

# Clinical efficacy and safety of ultra-short-course chemotherapy in treatment of spinal tuberculosis after complete debridement: an observational study

Guangwei Sun<sup>1,2,\*</sup>, Qian Wang<sup>3,\*</sup>,  
Qiang Liang<sup>1</sup>, Xiangwei Song<sup>4</sup>, Jian Chen<sup>5</sup>,  
Jiandang Shi<sup>1</sup>, Wenxin Ma<sup>1</sup>, Hucheng Yuan<sup>1</sup>,  
Weidong Jin<sup>1</sup> and Zili Wang<sup>1</sup> 

## Abstract

**Objective:** To evaluate the clinical efficacy and safety of ultra-short-course chemotherapy (<4 months) in treating spinal tuberculosis following complete debridement.

**Methods:** Clinical data of patients diagnosed with spinal tuberculosis, who underwent surgery with postoperative chemotherapy for <4 months at the General Hospital of Ningxia Medical University between January 2005 and March 2015, were retrospectively analysed. Clinical manifestations, American Spinal Injury Association grades, states of bone fusion and lesion healing, deformity correction, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels and adverse drug reactions, observed before and after surgery and at the final follow-up, were assessed.

**Results:** Sixty patients were included, comprising 26 male and 34 female patients aged 16–78 years (mean, 40.85 years). Patients received postoperative chemotherapy for 3–4 months (mean, 3.61 months) and were followed for 25–129 months (mean, 70.61 months). Spinal tuberculosis recurred after surgery in one patient, who was cured by subsequent surgery. At the final follow-up, no symptoms of tuberculosis, local pain, abscess or sinus were observed. Daily life and

<sup>5</sup>Department of Spinal Surgery, Shanghai Guolong Hospital, Shanghai, China

\*These authors contributed equally to this work.

## Corresponding author:

Zili Wang, Department of Spinal Surgery, General Hospital of Ningxia Medical University, 804 Shengli Street, Yinchuan 750004, China.

Email: drwangzili@yandex.com

<sup>1</sup>Department of Spinal Surgery, General Hospital of Ningxia Medical University, Yinchuan, China

<sup>2</sup>Department of Orthopaedics, Linfen People's Hospital, Linfen, China

<sup>3</sup>Hillsborough Community College, Tampa, FL, USA

<sup>4</sup>Department of Orthopaedics, The First Affiliated Hospital of Xinxiang Medical College, Xinxiang, China



working abilities were almost recovered in all patients. ESR and CRP levels were restored to normal, bone grafts fused, lesions healed and neurological functions were recovered. Postoperative chemotherapy-induced complications occurred in 10 patients (16.67%).

**Conclusions:** Complete debridement plus ultra-short-course chemotherapy for 3–4 months may be safe and efficacious in treating spinal tuberculosis, and requires further investigation.

### Keywords

Complete debridement, clinical efficacy, safety, spinal tuberculosis, ultra-short course chemotherapy

Date received: 8 April 2020; accepted: 29 September 2020

## Introduction

A conventional standard 9–18-month chemotherapy regimen has been mainly adopted by surgeons to effectively treat tuberculosis. However, the prolonged course of chemotherapy is likely to provoke drug toxicity, interruption of treatment, or modification of the regimen during the course of chemotherapy. In addition, prolonged chemotherapy may lead to decreased patient compliance and case supervision difficulties.<sup>1</sup> Consequently, extensive attention has been given to shortening the course of chemotherapy to eliminate adverse consequences during tuberculosis management. In the 1970s, short-course chemotherapy regimens for 6–9 months were successfully adopted by collaborative groups of the British Academy of Medical Sciences to effectively treat tuberculosis.<sup>2</sup> In 2014, Merle *et al.*<sup>3</sup> demonstrated that a 4-month chemotherapy regimen to treat tuberculosis yielded a lower withdrawal rate (2.7% versus 5.0%) and a lower rate of treatment failure (1.7% versus 14.6%) compared with a standard regimen. In treating spinal tuberculosis, the clinical efficacy and safety of short-course chemotherapy (<9 months) has been widely recognized by multiple scholars.<sup>4,5</sup>

