Intra-Articular Injection of Deproteinized Hemodialysate in Osteoarthritis of the Knee : A Case-Series

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Abstract

Objective : To report the efficacy of intra-articular injection of deproteinized hemodialysate including its side effects in a case-series of knee osteoarthritic (OA) patients.

Material and Method : Intra-articular injection of deproteinized hemodialysate was performed in 17 subjects (3 male and 14 female) with primary knee OA. Their average age was 63 years (min, max = 50, 80 yrs). The X-ray appearance was grade II-III according to Kellgren-Lawrence criteria.

Measurements : 100 mm visual analogue scale (VAS) and any side effects.

Results : The mean (95% CI) of the VAS before and after injection were 70.0 (59.9-80.1) and 42.7 (31.2-54.2) respectively, with a p-value of < 0.001. The mean difference in pain score was 27.35 (95% CI = 17.0-37.7). The symptoms of knee pain resolved in an average of 4.8 (2.9) days (min, max = 1, 10). No side effects were found.

Conclusion : Intra-articular injection of deproteinized hemodialysate is effective and safe. However, a further controlled trial with an adequate sample size should be performed to confirm the efficacy as well as to detect any adverse effects of this drug.

Key word : Intra-Articular Injection, Deproteinized Hemodialysate, Knee Osteoarthritis, Case-Series

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Osteoarthritis (OA) is the most common degenerative rheumatologic disease, resulting in significant morbidity and health care expense. This condition can cause pain or dysfunction in 20 per cent of the elderly[1]. Although it can affect any joint containing hyaline cartilage, troublesome symptoms

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occur most often in the weight-bearing joints of the lower extremities[2]. A study of knee OA in the elderly performed in Bangkok, revealed the prevalence of 34.5-45.6 per cent[3].

No specific modality of treatment is able to stop the osteoarthritic process[4]. Generally, the therapeutic goal has focused on reducing pain and improving function. There are many strategies for management of knee OA depending on the severity of the disease.

Intra-articular injection is considered to be effective in some conditions. For example, steroid yields significantly greater pain relief at one week after an injection but its effect is likely to be temporary and rapidly progressive joint failure has been observed after frequent and repeated injections[5]. Recent studies have demonstrated the efficacy of intra-articular injection of viscosupplementation in the treatment of knee OA with significant pain relief and improvement in knee function[6-8]. However, a small number of severe side effects have been reported, such as haemathrosis [9], phlebitis[10], restless leg syndrome and vertigo [11], and calcium pyrophosphate dehydrate crystal precipitation[12,13]. The cost, in particular, is rather high (one injection per week for 3-5 consecutive weeks). It might be inappropriate for developing countries with limited financial resources.

A deproteinized hemodialysate is derived from calf's blood. It is composed of peptides, oligosaccharides and nucleonic acid derivatives. It is a metabolically active substance with insulin-like efficacy. Deproteinized hemodialysate demonstrated effects on transportation into the cells and enhancement of utilization of glucose. It has been used in many conditions, e.g. organic brain syndrome[14], dementia[15], and tendinitis[16]. Routes of administration are intravenous, intramuscular or subcutaneous. Adverse effect reports have been generally mild and transient in nature, without any systemic effect. The objective of this study was to report the efficacy of intra-articular injection of deproteinized hemodialysate including its side effects in a case-series of knee OA patients.

MATERIAL AND METHOD

The study was performed in 17 subjects (3 male and 14 female) suffering from chronic knee OA. Their average age was 63 years (min, max = 50, 80 yrs). The inclusion criteria were age over 50 years, primary osteoarthritis of the medial femerotibial compartment, failed full conservative treatment, grade II-III X-ray appearance according to Kellgren-Lawrence criteria.

The exclusion criteria were severe articular inflammation, traumatic knee, patients who had substantial abnormalities in hepatic, renal or metabolic function or were immuno-compromized and patients who had a history of intra-articular knee injection in the 6 months preceding enrollment.

Demographic data were obtained from all patients; for example, the duration of their disease, the affected side and severity of knee pain using a 100 mm visual analogue scale (VAS). Patients were evaluated for knee effusion, bony enlargement and genu varus deformity by physical examination. This was done before and after the intervention. Then 10 ml of deproteinized hemodialysate with 2 ml of 2 per cent xylocaine was injected intra-articularly of the knee in every subject at the first visit. A follow-up appointment was given one week after injection in order to evaluate efficacy as well as any side effects, such as dizziness, headache, nausea, pruritus or a skin rash.

Statistical analysis

Descriptive analysis of mean, SD, 95 per cent CI of the VAS and percentage of demographic data were performed using the SPSS program version 11.0.

