Comparative Efficacy of Traditional Conservative Treatment and Ct-guided Local Chemotherapy for Mild Spinal Tuberculosis

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Abstract

Background: There are considerable differences in the treatment strategy for spinal tuberculosis, including conservative or surgical procedures. Conservative treatment is always suitable for most patients. This study aimed to compare the clinical efficacy of traditional conservative treatment with CT-guided local chemotherapy strategy of mild spinal tuberculosis.

Methods: This research retrospectively analysed 120 patients with spinal tuberculosis between January 2005 and January 2016 according to the diagnostic criteria of mild spinal tuberculosis. In total, 89 patients underwent traditional conservative treatment, 31 underwent CT-guided local chemotherapy. Clinical outcome, laboratory indexes, and radiological results were analysed to provide a clinical basis for the choice of mild spinal tuberculosis treatment.

Results: All cases achieved a clinical cure with 24 to 50 months followed up. Cobb angle of the two groups spinal tuberculosis segments was $6.25 \pm 3.11^\circ$, $5.69 \pm 2.58^\circ$ before treatment and $12.36 \pm 6.31^\circ$, $14.87 \pm 7.26^\circ$ after treatment, respectively. VAS scores were significantly decreased post-treatment. There was no obvious kyphosis, symptoms or neurological deficits at the final follow-up.

Conclusions: For mild spinal tuberculosis, traditional conservative treatment can achieve satisfactory results. The strategy combined with CT-guided local chemotherapy treatment is minimally invasive, beneficial for the drainage of paravertebral abscesses and pain relief.

Background

Spinal tuberculosis is the most common and serious form of tuberculosis lesion in skeleton result in severe complications including kyphosis and paralysis complications[1, 2]. Although the cure rate of spinal tuberculosis is high with the use of anti-tuberculosis drugs, there is still no consensus on the use of chemotherapy, surgical indications, and surgical methods related to spinal tuberculosis [3, 4]. The blind increase in surgical indications and over-operation have become problems that need to be solved urgently. How to properly select conservative treatment or surgery has gradually attracted the attention of clinicians. Several researchers have attempted to classify spinal tuberculosis in order to standardise the treatment strategy but not been widely accepted due to some shortcomings [5, 6].

Through a literature review and in an effort to summarise our relevant clinical experience, we have suggested a standard for the early diagnosis of mild spinal tuberculosis[6]. The patients in this study with traditional conservative treatment was compared to CT-guided local chemotherapy treatment. The efficacy and safety was evaluated to improve the treatment strategy for spinal tuberculosis.

Methods

The study was approved by the Institutional Ethics Review Board of the First Affiliated Hospital at Third Military Medical University and the Ethics Committee of the Zhoukou Union Orthopedic Hospital. Written
informed consent was obtained from all patients or their guardians and retrospectively registered. The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers. All patients received nutritional supporting treatment. Conservative treatment patients were not confined to bed but told to avoid strenuous exercise.

Between January 2005 and January 2016, 120 mild spinal tuberculosis cases were included by imaging, pathology, tuberculosis or gene chip by bacterial culture in this research. 89 patients underwent traditional conservative treatment (A group), another 31 cases were performed CT-guided local chemotherapy (B group). There were 72 males and 48 females with an average age of 28.26 ± 10.88 years (range 15–78 years). In total, there were 2 cervical, 33 thoracic, 26 thoracolumbar (involving T11-L2), 59 lumbar, and 2 lumbosacral (involving L5-S1) lesions. There was no significant difference in age and sex among the two groups (P>0.05). All patients underwent imaging examination (X-ray, CT, MRI). VAS score and kyphosis Cobb angle were measure before and after treatment in Table 1.