Since 1998, Professor Wang and his team have shortened the course of chemotherapy

in an attempt to enhance the efficacy and guarantee safety in the treatment of spinal tuberculosis, suggesting that it is feasible to adopt ultra-short-course chemotherapy (4.5 months on average) following radical debridement surgery in patients diagnosed with spinal tuberculosis.<sup>1</sup> However, whether the duration of chemotherapy in this protocol should be further shortened remains to be confirmed. Thus, the aim of the present study was to retrospectively analyse clinical data from patients diagnosed with spinal tuberculosis who underwent radical debridement in combination with ultra-short-course chemotherapy for 3–4 months at the General Hospital of Ningxia Medical University between January 2005 and March 2015, in order to evaluate the clinical efficacy and safety of this modified regime, thereby providing clinical evidence for the application of ultra-short-course chemotherapy after complete debridement in the treatment of spinal tuberculosis in clinical settings.

## Patients and methods

### Study population

Clinical data from patients with spinal tuberculosis, who were admitted to the Orthopaedics Department of the General Hospital of Ningxia Medical University,

Yinchuan, China between January 2005 and March 2015, were retrospectively analysed.

Inclusion criteria comprised: (1) diagnosis of spinal tuberculosis, validated according to histopathological examination or positive tuberculosis culture; (2) treatment with <4 months of ultra-short-course chemotherapy after complete debridement; (3) no active tuberculosis in other parts of the body; (4) no severe liver or kidney dysfunction; and (5) no immune diseases, such as active rheumatism, rheumatoid diseases, hepatitis B, ankylosing spondylitis, systemic lupus erythematosus, or similar conditions. Patients were excluded from the study if: (1) their condition could not be completely debrided; (2) incomplete clinical information was available; (3) the patient was lost to follow-up; (4) the patient had active tuberculosis; or (5) the patient had multi-drug resistant tuberculosis.

The present study was approved by the ethics committee of the General Hospital of Ningxia Medical University, and written informed consent was obtained from each patient.

### *Preoperative preparation*

Bed rest immobilization for 2–4 weeks (mean duration,  $3.13 \pm 0.79$  weeks) was instructed before surgery, and nutritional support was provided. All patients were administered 20 mg/kg/day streptomycin (S) by intramuscular injection, once daily; 5 mg/kg/day isoniazid (H), orally, once daily; 10 mg/kg/day rifampicin (R), orally, once daily; and 25 mg/kg/day pyrazinamide (Z) orally, once daily. The above quadruple (SHRZ) antituberculosis treatment regimen was administered for 2–4 weeks (mean, 3.1 weeks). Liver and kidney functions were monitored, and patients were closely observed to identify and treat incidental drug-related side effects. Surgery was performed when tuberculosis symptoms and

general condition of the patient were improved.

### *Surgical indications*

Indications for surgery included the following: spinal cord and nerve compression leading to dysfunction; presence of spinal instability and kyphosis deformity; large abscesses, cavities, dead bones, or sinus tract formation; poor response to non-surgical treatment. Patients presenting with one of the above conditions were eligible to receive surgical treatment.

### *Surgical procedures*

All patients underwent radical resection of the lesions by the present research team.<sup>6,7</sup> Surgical procedures including decompression, deformity correction, bone grafting and instrumentation were performed according to topical pathological changes, as previously described.<sup>8,9</sup> Lesions were debrided from the most severe side of vertebral body damage or larger side of the abscess to fully expose the abscess. First, a thick needle was inserted into the abscess and suction was applied to remove the pus. Subsequently, the cavity was cut open and the wall of the cavity was shaved with a large-head spatula to expose the bone fistula. The diseased vertebral body was identified along the bone fistula, the vertebral segment vessels were ligated and then the affected disc and damaged bone were exposed and resected. Spinal canal decompression was performed in patients with spinal cord injury, and granulated tissue and pus in the spinal canal were removed. When the lesion wall was resected, particularly the sclerotic wall, cutting, grinding and chipping procedures were adopted to completely and uniformly remove the sclerotic wall surface (approximately 2.0–4.0 mm). The pathological bone bridges were completely resected. Multiple cavities