RESULTS

Seventeen OA knee patients were enrolled in the study. The demographic data is shown in Table

Table 1. Demographic data of the seventeen knee OA subjects studied.

Data	No	%
Age (yr) (Mean, SD)	62.9 , 8.9	
Duration (yr) (Mean, SD)	2.2 , 1.9	
Sex		
Male	3	17.6
Female	14	82.4
Affected side		
Lt	2	11.8
Rt	4	23.5
Bilateral	11	64.7
X-ray grade		
II	10	58.8
III	7	41.2
Pain		
Squatting	6	35.3
Going up stairs	6	35.3
Level walking	5	29.4

1. The means (95% CI) of the VAS before and after intra-articular injection of deproteinized hemodialysate were 70.0 (59.9-80.1) and 42.7 (31.2-54.2) respectively (Fig. 1). Comparing the pain scores using a paired *t*-test, the difference was statistically significant with a p-value of < 0.001. The mean difference in pain score was 27.35 (95% CI = 17.0-37.7). The symptoms of knee pain resolved in an average of 4.8 (2.9) days (min, max = 1, 10) and joint effusion after the injection seemed to improve (Table 2). Concerning the side effects of this drug, the authors interviewed and evaluated every patient, and found no side effects.

DISCUSSION

Osteoarthritis is a degenerative change of the articular or hyaline cartilage which is relatively avascular tissue. Any defects that penetrate subchondral bone can heal with fibro-cartilaginous tissue, mainly composed of type I collagen. It has different biochemical and biomechanical properties than normal cartilage. It cannot resist mechanical stress for a long time and tends to deteriorate with time. These facts mean that if articular cartilage is injured, it cannot heal fully[17].

An intra-articular injection of a viscosuppliment has proven to be safe and effective in treating OA knee, resulting in significant pain relief and improvement in overall functions but it is expensive[7,8]. The present study reported the effect of intra-articular injection of deproteinized hemodialysate in pain reduction. It was composed of two fractions; the P1 fraction demonstrates insulin-like activity on glucose transportation into the cells, and the IPO fraction (Inositol phospho-oligosaccharides) demonstrates a positive effect on the glucose transport system[18,19] by activating GLUT1[20] and also activates glucose oxidation as well as the PDH complex. Therefore, it can increase oxygen and glucose transportation into cells as well as intracellular glucose utilization[21]. It also stimulates the aerobic route of energy metabolism. Hypoxia is a major contributor to the prevention of healing in most tissue damage in the human body; therefore it can improve tissue healing *via* this mechanism. The results of the present study revealed

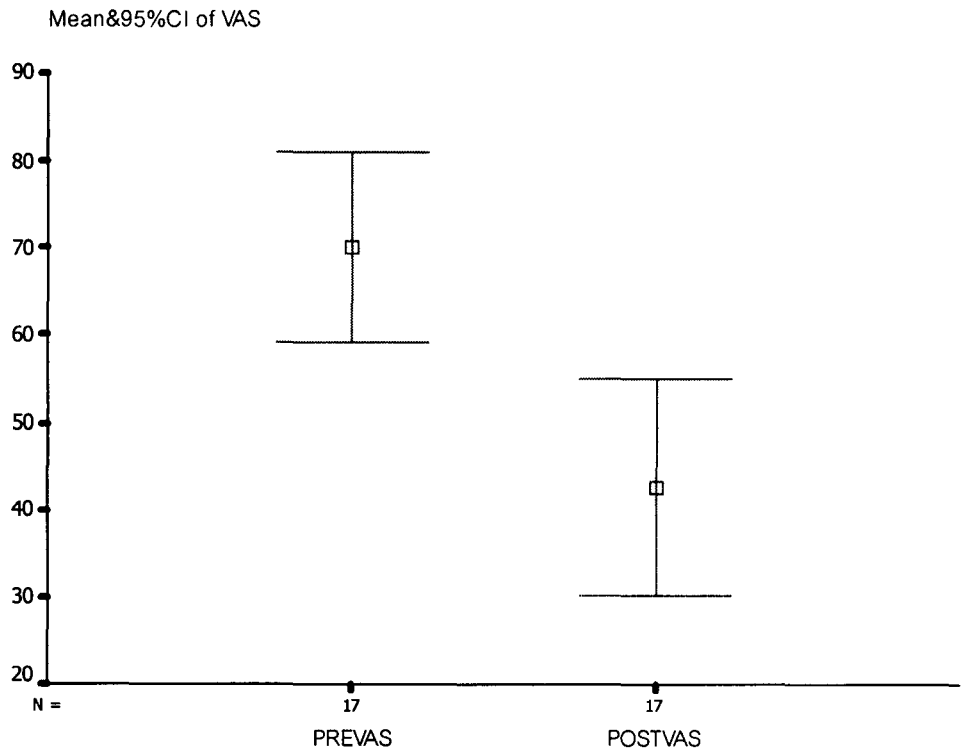

Fig. 1. The mean and 95 per cent CI of the VAS before and after intra-articular injection of deproteinized hemodialysate.

