



Estimation of ^{99m}Tc -ciprofloxacin accumulation indexes in bone and joint bacterial infections

Procena indeksa akumulacije ^{99m}Tc -ciprofloksacina u bakterijskim infekcijama kostiju i zglobova

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Abstract

Background/Aim. ^{99m}Tc -ciprofloxacin is a radiopharmaceutical preparation synthesized to improve diagnostic accuracy of bacterial infections in human tissues. It is mostly applied in diagnosis of bone and joint infections. Many papers have confirmed its sensitivity to infection, but newer papers argued its specificity. The aim of this study was to compare the results of visual analysis of scintigrams to semiquantitative calculations of accumulation indexes with the assumption that calculation of indexes would improve the specificity for bone and joint infections. **Methods.** We examined 40 patients, 25 with confirmed bone and joint bacterial infections and 15 patients with bone and joint diseases without bacterial infection. Scintigraphy was performed 5 minutes, 1, 4 and 24 hours after intravenous (*iv*) injection of ^{99m}Tc -ciprofloxacin. Scintigrams were analysed visually and by calculation and comparison of accumulation indexes values. **Results.** Visual sensitivity was 94%, but specificity only 47%. Index calculation achieved much higher specificity (100% after 1, 4 and 24 hours for cut off value of 1.50). All basic index values (5 min) in the patients with infections increased in 24 hours. In 8 patients without infection occurred a slight increase and in 7 patients decrease of basic index values. **Conclusion.** Calculation of accumulation index values is needed in the use of ^{99m}Tc -ciprofloxacin scintigraphy as it is the only way to improve specificity for bacterial bone infections. Visual interpretation of results is sensitive, but not specific due to accumulation of the drug in a high percent of non infected bone and joint lesions.

Key words:

organotechnetium compounds; radionuclide imaging; bone and bones; joints; infection; sensitivity and specificity.

Apstrakt

Uvod/Cilj. ^{99m}Tc -ciprofloksacin je radiofarmak koji je sintetisan radi povećanja tačnosti dijagnostike bakterijske infekcije ljudskog tkiva. Najviše se primenjuje u dijagnostici bakterijskih infekcija u kostima i zglobovima. Mnogi radovi potvrdili su da je osetljiv za otkrivanje infekcije, ali su noviji radovi osporili njegovu specifičnost. Cilj rada bio je da se uporede rezultati vizuelne analize scintigrama sa semikvantitativnim izračunavanjem indeksa akumulacije uz pretpostavku da će izračunavanje indeksa poboljšati specifičnost u dijagnostici infekcije kostiju i zglobova. **Metode.** Ispitano je 40 bolesnika, 25 sa potvrđenom bakterijskom infekcijom kostiju i zglobova i 15 bolesnika sa oboljenjem kostiju i zglobova bez bakterijske infekcije. Posle intravenskog (*iv*) davanja ^{99m}Tc -ciprofloksacina rađena je scintigrafija nakon 5 minuta, 1, 4 i 24 sata. Scintigrami su analizirani vizuelno i izračunavanjem i poređenjem vrednosti indeksa akumulacije. **Rezultati.** Vizualnom analizom dobijena je osetljivost 94%, a specifičnost samo 47%. Izračunavanjem indeksa postignuta je mnogo veća specifičnost (posle 1, 4 i 24 h 100% za graničnu vrednost 1,50). Sve vrednosti indeksa kod bolesnika sa infekcijom povećavale su se u toku 24 h, kod osam bolesnika bez infekcije pokazale su mali porast, a kod sedam smanjenje. **Zaključak.** Izračunavanje indeksa akumulacije neophodno je pri korišćenju ^{99m}Tc -ciprofloksacina i jedini je način da se poveća specifičnost scintigrafije. Vizuelna interpretacija rezultata je osetljiva, ali nespecifična zbog akumulacije radiofarmaka u znatnom procentu lezija kostiju i zglobova bez bakterijske infekcije.

Ključne reči:

organotehnećijumska jedinjenja; scintigrafija; kosti; zglobovi; infekcija; osetljivost i specifičnost.

Introduction

Diagnosis of bone and joint bacterial infections nowadays remains a diagnostic challenge. Standard radiological

methods (radiography, computerized tomography magnetic resonance images, ultrasonography) are not adequately sensitive or specific. Nuclear medicine methods – bone scintigraphy, leukocyte scintigraphy, gallium and monoclonal anti-

body scanning – are sensitive, but insufficiently specific since they are used to confirm inflammation that is not always caused by bacterial infection. In the middle of the last decade of the 20th century ^{99m}Tc labelled ciprofloxacin (^{99m}Tc -CIP) was introduced with hope to improve diagnostic specificity for bacterial infection¹⁻³. Recent papers have diminished its diagnostic value because of a lack of specificity, likewise other nuclear medicine radiopharmaceuticals⁴⁻⁶. All the above cited papers are mostly based on subjective visual estimation of scintigrams.