were excised and cut open. After complete debridement, the remaining interspace was formed into the shape of a regular rectangle or square, and a large piece of iliac bone was harvested and embedded as a strut graft. At 2 weeks postoperatively, various imaging examinations were performed, and the obtained images were used to determine whether the lesion was completely removed. Images were evaluated by two chief physicians (WDJ and ZLW) and the operating surgeons, according to the stated requirements. At 3 weeks following surgery, ambulation was started while the patients were wearing braces.

### **Implementation of ultra-short-course chemotherapy**

A regimen of SHRZ for 2 months/HRZ for 1–2 months was applied after surgery, using the same dose and route of administration as those used before surgery. A quadruple regimen of SHRZ was utilized as intensive chemotherapy, and a triple regimen of HRZ was adopted as consolidation chemotherapy. The whole course of chemotherapy was supervised. Supportive treatments were given to patients who experienced side effects, and the chemotherapy regimen was changed accordingly. If necessary, one or several of the drugs in the regimen were withdrawn temporarily. Anti-tuberculosis treatment was terminated when the lesion was determined to be cured. The indicators of healing were as follows: (1) systemic and local symptoms and signs had disappeared or were alleviated; (2) erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were restored normal; and (3) imaging examinations showed no tuberculosis lesions and bone fusion was achieved. These indicators were assessed at 15 days and 1 month after surgery, then once a month thereafter. If the first two of these indicators were normalized, the third

indicator was checked until the lesion was cured.

### **Follow-up outcomes**

A self-designed data collection system was adopted to establish a database of patients with spinal tuberculosis. Regular follow-up and supervision were carried out by a specifically assigned member (JDS) of the present team. Postoperative follow-up was performed at 6 months after surgery and once a year thereafter until 10 years after surgery. Follow-up observational parameters were as follows: (1) general condition; (2) ESR and CRP levels, and liver and kidney function parameters; (3) neurologic recovery; (4) bone fusion and lesion healing, measured using computed tomography (CT) and magnetic resonance imaging (MRI) scans, showing that the bone graft interface was blurred, trabecular bones were produced, the bone graft was corpulent, and the bone graft was remodelled; (5) kyphosis correction and long-term loss of correction; and (6) instances of failure to heal and relapse.

### **Statistical analyses**

Data are presented as mean  $\pm$  SD or  $n$  (%) prevalence, and were analysed using simple descriptive statistics.

## **Results**

### **Baseline data**

Data from a total of 60 patients with spinal tuberculosis were included in the study, comprising 26 male and 34 female patients aged 16–78 years (mean age,  $40.85 \pm 16.50$  years). Twenty-three patients had anorexia, weight loss, fever and night sweats; 26 patients developed fatigue; and 56 patients suffered from a painful lesion. According to the American Spinal Injury Association (ASIA) classification, two cases were

classified as grade B (nerve injury is located below the plane, including sensory function in the sacral segment without motor function); three as grade C (motor function is retained below the nerve injury plane, and the muscle strength of at least half of the key muscles is <Grade III); 15 as grade D (motor function is retained below the nerve injury plane, and at least half of the key muscles have muscle strength  $\geq$  Grade III); and 40 as grade E (sensory and motor functions are normal). Abscess formation was detected in 38 cases, sequestrum in 53 cases, sclerosis in 45 cases, pathological bone bridges in 10 cases and tuberculous cavity in 50 cases. No sinus formation was observed in any case. Lesions were identified in the cervical spine in one case, the thoracic spine in 28 cases, the lumbar spine in 29 cases and the sacral spine in two cases. A single segment was involved in 48 cases, double segments in six cases, and triple segments or more in six cases. Seventeen patients presented with kyphosis with a mean Cobb angle of  $29.82 \pm 8.62^\circ$ . The mean ESR was  $37.25 \pm 19.98$  mm/h (range, 23–71 mm/h), and the mean CRP level was  $27.13 \pm 14.05$  mg/l (range, 7.1–60 mg/l).

