

UTILITY OF MEASUREMENT OF GENTAMICIN RELEASE FROM PMMA BEADS IN WOUND DRAINAGE FLUID AFTER IN-VIVO IMPLANTATION

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Acute or chronic osteomyelitis in 188 patients was treated by surgical debridement and filling of the cavity with gentamicin-PMMA beads. The gentamicin concentration was measured in the total drainage fluid of the first postoperative day. There was no correlation between this concentration and the amount of implanted beads. It is impossible to predict preoperatively the gentamicin concentration which will be obtained in situ. The measurement of gentamicin concentration in the total drainage fluid of the first postoperative day and its comparison to the minimal bactericidal concentration of responsible pathogens, allow very early assessment of the effectiveness of the local antibiotherapy and if necessary, adaptation, of systemic antibiotherapy.

Keywords : PMMA beads ; gentamicin release.

Mots-clés : billes de ciment acrylique à la gentamicine ; libération de gentamicine.

INTRODUCTION

The theoretical indication for local antibiotherapy is the sensitivity of responsible pathogens to the antibiotic used. With gentamicin-polymethylmethacrylate (PMMA) beads, the standard antibiogram, which is based on an approximation of the Minimal Inhibitory Concentration (MIC), is not appropriate, because very high local concentrations of gentamicin can be obtained (7). It is thus logical to measure the Minimal Bactericidal Concentration (MBC) of the pathogens and to compare it with the local gentamicin concentration, which should be greater than the MBC (7).

This local gentamicin concentration can be evaluated by the gentamicin concentration in the drainage fluid of the first postoperative day after gentamicin-PMMA bead implantation, when maximal concentration is obtained (5, 6, 7).

MATERIAL AND METHODS

Acute or chronic osteomyelitis was treated in 188 patients by surgical debridement and filling the cavity with gentamicin-PMMA beads. The wound was closed over Redon drains with a limited 2-hour suction. No systemic aminoglycosides were given. The gentamicin concentration was measured in the total drainage fluid of the first postoperative day. This value was compared to the amount of implanted beads with a correlation test.

RESULTS

The results of measurement of gentamicin concentration for each amount of implanted beads are reported in table I. The correlation coefficient r between these two quantities is 0.1157. The correlation is not significant ($p = 0.057 > 0.05$ — unilateral test — fig. 1).

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Table I. — Amount of implanted beads and measured gentamicin concentration in the total drainage fluid during the first post-operative day

Amount of implanted beads	Number of patients	Gentamicin concentration ($\mu\text{g/ml}$)			
		Minimum	Maximum	Mean	Standard deviation
3	1			115,0	
10	3	30	105	151,3	92,2
15	2	19	190	43,0	13,0
17	1			16,0	
20	5	71	220	139,6	61,4
22	1			310,0	
24	1			260,0	
27	1			137,0	
28	1			18,0	
30	46	13	380	116,4	81,1
35	1			28,0	
40	2	51	114	75,5	33,5
44	1			78,0	
45	1			65,0	
46	1			40,0	
47	1			52,0	
48	4	33	73	171,5	79,8
50	4	60	160	123,0	99,2
52	3	77	203	218,0	137,4
54	1			44,0	
55	1			30,0	
59	1			190,0	
60	35	6	340	111,1	77,0
65	1			109,0	
72	1			190,0	
75	1			180,0	
78	1			67,0	
79	1			56,0	
80	2	62	69	108,0	52,0
85	1			32,0	
90	26	28	230	106,7	98,2
100	1			105,0	
120	11	38	190	61,8	51,2
150	6	2	200	90,3	63,4
156	1			420,0	
180	4	160	440	175,8	98,3
240	5	93	250	103,2	36,0
300	3	98	280	80,7	52,5
330	2	93	93	220,0	90,0
360	1			75,0	
390	2	92	230	142,5	77,5
Mean 79 \pm 72	n = 188	Minimum 2	Maximum 440	Mean 116,7	Standard deviation 88,4

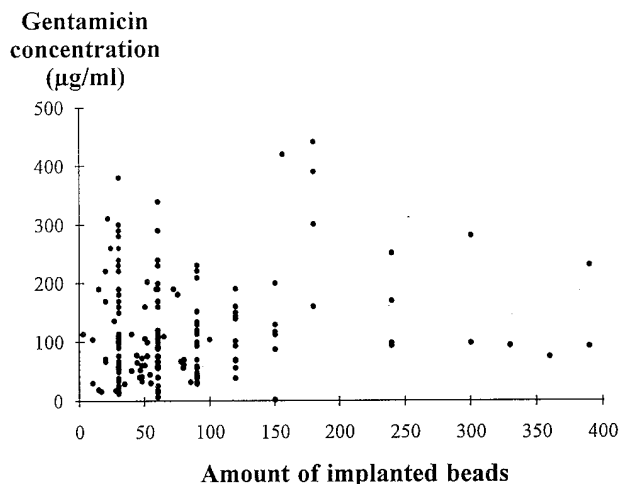


Fig. 1. — Correlation between measured gentamicin concentration in the total drainage fluid during the first postoperative day ($\mu\text{g/ml}$) and the amount of implanted beads.

DISCUSSION

The pharmacokinetics of gentamicin released from PMMA-cement *in vitro* is well known (4) : it is proportional to the contact surface between the cement and the surrounding tissues, to the amount of gentamicin contained in the cement and especially its concentration, and to the liquid flow around the beads. It decreases with time ; the peak concentration is obtained within the first day, and it can reach values from 400 to 600 mg/ml (4). The kinetics of gentamicin release from gentamicin-PMMA beads *in vivo* is comparable (2, 5, 6), but less predictable : Wahlig (6) reported values of 350 mg/ml after implantation of 87 beads, but Lidgren (2) found a concentration of only 17 mg/ml after implantation of 540 identical beads.

