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Lavori originali

Original articles

Comparison of incidence of sepsis in cancer patients that underwent systemic or loco-regional chemotherapy

Incidenza di episodi settici in pazienti oncologici sottoposti a chemioterapia sistemica o loco-regionale: confronto fra due semestri

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INTRODUCTION

Sepsis during neutropenia is frequent in cancer patients that underwent chemotherapy. Sepsis is the second cause of death in this kind of patients (1-3). In this study we evaluated the febrile patients in two different periods: January to June 2003 when a systemic chemotherapy was used; January to June 2004 when a loco-regional therapy performed with less toxic drugs was used. In this second period a supportive domiciliary care was started at our oncology department. The aim of the study was to demonstrate a reduction of infections related to the change of therapy and to understand the epidemiology of sepsis in order to manage more wisely empiric antibiotic therapy for febrile neutropenia.

PATIENTS AND METHODS

In this study we enrolled 247 patients in the first six months of 2003 and 398 patients in the first six months of 2004. In these two periods we analyzed 60 patients with fever in 2003 and 34 patient in 2004, respectively. Fever was defined as body temperature >38°C with chills. In these patients 3 blood cultures were drawn from peripheral vein and, when present, from a central

Table 1 - Patients' characteristics.

	2003 (first six months)	*2004 (first six months)*
Hospitalized Patients	247	398
Patients with fever	60 (24,3%)	34 (8,5%)
Positive blood culture	35	12
Mean age (range)	61 (40/82)	59,5 (38/81)
Oncological/Onco-hematological	24/11	10/2
Neutropenic/non neutropenic	18/17	3/9
Porth-a-cath	15	2
CVC	16	6

venous catheter (CVC) or a porth-a-cath before the start of empiric therapy. The same standard laboratory procedures were used in the two periods [4].
The characteristics of the patients enrolled in the study are summarized in Table 1. Sepsis was defined as two or more blood cultures positive for the same microorganism with the same susceptibility and signs and symptoms able to diagnose SIRS [5, 6]. Neutropenia was defined as white blood cells number below 1000/mmc. Informed consensus was asked to every febrile patient before starting this observational study. Ethical committee authorization was not required.

RESULTS

There was an increased number of patients admitted to this oncology unit in the first six months of 2004 (398 vs 247). In the first period examined, we found 60 episodes of fever: in this group of patients we were able to diagnose 35 sepsis; on the other hand in the second period studied we were able to found only 12 episodes of sepsis (1 polymicrobial) among 34 patients with fever. In Table 2 are listed the microorganisms isolated during the two periods studied. Coagulase negative staphylococci (CNS) were the microorganisms more frequently isolated followed by *Escherichia coli* and *Staphylococcus aureus*. In 2004, 9 CNS strains and 2 *S. aureus* strains were methicillin-resistant, 3 out of 7 *E. coli* were multi-drug resistant and the 2 *Enterobacter cloacae* isolated were extended spectrum beta-lactamases producers. No *Pseudomonas aeruginosa* isolate was found. Only one polymicrobial infection (CNS and *Enterococcus faecalis*) was observed in 2004. Patients with solid tumor or haemotological malignancies were in the same rate in the two groups studied. Patients with neutropenia were more frequent during 2003 with respect to 2004 (68,5 vs 25%). In 2003 more patients had a central venous catheter with respect to 2004. The loco-regional therapy has reduced the mean admission time from 9 days in 2003 to 5 days in 2004, respectively. More patients were treated at home in 2004 (150 *vs* 119). In 2004 only 8.5% of patients treated with loco-regional chemotherapy had fever, instead in 2003 during systemic chemotherapy 24.3% of the patients treated experienced fever. No CVC related infection was found.

DISCUSSION

The change from systemic to locoregional and less toxic chemotherapy has brought to a reduction of fever, neutropenia episodes and sepsis in the Oncology Department of Carrara Hospital, Carrara, Italy. Chemotherapy causes a re-

Table 2 - Microorganisms isolated from patients with sepsis in the two periods of observation.

	2003 (first six months)	*2004 (first six months)*
CNS	14	4
E. coli	7	2
S. aureus	5	2
Enterobacter cloacae	2	0
Streptococcus pneumoniae	2	0
Enterococcus faecalis	1	3
Klebsiella spp.	2	0
Pasteurella pneumotropica	1	0
Stenotrophomonas maltophilia	1	0
Streptococcus agalactiae	0	1
Streptococcus mitis	0	1
Total	35	13

duction of leukocytes, disruption of mucosal epytelium and other toxic effects that lead to an increased incidence of infections. The reduced incidence of neutropenia, less patients with CVC and the reduction of hospital admission time has reduced the incidence of sepsis in this oncology ward. The percentage of sepsis observed in the second period (8.5%) is in accord with the results found in literature (4-12). Although microorganisms causing sepsis in oncologic patients are considered endogen, the reduction of time passed by these patients in the hospital in 2004 might explain why there was a sharp reduction in the isolation of multi-drug resistant strains in the second period studied [6, 7, 9, 11]. The change in the management of chemotherapy in fragile patients as oncology patients might result in reduction of severe life-threatening bloodstream infection. The knowledge of the local epidemiology in an oncology department may help to use, in case of fever, a more effective empiric antibiotic therapy.

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Key words: sepsis, cancer patients, chemotherapy

SUMMARY

In this retrospective, non controlled trial we evaluated the incidence of sepsis in cancer patients in two different periods (January-June 2003 versus January-June 2004). The main difference in these two periods was that in our Oncology Department we changed from systemic chemotherapy to loco-regional chemotherapy using less myelosuppressive drugs and developed the domiciliary assistance. The aim of the study was to assess the incidence of sepsis in order to demonstrate a reduction of the infection related to the change of chemotherapy. In addition, this study may be able to describe the epidemiology of sepsis in cancer patients afferent to our Oncology Department. The incidence of sepsis was reduced in the second period from 24.3% to 6.2%. The pathogens more frequently isolated in this study were coagulase-negative staphylococci (CNS) followed by *Escherichia coli* and *Staphylococcus aureus*. Less invasive therapy may reduce infective complications of chemotherapy. The epidemiology of sepsis may be very helpful to design empiric therapeutic protocol for febrile patients that have received chemotherapy.

RIASSUNTO

In questo studio retrospettivo abbiamo valutato l'incidenza di episodi settici in pazienti oncologici in due diversi periodi (gennaio-giugno 2003 e gennaio-giugno 2004).
La scelta di questi due periodi è stata motivata dal fatto che nel nostro reparto abbiamo introdotto l'uso, sempre più frequente, di chemioterapia loco-regionale con farmaci meno mielotossici e abbiamo favorito lo sviluppo e l'ampliamento dell'assistenza domiciliare.
Lo scopo di questo studio è la valutazione dell'incidenza di episodi settici nei due periodi per dimostrare una riduzione delle infezioni correlata alle nuove metodologie terapeutiche. L'incidenza della sepsi è risultata ridotta nel secondo periodo da 24,3% a 6,2%. I patogeni più frequentemente isolati sono stati stafilococchi coagulasi-negativi, Escherichia coli, Staphylococcus aureus.
Concludiamo che una terapia meno invasiva riduce le complicanze infettive post-chemioterapia; inoltre, lo studio epidemiologico degli episodi settici in un reparto oncologico può essere di aiuto per la stesura di protocolli di terapia empirica per pazienti con neutropenia febbrile post-chemioterapia.

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