As shown in Table 1, the mean course of postoperative chemotherapy was

$3.61 \pm 0.47$  months (range, 3–4 months). The mean follow-up duration was  $70.61 \pm 28.37$  months (range, 25–129 months). At two weeks after surgery, plain or enhanced CT and MRI scans showed that the sclerotic wall, multiple cavities, pathological bone bridges and sequestrum, abscess, granulation tissue, caseous necrotic substance, sinus, and necrotic disc were completely removed compared with those signs observed before surgery (Figure 1A–C). The imaging results were determined by two chief physicians (WDJ and ZLW) and one surgeon (JDS).

### Postoperative chemotherapy-related symptoms

During postoperative chemotherapy, adverse reactions to anti-tuberculosis drugs occurred in 10 patients (16.67%). Five patients experienced gastrointestinal reactions, two had mouth numbness, two developed tinnitus, two had blurred vision, two experienced rash and one patient presented with liver dysfunction (Table 2). At the end of chemotherapy, no tuberculosis-related symptoms, such as fever, night sweats, or weakness, were observed in any patient. No local pain,

**Table 1.** Baseline demographic and clinical data in patients with spinal tuberculosis.

Parameter	Postoperative wound infection status	
	Without infection ( $n = 58$ )	With infection ( $n = 2$ )
Male/female	25/33	1/1
Mean age, years	38.75	72.50
Segment involvement (single/double/multiple segments)	48/6/4	0/0/2
Mean preoperative ESR, mm/h	45	36.98
Mean preoperative CRP level, mg/l	28.5	21.50
Surgical approach (anterior/posterior/anterior plus posterior)	14/4/42	0/0/2
Mean preoperative albumin, g/l	35.33	31

Data presented as mean or  $n$  prevalence.

ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.



**Figure 1.** Representative images from a 29-year-old female patient diagnosed with spinal tuberculosis in T10–11. Surgical treatment comprised one-stage posterior T10, 11 pedicle screw fixation, posterolateral fusion and anterior complete removal of tuberculosis lesion, and strut grafting using the iliac bone: (A and B) preoperative sagittal computed tomography (CT) scan and magnetic resonance image (MRI) showing T10–11 vertebral body destruction with abscess and sequestrum formation; (C) sagittal CT image obtained 2 weeks after surgery showing complete debridement and reliable bone grafting; (D) sagittal CT image obtained 4 months after surgery showing bone healing (antituberculosis drugs were consequently withdrawn); (E and F) CT images at 5 years after surgery showing bone healing and remodelling.

abscess or sinus was reported. Normal daily life and working abilities were recovered. The mean ESR level was  $8.08 \pm 4.70$  mm/h, and mean CRP level was  $1.06 \pm 0.51$  mg/l. Ultrasonography demonstrated no cold abscess formation, and CT scanning at 4 months postoperatively revealed that the bone graft interface was blurred, trabecular

bones were produced, and no new tuberculosis lesion was formed (Figure 1D).

#### *Follow-up outcome assessment*

During the final follow-up visit, all patients were cured and free of symptoms, such as fever, night sweats, weakness or local pain.

**Table 2.** Adverse drug reactions in 10 patients with spinal tuberculosis.

Patient	Adverse reaction						Drug associated with adverse reaction
	Gastrointestinal reaction	Numb mouth	Tinnitus	Blurred vision	Rash	Liver dysfunction	
1		+		+			INH
2						+	RFP
3	+				+		RFP
4		+		+			INH
5			+		+		SM
6	+						-
7			+				SM
8	+						-
9	+						-
10	+						-

+, adverse reaction; -, specific drug causing adverse reaction was unknown, symptoms disappeared after symptomatic treatment; INH, isoniazid; RFP, rifampicin; SM, streptomycin.

**Table 3.** Recovery of postoperative American Spinal Injury Association (ASIA) neurological function grade in 60 patients with spinal tuberculosis.