The inclusion criteria of mild spinal tuberculosis were as follows: active spinal tuberculosis, mild systemic and local symptoms; single central vertebral or two margin vertebral tuberculosis; spinal appendage tuberculosis without spinal canal involvement; mild bone destruction (< 1/3 vertebral height, no large sequestrum, smaller paravertebral abscess less than 5 cm in diameter); no retropharyngeal, single vertebral involvement with central lesion or multivertebral involvement with edge type lesion; neurological deficits according with American Spinal Injury Association (ASIA) D or normal; no obvious kyphosis (Cobb angle < 30°); and no obvious spinal instability. The exclusion criteria were as follows: severe bone destruction (> 1/3 vertebral height), significant kyphosis (Cobb angle ≥30°), obvious neurological deficit (worse than ASIA D), large abscesses and sequestrum requiring debridement, bone grafting and internal fixation, complicated spinal tumour or active pulmonary tuberculosis, and poor tolerance or compliance. The traditional conservative treatment (A group): the 89 patients without paravertebral abscesses or psoas gravitation abscess were accepted four drug anti-tuberculous chemotherapy, i.e. HREZ (rifampicin, 15 mg/kg, maximum, 600 mg/day; isoniazid, 6 mg/kg, maximum 300 mg/day; ethambutol, 25 mg/kg, maximum 750 mg/day; pyrazinamide, 25 mg/kg, maximum 750 mg/day) for at least 18 months. In order to improve the compliance and convenience of patients outside the hospital, all patients and their families received education and training to make clear the importance of early, regular, appropriate, whole-course, and combined medication, and to supervise the patients’ medication. The CT-guided local chemotherapy (B group): the 31 patients appeared obvious paravertebral abscesses or psoas gravitation abscess, in the prone or lateral position, a CT positioning scanner was used to select the best puncture point. The punctures were performed above the transverse process and into the intervertebral space and paraspinal abscess. Under local anaesthesia, puncture was performed with an 18G puncture needle to reach the lesion position. After CT reconfirmation, the guide wire and expansion tube were taken out and the double-lumen tube was placed inside. The patient was observed for 30 minutes. Vital signs were monitored and antibiotics were used to prevent infection for three days after the operation (1 g rifamycin sodium or 0.6 g isoniazid was added to 500 ml saline for 24 hours under continuous infusion). Four drug anti-tuberculous chemotherapy HREZ was performed following the same procedure as that for group A.
All patients were followed up (1, 3, 6, 9, 12, 18 months after treatment, and then once a year thereafter). Observed clinical symptoms, signs, and ESR, liver and kidney function were monitored. Radiology (X-ray, CT) was used to evaluate kyphosis. A visual analogue scale (VAS) was used to assess pain improvement, along with a neurological status test according to the American Spinal Injury Association (ASIA) impairment scale. Cure definition was as follows: follow-up more than 18 months, good body condition, normal temperature, good appetite, normal ESR, no obvious local symptoms, no abscess or sinus, X-ray shows abscess disappearance or calcification, no sequestrum or absorption, and lesion edge clear or joint fusion [G,H].

All analyses were performed using the SPSS statistical software package (version 14.0, SPSS Inc, Chicago, IL, USA). The before treatment and final follow-up kyphotic angles and VAS scores were compared with repeated measures analysis of variance among groups, and then using the Student-Newman-Keuls test to compare each group. Gender was statistically analysed using the $\chi^2$ test, and age was statistically analysed using analysis of variance. $P < 0.05$ was considered to indicate a significant difference.

**Results**

All patients were followed up for 24–50 months. In the traditional conservative treatment (A group), one month later, the ESR dropped in 85 patients, and then returned to a normal level at three months. At three months follow-up, ESR increased in four lumbar patients, accompanied by obvious pain, aggravated bone destruction, progressive kyphosis, unabsorbed paravertebral abscess. These patients underwent further surgical treatment. The drug sensitivity test indicated they were infected with resistant spinal tuberculosis, so chemotherapy drugs were adjusted, and the patients were declared cured 18 months after surgery. All patients were able to follow the chemotherapy regimen for 18 months and achieved clinical cure (95.51%) (Fig. 1), except the 4 patients infected with resistant spinal tuberculosis had been treated with correction, bone grafting surgery.

