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Oral Therapy with Rifampin Associated with Minocycline or Moxifloxacin in Vertebral Osteomyelitis due to Gram-positive Micro-organisms: a Retrospective Study of 63 Cases[1]

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Abstract

Background:
IDSA guidelines about vertebral osteomyelitis (VO) recommend parenteral antimicrobial therapy (PAT) as the standard treatment for gram-positive pathogens (GPP). In this setting, a switch to oral antimicrobial therapy (OAT) with excellent bioavailability could be considered. However, among fluoroquinolones, moxifloxacin is not recommended in staphylococcal VO, and among tetracycline, only doxycycline is considered with rifampin, for brucelar VO. Our study aims to review the efficacy and safety of rifampin OAT associated with moxifloxacin (Rif-Mox) or minocycline (Rif-Mino) in the treatment of VO due to GPP.
Methods:
Observational, retrospective study in a Belgian teaching hospital, over 10 years. All charts with a diagnosis of VO were reviewed.
Patients with VO who received definite OAT with Rif-Mox or Rif-Mino were included. An episode of VO caused by the same species within 24 months after the initial episode represented a relapse; other situations were considered as recurrences.
Results:
Seventy-four/655 charts matched our inclusion criteria. Eleven were rejected: missing data 6 cases; death before the end of treatment 5 cases, including one death related to VO. Key data are shown in the Figure.
Fifty-three and 10 patients received Rif-Mox and Rif-Mino OAT, respectively. The median duration of PAT and OAT were 15 days and 64 days, respectively and the global treatment median duration was 89 days. The duration of PAT was essentially driven by the presence of an associated bacteremia or endocarditis, particularly in cases due to Staphylococci. Interestingly, OAT without initial PAT was performed in 6 cases without failure.
The follow-up after end of therapy was ≥2 years. There was no recurrence or relapse in Rif-Mino group. In Rif-Mox group, there was 1 recurrence occuring 6 months after the end of therapy. Two others recurrences were observed > 24 months after the end of therapy and were not notified.
No treatment was stopped because of intolerance or significant adverse events.
Conclusion:
OAT with Rif-Mox or Rif-Mino was safe, well tolerated and achieved a high level of cure in VO due to GPPs, including cases with spinal hardware infection.

Background

Spondylodiscitis tends to have an increased incidence over the last decades, and can leads to long term disabilities. Although guidelines exist, there is still no general agreement on management. IDSA guidelines about VO recommend parenteral antimicrobial therapy (PAT) as the standard treatment for Gram-positive pathogens (GPP). In this setting, a switch to oral antimicrobial therapy (OAT) with excellent bioavailability could be considered. However, among fluoroquinolones, moxifloxacin is not recommended in staphylococcal VO, and among tetracyclines, only doxycycline is considered with rifampin, for brucelar VO.

Methods

We performed a retrospective, monocentric, observational study in a Belgian teaching hospital, the CHU of Liège.
655 charts was collected between 1st January 2005 and 31 December 2015 in which the diagnosis of spondylodiscitis or vertebral osteomyelitis was evoqued.
Inclusion criteria: patients with clinical and imaging signs of infectious spondylodiscitis, whatever we had microbiological confirmation or not, who had oral step down after a course of intravenous therapy and received rifampin in association with minocycline or moxifloxacin.
We defined relapse as recurring symptoms with the same organism found, and the same spine level involved within 24 months after the end of treatment. A recurrence was a new infectious episode, without especially the same germ and localization.

Results

Seventy-four charts on 655 matched our inclusion criteria. 11 were rejected: missing data 6 cases; death before the end of treatment in 5 cases.
Patients' characteristics are summarized in table 1.
Most of the patients had acute presentation and hematogenous spread.

Almost every patients had back pain at diagnosis and 63,5% had associated bacteremia. 42,9% had associated abcesses (Table 2).
53 and 10 patients received Rif-Mox and Rif-Mino OAT, respectively.
Five patients received direct oral antibiotherapy without initial intravenous therapy; 15 patients received empirical intravenous therapy before switch to oral therapy (Table 3).

The most frequent microorganism was *Staphylococcus aureus*. In second place, it was coagulase-negative Staphylococci (CoNS) (figure 1 and figure 2).
Polymicrobial infections included 2 cases of CoNS + *Propionibacterium acnes*; 1 case of *Streptococcus* + *Propionibacterium acnes*; 2 cases of MSSA + *Propionibacterium acnes*; and 1 case of *Propionibacterium acnes* + *Peptostreptococcus*.