Preoperative ASIA classification	n	ASIA classification at the final follow-up				
		A	B	C	D	E
A	0					
B	2				2	0
C	3				1	2
D	15					15
E	40					40

ASIA grade A, no sensory and motor function in the sacral segment of spinal cord (S4 and S5); B, nerve injury is located below the plane, including sensory function in the sacral segment without motor function; C, motor function is retained below the nerve injury plane, and the muscle strength of at least half of the key muscles is < Grade III; D, motor function is retained below the nerve injury plane, and at least half of the key muscles have muscle strength  $\geq$  Grade III; and E, sensory and motor functions are normal.

All patients were recovered and had normal daily life and work abilities. The mean ESR level was  $4.53 \pm 4.13$  mm/h and the mean CRP level was  $1.08 \pm 0.72$  mg/l. Two patients had postoperative wound infection, which was subsequently cured after debridement and drainage. The ASIA grades were improved after surgery: grade B was improved to grade D in two cases, grade C was improved to grade D in one case and grade E in two cases, and grade D

was improved to grade E in 15 cases (Table 3). CT scans showed that all patients had bone healing and remodelling (Figure 1E and F). Following surgery, the mean Cobb angle was  $14.82 \pm 6.22^\circ$  (range,  $5-26^\circ$ ) in 17 patients with kyphosis, and at the final follow-up assessment, the mean Cobb angle was  $17.66 \pm 5.06^\circ$  (range,  $9-33^\circ$ ). The degree of correction was  $15.00 \pm 7.26^\circ$ , the loss of correction was  $2.84 \pm 3.72^\circ$ , and the rate of correction

loss was 9.52%. The overall correction rate was 50.30% ( $n = 17$ ) and the deformity correction was satisfactory.

### Postoperative recurrence

Postoperative recurrence involving spinal tuberculosis in L4–5 occurred in one patient. The patient was initially treated by posterior internal fixation, anterior debridement and iliac bone grafting. At 4 months after surgery, the lesion was healed and drugs were withdrawn. At 6 years post-surgery, tuberculosis recurred in L4–5, which was treated by anterior debridement and bone grafting. After surgery, the patient was treated with SHRZ for 2 weeks followed by HRZ for 22 weeks and was cured after 24 months.

### Discussion

In the present study, 60 patients with spinal tuberculosis underwent 3–4-month postoperative chemotherapy on the basis of complete debridement. The long-term follow-up showed that only one patient (1.67%) experienced a recurrence, and all other patients (98.3%) were effectively cured. The Cobb angle was improved after surgery in 17 patients with thoracolumbar kyphosis, with a correction rate of 50.30%. The ASIA grades were improved, and daily life and work abilities were recovered in all patients. Bone fusion was achieved, lesions were healed, and outcomes were satisfactory. Compared with the results of Jin *et al.*<sup>10</sup> and Cui *et al.*<sup>11</sup> in the treatment of spinal tuberculosis by debridement, the recurrence rate in the present study was relatively low even though ultra-short-course chemotherapy was adopted. Notably, Jin *et al.*<sup>10</sup> and Cui *et al.*<sup>11</sup> adopted antituberculosis treatment with a duration of 1–1.5 years. Spinal tuberculosis cannot be efficiently treated by prolonging the course of chemotherapy alone without paying attention to the