In the CT-guided local chemotherapy (B group), the drainage time was three weeks to three months in patients with catheter drainage, local intensified chemotherapy and with combined drug treatment for 18 months. The extraction standard of the drainage tube was drainage pus less than 5 ml/day, observed continuously for 3 days, ESR < 20 mm/h and abscess disappearance by CT or MRI re-examination. During the treatment period, all patients were treated successfully without cross-infection. At one month follow-up, one patient showed increased ESR, aggravated pain, and progressive kyphosis, then underwent surgical treatment. The drug sensitivity test indicated it was due to resistant spinal tuberculosis, so the chemotherapy drugs were adjusted and the patient was cured 18 months later. The remaining patients were clinically cured and the abscesses disappeared. MRI showed a vertebral signal similar to the surrounding normal vertebral body (Fig. 2).

In the conservative treatment group (Group A), most patients still had pain at the first month follow-up. At three months follow-up, X-rays showed that the bone was stable in the vertebral destruction area, the
marginal bone appeared sclerotic, the pain had disappeared, and MRI showed no obvious abscess. At six months follow-up, 36 patients showed interbody fusion. At nine months follow-up, 67 showed bone fusions. At 18 months follow-up, there were 85 cases of interbody fusion, the disease was cured except the 4 resistant spinal tuberculosis.

In the CT-guided puncture/irrigation combined conservative treatment groups (Group B), the abscess disappeared and the pain symptoms were relieved one month postoperatively except the one resistant spinal tuberculosis. At three to six months postoperatively, the lesion showed marginal sclerosis and intervertebral fusion. Vertebral body fusion was observed at one year follow-up except the one resistant spinal tuberculosis.

The VAS scores of two groups were significantly decreased post-treatment and at last follow-up, indicating that the two methods significantly improved pain symptoms, but with no significant differences between the two groups (Table 2). At the last follow-up, the average Cobb angle was $12.36 \pm 6.31^\circ$ in conservative treatment (Group A), $14.87 \pm 7.26^\circ$ in CT-guided local chemotherapy (Group B), with no significant differences. Compared with the pretreatment Cobb angle, mild residual kyphosis was observed in the two groups but no significant differences between them. No obvious symptoms of neurological deficits were observed, and all patients returned to normal daily activities (Table 3).

**Discussion**

Spinal tuberculosis diseases was similar to internal medicine diseases, and the best basic treatment is chemotherapy, rest, and immobilisation. It was advocated chemotherapy alone at the beginning until Hodgson and Stock advocated debridement and bone grafting fusion surgery [9]. Surgery should be considered in cases of unstable spine to prevent kyphosis, progressive symptoms of spinal cord nerve damage to avoid paralysis. The final neurological improvement is significantly affected by patients suffering from tuberculosis of spine, vertebral involvement, AIS grade, bladder and bowel involvement and its duration [10]. Complete debridement and decompression can reduce the paralysis, re-establish spinal stability and correct the deformity, as well as shorten the treatment cycle, reduce adverse drug reactions, and improve quality of life [11, 12].

Although surgical strategy has significant advantages in terms of preventing kyphosis progression and neurological deficits, surgical treatment also has many disadvantages such as considerable trauma, risk to important organs, blood vessels and nerves, postoperative complications, economic burden and so on. Selecting the appropriate treatment programme for spinal tuberculosis is challenging for surgeons [13, 14]. The choice of surgery or drug therapy has yet been reached an agreement. Many studies have reported satisfactory results for the treatment of spinal tuberculosis with simple chemotherapy, and about 80% of patients achieved spontaneous fusion. Chemotherapy became one essential foundation for the treatment of spinal tuberculosis [15, 16]. The antitubercular drugs are the key stones in the management of tuberculosis of spine, similar as soft tissue tuberculosis management, limited role of surgery [17]. For patients without serious complications, drug chemotherapy can achieve satisfying short
and long-term effects. Moreover, the conservative treatment is suitable for most patients, as an early incarnation of the concept of individualised treatment. Bhojraj et al. [18] reported more than 98% spinal tuberculosis patients can be cured by simple chemotherapy and avoided surgery. No significant difference in functional outcome was found between conservative management and surgery for cases with uncomplicated spinal tuberculosis [19].