The efficiency of antibiotherapy, either local or systemic, depends on the antibiotic concentration obtained *in situ*. For gentamicin, the bactericidal activity depends especially on the local concentration obtained during the first postimplantation or postinjection hours (3). The advantage of gentamicin-PMMA beads is that they release maximal concentrations of gentamicin during this period.

The measurement of local gentamicin concentration in the total drainage fluid of the first post-

operative day is only an approximation, because it cannot measure the actual peak concentration. However, this method is the only one that can be used safely *in vivo*, and it is known to be reliable (1).

The present measured concentrations, compared to the amount of implanted beads are unpredictable. This is not surprising : as the debridement cavity was *filled* with beads, the ratio between the amount of implanted beads, i.e. the amount of implanted gentamicin and the total contact surface of the cement with the surrounding tissues, and the volume of the cavity, remains approximately constant. But the liquid flow around the beads is variable, and this factor alone controls the concentration obtained.

It is obvious that complete filling of the debridement cavity permits a higher concentration than incomplete filling, as a lower quantity of gentamicin is released in the same volume. In other words, it is impossible to know preoperatively the gentamicin concentration which will be obtained *in situ*, and its bactericidal activity.

The measurement of gentamicin concentration in the total drainage fluid of the first postoperative day, allows measurement of this bactericidal activity *in situ* in the first postoperative hours. Comparison to the MBC of responsible pathogens allows very early assessment of the effectiveness of the local antibiotherapy and, if necessary, institution of systemic antibiotherapy with gentamicin or other antibiotics if the local concentration of gentamicin is too low.

CONCLUSION

The measurement of gentamicin release by means of the concentration of gentamicin in the total drainage fluid of the first postoperative day, is a useful criterion in the management of systemic antibiotherapy, after implantation of gentamicin-PMMA beads for acute or chronic osteomyelitis.

REFERENCES

1. Jenny G., Taglang G. Traitement local de l'infection osseuse par des billes de ciment acrylique à la gentamycine. *Acta Orthop. Belg.*, 1979, 45, 57-68.

2. Lidgren L. Discussion. In: Contzen H. Gentamycin-PMMA-Kette. Gentamycin-PMMA-Kugeln. Symposium München 1976, VLE Verlag, 1977, p.34.
3. Sorensen T. S., Sorensen A. I. Bactericidal activity of gentamicin against *S. aureus*; in vitro study questions value of prolonged high concentrations. *Acta Orthop. Scand.*, 1993, 64, 82-84.
4. Wahlig H., Hameister W., Grieben A. Über die Freisetzung von Gentamycin aus Polymethylmethacrylat. I: Experimentelle Untersuchungen in vivo. *Langenbecks Arch. Chir.*, 1972, 331, 193-197.
5. Wahlig H., Dingeldein E. Gentamicin-polymethacrylate beads. Experimental and pharmacokinetic investigations. *Chemotherapy*, 1978, 2, 1021-1028.
6. Wahlig H., Dingeldein E., Bergman R., Reuss K. The release of gentamicin from polymethylmethacrylate beads. *J. Bone Joint Surg.*, 1978, 60-A, 270-272.
7. Walenkamp G. H. I. M. Gentamicin-PMMA-beads. Drukkerij Cliteur, Amsterdam, 1983.

SAMENVATTING

J. Y. JENNY, G. JENNY, J. LAMBERT, J. GAU-DIAS, I. KEMPF. Nut van de meting van de uit PMMA-kralen losgekomen gentamicine in het drainagevocht, na in vivo implantatie.

Honderdachtentachtig patiënten, met een acute of chronische osteomyelitis werden heelkundig behandeld met debridement en opvulling van de excisieholte met Gentamicine PMMA-kralen. De lokale Gentamicine-concentratie werd gemeten d.m.v. het doseren van concentratie in het drainagevocht van de eerste 24 U.

Er werd geen correlatie gezien tussen deze concentratie en het aantal ingebrachte parels. Men kan vóór de ingreep niet voorzien welke Gentamicine-concentratie er in situ zal bereikt worden. Het doseren van de Gentamicine in het drainagevocht van de eerste 24 post-operatieve uren en de vergelijking met de minimale kiemdodende concentratie toont de reële doelmatigheid van lokale antibiotherapie aan, die al dan niet met een algemene antibiotherapie zal moeten aangevuld worden.

RÉSUMÉ

J. Y. JENNY, G. JENNY, J. LAMBERT, J. GAU-DIAS, I. KEMPF. Utilité de la mesure de la libération de gentamicine à partir de billes de ciment acrylique dans le liquide de drainage après implantation in-vivo.

Cent quatre-vingt huit patients porteurs d'une ostéomyélite aiguë ou chronique ont été opérés par débridement chirurgical et remplissage de la cavité d'excision par billes de ciment acrylique à la gentamicine. La concentration locale de gentamicine a été appréciée par le dosage de sa concentration dans le liquide de drainage des 24 premières heures. Aucune corrélation n'a été observée entre cette concentration et le nombre de billes implantées. Il est impossible de prédire avant l'intervention la concentration de gentamicine qui sera obtenue in situ. Le dosage de la gentamicine dans le liquide de drainage des 24 premières heures et sa comparaison avec la concentration minimale bactéricide des germes en cause permet d'apprécier l'efficacité réelle de l'antibiothérapie locale et d'adapter si nécessaire une antibiothérapie générale complémentaire.