Table 2. Joint effusion comparison between before and one week after injection presented as number.

Joint effusion	Before	%	One week after	%
Minimal	6	35.3	9	52.9
Moderate	10	58.8	8	47.1
Marked	1	5.9	-	-

that deproteinized hemodialysate can decrease symptoms of knee pain with evidence of a statistically significant difference between pre and post pain VAS (p-value < 0.001). The major effect should come from increasing oxygen and glucose transportation into the cells.

Concerning the frequency and severity of undesired drug effects (UDE), 208 of degree I and II were reported from 44 clinical studies with parenteral application of deproteinized hemodialysate, conducted by order of Nycomed Arzneimittel GmbH. This corresponds to a frequency of 6 per cent in a total of 3,458 patients treated with deproteinized hemodialysate, compared to the rate of 3.3 per cent obtained in the placebo groups[22]. Those commonly reported UDE of deproteinized hemodialysate included dizziness, headache, heat sensations, nausea and reddening of skin. In addition, Kanowski reported that deproteinized hemodialysate had the relatively low rate of side effects and suggested this drug to be a very favorable benefit-risk ratio[14]. The results of the present study did not show any side effects due to the small sample size.

Regarding to the methodology, the present study did not have a control group, so some bias might have occurred. Therefore, a further controlled trial with an adequate sample size should be performed to confirm the efficacy as well as to detect the adverse effects of this drug.

In summary, the authors reported a case-series of the effects of intra-articular injection of deproteinized hemodialysate. It decreased knee pain and reduced joint swelling. In addition, the authors did not find any serious adverse effect. Because deproteinized hemodialysate costs less compared to other viscosupplement drugs, it may be another alternative treatment for knee OA patients. It can save money, shorten the duration of the treatment period and improve the quality of health care for knee OA patients.

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ประสิทธิผลของยาฉีดเข้าข้อ deproteinized hemodialysate ในผู้ป่วยข้อเข่าเสื่อม : รายงานชุดผู้ป่วย

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วัตถุประสงค์ : เพื่อรายงานประสิทธิผลของยาฉีดเข้าข้อ deproteinized hemodialysate ในการรักษาผู้ป่วยข้อเข่าเสื่อม รวมทั้งผลข้างเคียงของยา

วัสดุและวิธีการ : ทำการฉีดยา deproteinized hemodialysate เข้าข้อเข่าผู้ป่วยโรคข้อเข่าเสื่อมจำนวน 17 ราย (ชาย 3 ราย, หญิง 14 ราย) อายุเฉลี่ย 63 ปี (ค่าต่ำสุด, สูงสุด = 50, 80 ปี) โดยผู้ป่วยมีภาพถ่ายรังสีข้อเข่าเกรด II – III ตามการแบ่งระยะโรคของ Kellgren – Lawrence

วิธีวัด : แบบประเมินอาการปวด (Visual analogue scale) 100 มม. รวมทั้งผลแทรกซ้อนที่เกิดขึ้น

ผล : ค่าเฉลี่ยและค่าความเชื่อมั่น 95% ของคะแนนความปวดก่อนและหลังฉีดยามีค่าเท่ากับ 70.0 (59.9–80.1) และ 42.7 (31.2– 54.2) ตามลำดับ โดยมีค่าพีน้อยกว่า 0.001 ค่าเฉลี่ยผลต่างของคะแนนความปวดมีค่าเท่ากับ 27.35 (95% CI = 17.0–37.7) ผู้ป่วยรู้สึกว่าอาการปวดลดลงเฉลี่ย 4.8 (2.9) วัน (ต่ำสุด, สูงสุด = 1, 10 วัน) รายงานนี้ไม่พบผลแทรกซ้อนของยา

สรุป : การฉีดยา deproteinized hemodialysate เข้าข้อเข่าผู้ป่วยมีความปลอดภัยและประหยัด อย่างไรก็ตามควรมีการศึกษาต่อเนื่อง โดยมีกลุ่มควบคุมเปรียบเทียบ และมีจำนวนขนาดตัวอย่างที่มากเพียงพอ เพื่อศึกษายืนยันถึงประสิทธิผลของยานี้ รวมทั้งศึกษาผลข้างเคียงที่อาจเกิดขึ้นได้

คำสำคัญ : การฉีดยาเข้าข้อ, deproteinized hemodialysate, ข้อเข่าเสื่อม, รายงานชุดผู้ป่วย

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