The indication for the conservative treatment of spinal tuberculosis has always been controversial. Conservative treatment should be suitable for patients without obvious kyphosis, spinal instability, and progressive dysfunction of the spinal cord. In our past research, we characterised a subtype of spinal TB called ‘mild spinal TB’ in great detail and selected the study population accordingly to improve the clinical classification and treatment of spinal tuberculosis [6]. In a prospective study by Kotil 44 [20], patients without neurological deficits and significant kyphosis were treated effectively with anti-tuberculosis drugs. The results showed that 42 patients (95.4%) were clinically cured without any significant kyphosis after only chemotherapy. In our patients, the average number of spinal tuberculosis levels involved was 2.5 (range from one to five levels); this was associated with excellent results by non-surgical treatment for thoracic spinal tuberculosis [18]. Single vertebral involvement with a central lesion or multvertebral involvement (fewer than three) with edge type lesions are indications for conservative treatment. Except for these strict mild spinal tuberculosis standards, we found that patients who underwent CT-guided local chemotherapy for spinal tuberculosis involving four levels with a small paravertebral abscess or psoas gravitation abscess (less than 5 cm in diameter), without obvious kyphosis and no obvious spinal instability. Those patient also achieved satisfactory results by CT puncture treatment.

Although mild kyphosis was observed, there were no obvious symptoms in the two groups. With progress in treatment concepts, mild spinal tuberculosis is no longer treated surgically in recent years, but rather most patients are treated by simple chemotherapy and achieve satisfactory results. The existence of tuberculosis cold abscess always causes toxemia, abnormal inflammatory laboratory indicators, increased consumption and pain. It’s theoretically possible that traditional drug chemotherapy is not easy to obtain early control of abscess, the CT puncture treatment can play the purpose of rapid recovery of eliminate pus and pain relief. But in this study, the VAS scores decreased significantly and pain was relieved at follow-up under conservative treatment, with no significant differences between the two groups. It is very likely that patients in the traditional chemotherapy group had less or small abscess, and the chemotherapy drugs could be effectively controlled TB infection in the early stage. Minimally invasive surgery involved computed tomography (CT)-guided percutaneous catheter drainage and percutaneous catheter infusion chemotherapy carries advantages in terms of less invasiveness, precise drainage, and enhanced local drug concentration. While the technique has not been fully characterized and clinically prove, its use in addition to conservative chemotherapy and open debridement and instrumental fixation may be recommended for patients with paravertebral or psoas abscesses and spinal tuberculosis [21].

With the development of the economy, the health consciousness of patients has gradually improved, and various diagnostic techniques have been applied to the clinic. These affordable and simple actions and district levels could facilitate earlier diagnosis [22]. Diagnosis of spinal tuberculosis (TB) in the early
(inflammatory) stage is essential to prevent the development of spinal deformity and neurological deficit [23]. Due to this, the early diagnosis rate of spinal tuberculosis has been significantly enhanced. Before the symptoms of kyphosis, gravitation abscess, neurological deficits, and spinal instability occur, patients can be diagnosed and treated early. The CT puncture treatment technique has some advantages of less traumatic or risky, beneficial for obtaining specimens, detecting drug resistance and accomplishing early individualised treatment.