The follow-up after end of therapy was ≥2 years.

There was no recurrence or relapse in Rif-Mino group.
In Rif-Mox group, there was 1 recurrence occuring 6 months after the end of therapy. Two others recurrences (vs re-infection) were observed > 24 months after the end of therapy and were not notified.
Seven patients died during the 24-months follow-up after completion of therapy, none from VO.

No treatment was stopped because of intolerance or significant adverse events.
The duration of parenteral therapy was essentially driven by the presence of an associated bacteremia or endocarditis, particularly in cases due to Staphylococus aureus.
Interestingly, OAT without initial PAT was performed in 5 cases without failure.
Those data tends to confirm our results of treatment of bone and joint infections with moxifloxacin (unpublished data).

Figure 1: Minocyclin group, N=10

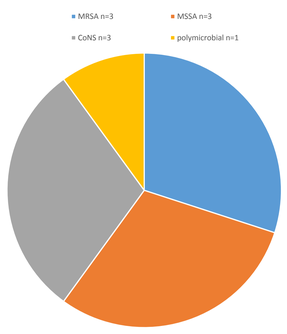

Figure 2: Moxifloxacin group, N=53

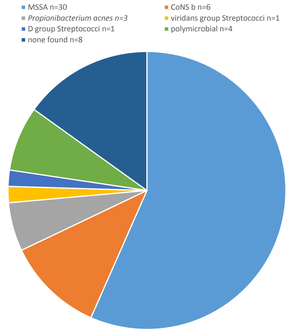

Table 1: Patient's characteristics

Number of patients	63
Male/female	43/20
Age (median [range])	65 [28,2-86,5]
Comorbidities	48
Diabetes	12
Lymphopenia	2
Chronic renal failure (GFR<45ml/min)	9
Immunocompromised	7
Spinal hardware	6
Neoplasia	10
treatment in progress	*1*
Alcoholism	14
Drug use	2
Active smoking	22

Table 2: clinical presentation

Onset circumstances	
Spontaneous	52 (82,5%)
Post surgical/procedure	10 (15,8%)
Contigous to wound	1 (1,6%)
Early post operative (<3 weeks) hardware-associated infection	3 (4,7%)
Onset presentation	
Acute[a]	30 (47,6%)
Subacute[b]	14 (22,2%)
Chronic[c]	19 (30,1%)
Clinical signs at diagnosis	
Fever >38°C	20 (31,7%)
Back pain	59 (93,6%)
Neurological impairement	7 (11,1%)
Sepsis[d]	3 (4,7%)
Septic shock	0 (0%)
Associated pathologies	
Positive blood cultures	40 (63,5%)
Endocarditis	6 (9,5%)
Abscess	27 (42,9%)
Drained	15/27
Surgical drainage	8/15
CT guided drainage	7/15

[a] symptoms for < 2 weeks
[b] symptoms for 2 to 6 weeks
[c] symptoms for > 6 weeks
[d] 2016 definition

Table 3: treatment

Documented intravenous therapy	43
Vancomycine	10 (23,2%)
Ceftriaxone	3 (7%)
Flucloxacillin	25 (58,1%)
Penicillin alone	2 (4,6%)
Penicillin + aminoglycoside	3 (7%)
Treatment duration ; days	values
Intravenous course	15 [4-109][a,b]
Oral course	64 [4-172][a]
Total antibiotherapy	89 [39-213][a]

[a] median [range]
[b] 58 patients had initial intravenous therapy

Table 4: Follow up

Moxifloxacin group	53
Recurrence	1 (1.9%)
Relapse	0
Death within 24 months of follow-up	6[a]
Minocycline group	10
Recurrence	0
Relapse	0
Death within 24 months of follow-up	1[b]

[a] One case due to associated infection (uncontrolled prosthetic joint infection); 5 cases due to other or unknown cause
[b] Not VO related

Conclusion

Oral antibiotherapy with rifampin – moxifloxacin or rifampin – minocycline was safe, well tolerated and achieved a high level of cure in vertebral osteomyelitis due to Gram-positive pathogens, including cases with spinal hardware infections.

[1] we presented initially 64 cases, but after data reviewing, due to encoding error, only 63 cases matches our inclusion criterium

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