surgical method. Incomplete debridement is a risk factor for postoperative recurrence and non-healing in patients diagnosed with spinal tuberculosis.<sup>12,13</sup> In the present study, the sequestrum was removed, and abscess, granulation tissue, caseous necrotic substance, sinus and necrotic discs were also eliminated to approximately 4 mm of the sclerotic wall surface. In addition, multiple cavities and pathologic bone bridges were removed until the sub-normal bone appeared.<sup>6</sup> The sclerotic wall is made up of dense laminae and is a bony barrier between the centre of the lesion and the diseased vertebra, which limits the absorption of antituberculosis drugs into the lesion.<sup>14</sup> Complete debridement can eliminate the sclerotic walls and facilitate the uptake of tuberculosis drugs to effectively kill residual *Mycobacterium tuberculosis*.<sup>15</sup> In addition, complete debridement can simplify the process of tuberculosis healing and can speed up bone graft fusion. The presence of dormant bacteria has been considered as the main cause of tuberculosis recurrence.<sup>16–18</sup> In contrast, complete debridement can eliminate dormant bacteria in the lesion and remove the source of recurrence. Antituberculosis drug treatment plays a pivotal role in the treatment of spinal tuberculosis.<sup>19–21</sup> First-line antituberculosis drugs can effectively treat spinal tuberculosis, kill *M. tuberculosis* during its phases of both rapid proliferation and slow growth, and have strong antibacterial activities, relatively few side effects, and relatively long half-lives. The combination of rifampicin with streptomycin and isoniazid enhances the therapeutic efficacy of these drugs, and combined use of pyrazinamide and other first-line antituberculosis drugs can enhance the antibacterial activity of the other drugs.<sup>22</sup> Therefore, chemotherapy regimens containing first-line antituberculosis drugs, SHRZ for 2 months/HRZ for 1–2 months, were adopted in the present study. A quadruple regimen of SHRZ was chosen during



the phase of rapid proliferation to kill *M. tuberculosis* quickly, and then a triple regimen of HRZ was adopted during the phase of slow growth to prevent the resurgence of *M. tuberculosis*.

Patient compliance with standard chemotherapy regimens is poor due to the long course of treatment and extensive adverse reactions to chemotherapy drugs. As recommended by the World Health Organization, the use of directly observed treatment short-course (DOTS) is an effective strategy to improve the healing rate in tuberculosis patients receiving chemotherapy.<sup>23</sup> DOTS chemotherapy was also employed in the present study as follows: (1) a patient database was established and supervised by a specifically assigned professional; (2) the supervisor monitored patients taking the medicines; (3) follow-up cards were given to patients to guide them to take medicines and present at a follow-up visit according to information on the cards; (4) the patients were supervised by regular text messages, phone calls, and via the internet. The findings in the present study demonstrated that ultra-short-course chemotherapy (less than 4 months) in combination with complete debridement may yield a high level of clinical efficacy and safety in the treatment of spinal tuberculosis. Nevertheless, the current results may be limited by the fact that this was a retrospective study conducted at a single centre involving a small sample size and relatively short chemotherapy duration. Therefore, further multicentre, large-sample prospective studies are urgently required to validate the current results.

## Conclusions

Postoperative ultra-short-course chemotherapy for 3–4 months may be an efficacious treatment of spinal tuberculosis. Complete debridement combined with ultra-short-course chemotherapy may

enhance clinical efficacy, lower the recurrence rate, lower the incidence of adverse drug reactions, reduce treatment cost and increase patient compliance. The therapeutic safety and efficacy shown in the present study requires validation by clinical trials with a large sample size.

## Acknowledgments

We thank the reviewers and editors for their helpful comments on this article.


## Declaration of conflicting interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the National Natural Science Foundation of China (grant number 81660370, and grant number 81460336), and Ningxia Hui Autonomous Region focus on Research and Development Program (grant number 2016-25).

## ORCID iD

Zili Wang  <https://orcid.org/0000-0002-9309-0898>

## References

1. Wang Z, Shi J, Geng G, et al. Ultra-short-course chemotherapy for spinal tuberculosis: five years of observation. *Eur Spine J* 2013; 22: 274–281.
2. Controlled clinical trial of short-course (6-month) regimens of chemotherapy for treatment of pulmonary tuberculosis: East African/British medical research councils. *Lancet* 1972; 299: 1079–1085.
3. Merle CS, Fielding K, Sow OB, et al. A four-month gatifloxacin-containing regimen for treating tuberculosis. *N Engl J Med* 2014; 371: 1588–1598.
4. Controlled trial of short-course regimens of chemotherapy in ambulatory treatment of spinal tuberculosis: results at three years