One persistent controversy in the treatment of spinal tuberculosis is the absence of a general classification system to guide clinical protocols. In order to standardise treatment strategies, a few researchers have attempted to classify spinal tuberculosis, but this has not been widely accepted because of some shortcomings. The classic pathological types (edge type, central type, sub-ligament type, accessory type) are too simple, making it difficult to guide clinical surgical decisions and prognosis.

In 2001, Mehta et al. [24] divided thoracic vertebrae into four types based on MRI signs, and recommended surgical procedures according to the different type. However, the classification system only included the thoracic vertebrae. In 2008, a retrospective study analysed 76 patients with spinal tuberculosis, and put forward a new classification (GATA) according to abscesses, neurological deficit, vertebral collapse, kyphosis, spinal instability, and disc degeneration [5]. This new classification system is considered to be a practical guide for spinal tuberculosis treatment planning [25]. Nonetheless, the classification does not include spinal adnexal tuberculosis, as this criterion is too complex to master in the clinic. Non-surgical measures have been successful in the treatment of spinal tuberculosis patients without the use for bracing [18, 26].

We found that there was no obvious difference between traditional conservative treatment with drug anti-tuberculous chemotherapy and CT-guided local chemotherapy to delay kyphosis, spinal instability, and neurological deficits in mild spinal tuberculosis by comparison. Although surgical treatment for spinal tuberculosis abscess can lead to satisfactory clinical outcomes [27]. The treatment by CT puncture and catheterisation is minimally invasive, beneficial for the drainage of paravertebral abscesses, and reduce the possibility of conventional surgical debridement for tuberculosis abscesses. Moreover, this strategy reduces tuberculosis infection, consumption, pain, and complications related to prolonged bed rest, also enhanced recovery of mild spinal tuberculosis. Theoretically, it has advantages over single drug chemotherapy in the treatment of abscesses. In particular, it is conducive to test for drug-resistant tuberculosis in abscess specimens to diagnose, guide and adjust the chemotherapy regimen if necessary. Spinal tuberculosis is a global disease, timely diagnosis with clinical, imaging, microbiological, histopathological features and complete course of anti-tubercular treatment along with symptomatic treatment appears to be safe and effective [28].

Although satisfactory outcomes were obtained in this study, several limitations exist. First, this was a retrospective study without random assignment of patients, a short follow-up period and small sample size, which may affect the reliability of the results. Second, the study did not include patients with neurological deficits, serious kyphosis, or large abscesses, which may cause a certain degree of bias. Third, need random controlled and prospective studies in future with large patient populations to prove.
Conclusions

For patients diagnosed with mild spinal tuberculosis, conservative treatment can achieve satisfactory results. The strategy combined with CT-guided local chemotherapy treatment is minimally invasive, beneficial for the drainage of paravertebral abscesses, pain relief and enhanced recovery of mild spinal tuberculosis.

Declarations

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Availability of data and materials

All data used in the study are available at the request of the editors and reviewers. If someone wants to request the data from this study please contact M.D. Wenbo Diao.

Authors’ contributions

Yangyang Guo※※ and Meitao Xu※※ contributed equally to this work and should be considered co-first authors; they designed the study and case review and wrote this article. Zehua Zhang※※ and Wenbo Diao※※ are both corresponding authors; they were responsible for performing the study. Lei Li※ and Bin Gu※ helped follow up patients, collect data and perform statistical analysis in this work. All authors are familiar with the contents of the final draft and take responsibility for the authenticity of the data used in the paper. All authors read and approved the final manuscript.

Ethics approval and consent to participate

We confirm that all methods were performed in accordance with the relevant guidelines and regulations. All patients consented to their data being used in this study. The study was approved by the Institutional Ethics Review Board of the First Affiliated Hospital at Third Military Medical University and the Ethics Committee of the Zhoukou Union Orthopedic Hospital. Written informed consent was obtained from all
patients or their guardians and retrospectively registered. The informed consent for participants below 16 years of age was obtained from their parent and/or legal guardian.