The aim of this study was to compare the results of visual analysis of scintigrams to semiquantitative calculations of accumulation indexes with the assumption that calculation of indexes would improve specificity for bone and joint infections.

Methods

We examined 40 patients, divided into the group A (n = 25) with confirmed bone and joint bacterial infections (patients with osteomyelitis, arthritis, infected prosthesis, and spondylodiscitis) and the group B (n = 15) with pathological noninfective changes (patients with arthrosis, non-infected prosthesis and trauma). Infections were diagnosed on the basis of clinical findings, laboratory and diagnostic results and in all patients confirmed by microbiological analysis. In the group B, infections were excluded by the same methods as for the infection group, except the microbiological analysis. Scintigraphy was performed by using 1 mg ciprofloxacin labelled with 740 MBq of ^{99m}Tc (Institute of Nuclear Sciences Vinča, Serbia). Scintigraphy was performed after 5 minutes, and 1, 4 and 24 hours after intravenous (*iv*) injection. Scinti-

grams were analysed visually and accumulation indexes were calculated after all imaging time periods. Visual score (VS) was semiquantitative: value 0 – normal accumulation, 1 – slightly increased accumulation, and 2 – increased accumulation of ^{99m}Tc -CIP. For all calculations regions of interest were constructed over pathological area without concern about visual finding (normal or increased accumulation of ^{99m}Tc -CIP) and on contralateral side (in the axial skeleton an area adjacent to the lesion). The statistical Friedman test and Wilcoxon signed rank test were used to test differences between the results after all imaging times in both groups, while Mann Whitney U test was used to test differences between the groups with and without infections.

Results

In 21 patients with infection, visual abnormal findings (score 1 and 2) were recorded after 4 h (sensitivity 84%) and in 24 patients after 24 h (sensitivity 96%). In all the patients of this group accumulation index increased with time (Table 1, Figure 1). In the patients without infection 9 out of 15 patients had false positive visual finding up to 4 h (specificity 40%) with a slight improvement after 24 h (specificity 47%). The index values in all control patients did not exceeded 1.50. In 7 patients the index gradually decreased, and in 8 patients slightly increased (Table 2). A statistical difference between index values in the group A was found ($p < 0.01$) except the values between 5 min and 1 h ($p > 0.05$). A statistical difference between index values in both groups was significant ($p < 0.01$). Any values of index in the group A were increased with time up to 24 h. The lowest increasing value was 0.07 and the highest one 0.39. Index values in the

Table 1
Visual scores (VS) and accumulation index (AI) values in patients with infection

Patient (number)	Time after <i>iv</i> injection of ^{99m}Tc -ciprofloxacin							
	5 min		1 h		4 h		24 h	
	VS	AI	VS	AI	VS	AI	VS	AI
1	2	1.85	2	2.02	2	2.18	2	2.18
2	2	2.05	2	2.09	2	2.09	2	2.16
3	2	2.08	2	2.18	2	2.34	2	2.34
4	2	2.23	2	2.36	2	2.58	2	2.61
5	2	1.94	2	1.85	2	1.87	2	2.06
6	2	1.73	2	1.67	2	1.70	2	1.80
7	2	1.50	2	1.67	2	1.71	2	1.71
8	2	3.55	2	3.52	2	3.71	2	3.75
9	2	2.00	2	2.02	2	2.11	2	2.15
10	2	2.60	2	2.50	2	2.56	2	2.72
11	2	2.85	2	2.72	2	2.81	2	3.08
12	2	1.64	2	1.67	2	1.71	2	1.71
13	2	3.25	2	3.03	2	3.15	2	3.33
14	2	1.52	2	1.60	2	1.73	2	1.73
15	2	1.96	2	1.91	2	2.00	2	2.22
16	1	1.27	1	1.40	1	1.50	1	1.66
17	1	1.43	1	1.53	1	1.56	1	1.63
18	2	1.96	2	1.96	2	2.05	2	2.22
19	2	2.00	2	2.02	2	2.03	2	2.08
20	1	1.52	1	1.53	1	1.55	1	1.66
21	2	1.70	2	1.81	2	1.82	2	1.82
22	0	1.27	0	1.29	0	1.39	1	1.50
23	0	1.12	0	1.33	0	1.41	0	1.43
24	0	1.52	0	1.56	0	1.57	1	1.63
25	0	1.35	0	1.45	0	1.54	1	1.66

