

Sp15: How long should drug therapy be given in patients responding well to anti-tubercular medications?

RN Dunn, B Ndeleva, HS Chhabra, S Rajasekaran

Recommendation:

There is increasing recent evidence to support 6 month (2RHZE/4RH) chemotherapy in clinically responding patients, especially when combined with radical surgical debridement. However, little is reported on concomitant TB-HIV infection.

Level of Evidence: moderate

Delegate Vote

Rationale:

Since the adoption of intensive RHZE 2 months and RH continuation phase, most authors report a 9-12 month chemotherapy duration.[1-3]

Prior to this, MRC studies using PAS and Streptomycin as part of the therapy studied shorter courses of 6 and 9 months combined with radical surgery. At multiple sites, with 5 year outcomes the authors reported similar results irrespective of duration. [4, 5]

Rajeswari in an older study regarded 9 months as a short course, with streptomycin, RHE, and in a study of 33 patients reported that with surgery, was effective.[6]

Ramchandran raised concern in a small study of 34 patients where 5/8 patients treated with 6 months 2RHZE/4RH had a relapse, whereas the 30 patients with 9 months chemotherapy had no relapse.[7]

Cormican confirmed this concern in a small series of 21 patients where MRI was performed at 6 and 12 months after initiation of chemotherapy (2RHZE/RH). They suggested 6 months may not be adequate to achieve disease resolution.[8]

Jain reported on 51 patients with 8 month chemotherapy with MRI confirmed healing as the endpoint. They found only 35% had confirmed healing at 8 months and concluded that it was unscientific to stop chemotherapy at a fixed time point. [9]

Dai reported on anterior surgery and three drugs (RHE) for a full 9 months with all 57 cases healing and favourable outcome with a 5.5 year follow up. [10]

More recently there have been more reports on 6 month duration, usually in combination with radical debridement of the septic focus.

Wang randomised 185 radically debrided patients to short course (average 4.5 months and standard 9 months. Both groups has 2 months streptomycin, HRZ followed by HRZ continuation. The average follow up was 69 months. Pain, blood parameters, ability to work, ADLs were similar. However there were increased drug side effects in the longer duration group. The concluded that with thorough debridement, grafting and fixation, short course was of benefit.[11]

Nene compared 6 and 9 month courses in a randomised pilot study with 2RHZE / RH with 28/42 having surgery in 12 month group and 18/52 in the 6 month group. The outcome was similar at 24 months follow up, with no recurrence of disease.[12]

Aryal in a meta analysis of 8 papers and considerable heterogeneity found equivalent healing rates with 6 months therapy as compared to ≥ 9 months. [13]

Lin performed a meta-analysis on the Chinese population, identifying 6 Chinese papers with 851 patients where many appeared to have undergone surgery but not explicitly reported. They found no significant difference in patient outcome undergoing ≤ 6 months as opposed to ≥ 9 -18 months, with lower side effects. [14]

Van Loenhout-Rooyackers performed a literature review to assess the relapse rate with 6 months versus greater than 6 months. There were no relapses in the 6 month group and they concluded that 6 months is probably sufficient. [15]

References:

1. PM, M., et al., *Spinal tuberculosis among human immunodeficiency virus-negative patients in a Kenyan tertiary hospital: a 5-year synopsis*. The spine journal : official journal of the North American Spine Society, 2011. 11(4): p. 265-9.
2. Gupta, A. and M. Arora, *Comparison of Outcomes of Anti-Tubercular Chemotherapy Prescribed for 9 months and 12 months in POTT's Spine*. Journal International Medical Sciences Academy, 2020. 33(4): p. 226 – 233.
3. Park, D.W., et al., *Outcome and management of spinal tuberculosis according to the severity of disease - A retrospective study of 137 adult patients at Korean teaching hospitals*. SPINE, 2007. 32(4): p. E130-E135.
4. SS, U., S. MJ, and Y. AC, *Duration of antituberculosis chemotherapy in conjunction with radical surgery in the management of spinal tuberculosis*. Vol. 21. 1996, United States. 1898-903.
5. J, D., *Five-year assessment of controlled trials of short-course chemotherapy regimens of 6, 9 or 18 months' duration for spinal tuberculosis in patients ambulatory from the start or undergoing radical surgery. Fourteenth report of the Medical Research Council Working Party on Tuberculosis of the Spine*. Vol. 23. 1999, Germany. 73-81.
6. Rajeswari, R., et al., *Short-course chemotherapy in the treatment of Pott's paraplegia: report on five year follow-up*. INTERNATIONAL JOURNAL OF TUBERCULOSIS AND LUNG DISEASE, 1997. 1(2): p. 152-158.
7. Ramachandran, S., et al., *The treatment of spinal tuberculosis: a retrospective study*. INTERNATIONAL JOURNAL OF TUBERCULOSIS AND LUNG DISEASE, 2005. 9(5): p. 541-544.
8. L, C., et al., *Current difficulties in the diagnosis and management of spinal tuberculosis*. Postgraduate medical journal, 2006. 82(963): p. 46-51.
9. Jain, A.K., et al., *Efficacy of extended DOTS category I chemotherapy in spinal tuberculosis based on MRI-based healed status*. INDIAN JOURNAL OF ORTHOPAEDICS, 2012. 46(6): p. 633-639.
10. Dai, L.-Y., et al., *Chemotherapy in Anterior Instrumentation for Spinal Tuberculosis: Highlighting a 9-Month Three-Drug Regimen*. WORLD NEUROSURGERY, 2010. 73(5): p. 560-564.
11. Z, W., et al., *Ultra-short-course chemotherapy for spinal tuberculosis: five years of observation*. European spine journal : official publication of the European Spine

- Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society, 2013. 22(2): p. 274-81.
12. Nene, A.M., et al., *Six <i>versus</i> 12 Months of Anti Tubercular Therapy in Patients With Biopsy Proven Spinal Tuberculosis*. SPINE, 2019. 44(1): p. E1-E6.
 13. Aryal, A., et al., *Is 6 months of Antitubercular Chemotherapy as Effective as More Than 6 months Regimen in Spinal Tuberculosis? A Systematic Review and Meta-Analysis*. ASIAN SPINE JOURNAL, 2021.
 14. Lin, L., Z. Ke, and S. Cheng, *Efficacy and safety of short-term chemotherapy for patients with spinal tuberculosis undergoing surgery in Chinese population: a meta-analysis*. JOURNAL OF ORTHOPAEDIC SURGERY AND RESEARCH, 2021. 16(1).
 15. van Loenhout-Rooyackers, J., A. Verbeek, and P. Jutte, *Chemotherapeutic treatment for spinal tuberculosis*. INTERNATIONAL JOURNAL OF TUBERCULOSIS AND LUNG DISEASE, 2002. 6(3): p. 259-265.