcemia of malignancy [14]. As far as we know, there have been no reports on the use of calcitonin in calcifying tendinitis, except where this occurs in hemodialysis patients. In this study, 38 cases of calcifying tendinitis of the shoulders have been treated with calcitonin. In 36 cases (94%), shoulder function became good or fair, and in 28 cases (74%) the calcific deposits significantly im-

proved. We did not experience any clinical complications during the treatment. It is worth mentioning that in 19 shoulders (50%), the calcified depoints completely disappeared, the patients became pain-free, and the functional scores became good. Moreover, we showed that the effect of calcitonin was different in the shape of the calcific deposit. Namely, our therapy is likely to be more effective for fluffy type deposits rather than defined type. Recently, acetic acid iontophoresis therapy and physiotherapy alone (sham therapy) have been tested for shoulder calcifying tendinitis [15]. In this report, neither therapy reduced shoulder calcifications significantly. Furthermore, although acetic acid iontophoresis improved shoulder pain, shoulder-related ADL and ROM in comparison with sham therapy, neither therapy produced significant differences in these clinical parameters. Taking these results into account, our observations are encouraging and are in keeping with the findings of Jerosch et al. [3] who emphasized that removal of the calcific deposit is important for consistent success in treating this disease.

In dialysis patients, calcitonin decreases the serum calcium (Ca) and phosphate (P) levels [14]. The etiology of calcifying tendinitis is unclear, as is the mechanism of action of calcitonin in this disease. However, it is probable that this treatment reduces the concentration of both Ca and P in the extracellular fluid, thus reducing the likelihood that calcium will be deposited in soft tissues such as tendon or muscle. Further investigations are necessary to clarify the mechanism of action of calcitonin at the serological, pathological, and molecular levels.

We found that this treatment results in rapid clinical improvement with resolution of calcification in patients who have symptomatic calcifying tendinitis of the shoulder. Furthermore, it is fortuitous that calcitonin has little interaction with other drugs, making it potentially easier to use than cimetidine. However, it is difficult to assess the true benefit of calcitonin therapy compared to other conservative therapies, since there was no control group in this study. In order to assess the true benefits of calcitonin therapy, a large-scale double-blind randomized clinical trial with different treatment protocols or placebo is required in the future.

In conclusion, our data suggest that calcitonin may be useful in the treatment of calcifying tendinitis of the shoulder, with benefits in both clinical and radiological parameters.

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