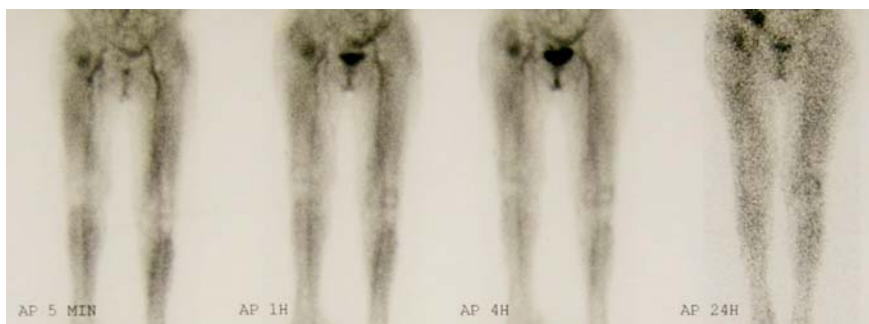


Fig. 1 – Infection of right cox prosthesis (patient N°1) in the group with infection: visual score in any time periods of imaging „2” with index values: 1.82, 2.02, 2.18, 2.18, respectively).

Table 2
Visual scores (VS) and accumulation index (AI) values in patients without infection

Patient (number)	Time after <i>iv</i> injection of ^{99m} Tc-ciprofloxacin							
	5 min		1 h		4 h		24 h	
	VS	AI	VS	AI	VS	AI	VS	AI
1	1	1.30	1	1.30	1	1.30	1	1.25
2	0	1.18	0	1.18	0	1.12	0	1.00
3	2	1.37	2	1.33	2	1.30	2	1.25
4	0	1.07	0	1.11	0	1.15	0	1.13
5	1	1.23	1	1.24	1	1.33	1	1.36
6	1	1.35	1	1.33	1	1.25	1	1.16
7	0	1.15	0	1.16	0	1.16	0	1.17
8	1	1.36	1	1.37	1	1.34	1	1.35
9	0	1.15	0	1.25	0	1.25	1	1.26
10	1	1.50	1	1.48	1	1.37	0	1.27
11	0	1.25	0	1.16	0	1.16	0	1.17
12	0	1.10	0	1.11	0	1.13	0	1.10
13	1	1.29	1	1.29	1	1.31	1	1.32
14	1	1.28	1	1.30	1	1.30	1	1.30
15	1	1.06	1	1.06	0	1.17	0	1.18

group B were constantly decreasing in 8 patients (ratio 0.01 – 0.23). In other patients the index increased (maximal increasing value 0.13). Specificity in all the patients for the cut off value of 1.50 was 100% (Table 3).

analysed values after 1, 4 and 24 h in 11 patients with infection and in 9 patients without infection. They did not find significant differences, although mean index values were higher in patients with infection. It is not unreason-

Table 3
Visual and index sensitivity and specificity in any imaging time periods

Sensitivity and specificity	Time after <i>iv</i> injection of ^{99m} Tc-ciprofloxacin			
	5 min	1 h	4 h	24 h
Sensitivity				
visual	84%	84%	84%	96%
index	80%	84%	92%	96%
Specificity				
visual	40%	40%	40%	47%
index	93%	100%	100%	100%

Discussion

Our results of visual interpretation of scintigrams are in compliance with papers that have confirmed low specificity of ^{99m}Tc-CIP scintigraphy. Dumarey et al.⁴ first argued previous results of Britton et al.³, but later, Sarda et al.^{5,6} confirmed their findings. Accumulation indexes were rarely calculated before by other authors and were published only in abstracts. Recent papers of Sarda et al.^{5,6} deal with the use of indexes in similar way as our work. In their paper based on human data, only patients with visually positive scintigraphic findings were selected for index calculation⁶. They

able, but a larger sample of patients would cause different statistics. Singh et al.⁷ presented their results using different preparation of ciprofloxacin and they correspond to our findings. Our results imply that calculation of accumulation indexes is the only reasonable way to use ^{99m}Tc-CIP. That would not provide an absolute reliable differentiation of bone infection from other bone diseases, but would certainly improve specificity of scintigraphy. We do not state that specificity would always be 100% because it is possible that a patient with noninfective inflammation has index values higher than 1.50, but it is certain that it is far higher than visual specificity.

Conclusion

Calculation of accumulation index values is needed in the use of ^{99m}Tc -ciprofloxacin since it is the only way to im-

prove specificity of scintigraphy for bone and joint infections. Visual interpretation of results is sensitive, but not specific due to a high percent accumulation in non-infected bone and joint lesions.

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