**Consent for publication**

Not Applicable.

**Competing interests**

The authors declare that they have no competing interests.

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Tables

Table 1.

Patient Data.

| Group     | Group A  | Group B  | P value |
|-----------|----------|----------|---------|
|           | n=89     | (n=31)   |         |
| Gender    |          |          | 0.496a  |
| Male      | 55       | 17       |         |
| Female    | 34       | 14       |         |
| Age       | 28.08 ± 10.78 | 26.87±9.56 | 0.531b  |
| Distribution |        |         |         |
| Cervical  | 2        | 0        |         |
| Thoracic  | 21       | 10       |         |
| Thoracolumbar | 14   | 12       |         |
| Lumbar    | 50       | 9        |         |
| Lumbosacral | 2      | 0        |         |

There was no significant difference in gender between the two groups (Chi-square test, p > 0.05).

There was no significant difference in age between the two groups (Analysis of variance, p > 0.05).

Table 2.

Comparison of VAS score before and after treatment between the two groups.

| Group     | Before treatment | Last follow-up |
|-----------|------------------|----------------|
| Group A   | 5.61 ± 1.63      | 2.06 ± 1.07    |
| Group B   | 5.23 ± 1.23      | 1.81 ± 1.01    |
| P value   | 0.075a           | 0.384b         |

There was no significant difference in VAS score before treatment between the two groups (Analysis of variance, p > 0.05).
There was no significant difference in VAS score at last follow-up between the two groups (Analysis of variance, p > 0.05).

### Table 3.

Comparison of Cobb angle before and after treatment between the two groups.

| Group   | Before treatment | Last follow-up |
|---------|------------------|----------------|
| Group A | 6.25 ± 3.11°     | 12.36 ± 6.31°  |
| Group B | 5.69 ± 2.58°     | 14.87 ± 7.26°  |
| P value | 0.061<sup>a</sup> | 0.093<sup>b</sup> |

<sup>a</sup> There was no significant difference in Cobb angle before treatment between the two groups (Analysis of variance, p > 0.05).

<sup>b</sup> There was no significant difference in Cobb angle at last follow-up between the two groups (Analysis of variance, p > 0.05).

### Figures

![Figures](attachment:image.png)
Figure 1

(a) Sagittal magnetic resonance imaging (MRI) showing a 22-year-old male with mild spinal tuberculosis at the L2 vertebral body. The patient was treated with standard first-line antituberculosis drugs for 18 months. (b) At 6 months follow-up sagittal MRI showed significant edema at the L2 and L3 levels, bone destruction exacerbated without obvious abscess, nerve dysfunction, kyphosis and spinal instability. Conservative treatment was continued. (c) Sagittal MRI showing significant absorption and a clear lesion edge at 18 months follow-up. (d) Anteroposterior radiography data two years after 18 month of standard chemotherapy treatment. The patient was considered cured and solid fusion appeared at the L2/3 levels, without any complications such as kyphosis or spinal instability.

Figure 2

(a) Sagittal and coronal MRI images showing a 31-year-old male with mild spinal tuberculosis at the T8 ~ T11 levels. Tuberculosis accumulated in the vertebral body and intervertebral space with a smaller paravertebral abscess; no distinct kyphosis was observed. (b) Sagittal and axial CT scan showing tuberculosis of the thoracic vertebra. An abscess was treated with CT puncture, followed by two months of drainage. (c) At one year follow-up, sagittal and coronal MRI showed significant bone destruction and intervertebral space reduction, but the tuberculosis abscess has disappeared. (d) Four years after combined treatment with CT guided puncture, catheter drainage and 18 months of standard chemotherapy, sagittal CT and MRI showed a solid fusion at the T8/T9, T10/11 levels and destruction of the thoracic vertebrae. The paravertebral abscesses had disappeared at the T8 ~ T11 levels, with no significant progression of local kyphosis.