- of a study in Korea. Twelfth report of the Medical Research Council Working Party on tuberculosis of the spine. *J Bone Joint Surg (Br)* 1993; 75: 240–248.
5. A controlled trial of six-month and nine-month regimens of chemotherapy in patients undergoing radical surgery for tuberculosis of the spine in Hong Kong. Tenth report of the Medical Research Council Working Party on Tuberculosis of the Spine. *Tubercle* 1986; 67: 243–259.
  6. Jin W, Wang Q, Wang Z, et al. Complete debridement for treatment of thoracolumbar spinal tuberculosis: a clinical curative effect observation. *Spine J* 2014; 14: 964–970.
  7. Jin W, Wang Q, Wang Z, et al. Compare of complete and incomplete radical debridement for thoracolumbar spinal tuberculosis. *Chin J Orthop* 2014; 34: 196–203 [In Chinese, English abstract].
  8. Shi JD, Wang Q and Wang ZL. The range of fusion and internal fixation for thoracic and lumbar tuberculosis. *Chin J Orthop* 2016; 36: 745–752 [In Chinese, English abstract].
  9. Shi JD, Wang Q and Wang ZL. Primary issues in the selection of surgical procedures for thoracic and lumbar spinal tuberculosis. *Orthop Surg* 2014; 6: 259–268.
  10. Jin G, Yao L, Cui Y, et al. Study on the risk factors associated with postoperative recurrence of spinal tuberculosis. *Chin J Spine Spinal Cord* 2007; 17: 516–519 [In Chinese].
  11. Cui X, Ma Y, Chen X, et al. The causes and surgical strategy of spinal tuberculosis retreatment. *Chin J Orthop* 2017; 37: 65–73 [In Chinese].
  12. Khoo LT, Mikawa K and Fessler RG. A surgical revisit of Pott distemper of the spine. *Spine J* 2003; 3: 130–145.
  13. Rajasekaran S, Soundararajan DCR, Shetty AP, et al. Spinal tuberculosis: current concepts. *Global Spine J* 2018; 8: 96S–108S.
  14. Wang Q and Ma WX. Osteoarticular tuberculosis: bone Lesions drug distribution characteristics and sustained-release material. *Chinese Journal of Tissue Engineering Research* 2015; 19: 7859–7859 [In Chinese].
  15. Ge Z, Wang Z and Wei M. Measurement of the concentration of three antituberculosis drugs in the focus of spinal tuberculosis. *Eur Spine J* 2008; 17: 1482–1487.
  16. Drusano GL, Neely M, Van Guilder M, et al. Analysis of combination drug therapy to develop regimens with shortened duration of treatment for tuberculosis. *PLoS One* 2014; 9: e101311.
  17. Koul A, Vranckx L, Dendouga N, et al. Diarylquinolines are bactericidal for dormant mycobacteria as a result of disturbed ATP homeostasis. *J Biol Chem* 2008; 283: 25273–25280.
  18. Singh R, Manjunatha U, Boshoff HIM, et al. PA-824 kills nonreplicating Mycobacterium tuberculosis by intracellular NO release. *Science* 2008; 322: 1392–1395.
  19. Rajasekaran S and Khandelwal G. Drug therapy in spinal tuberculosis. *Eur Spine J* 2013; 22: 587–593.
  20. Nene AM, Patil S, Kathare AP, et al. Six versus 12 months of anti tubercular therapy in patients with biopsy proven spinal tuberculosis: a single center, open labeled, prospective randomized clinical trial-a pilot study. *Spine (Phila Pa 1976)* 2019; 44: E1–E6.
  21. Ali A, Musbahi O, White VLC, et al. Spinal tuberculosis: a literature review. *JBJS Rev* 2019; 7: e9.
  22. Yin CY, Leng DL and He ZG. Advances in the research of anti-tuberculosis drugs. *Journal of Shenyang Pharmaceutical University* 2015; 32: 77–83 [In Chinese].
  23. Steffen R, Menzies D, Oxlade O, et al. Patients' costs and cost-effectiveness of tuberculosis treatment in DOTS and non-DOTS facilities in Rio de Janeiro, Brazil. *PLoS One* 2010; 5: e14014.