

INFECTIONS IN CHILDHOOD ALL 222 FEBRILE NEUTROPENIC EPISODES

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Fever and Neutropenia

- **Fever**

- Single temperature of 38.5°C
- or
- Two temperatures of 38°C or higher within 24 hour period

- **Neutropenia (Granulocytopenia)**

- Absolute neutrophil count (ANC) $<1500/\text{mm}^3$ (neutrophils + band forms)
- ANC $<1000/\text{mm}^3$ mild neutropenia
- **ANC $<500/\text{mm}^3$ moderate neutropenia**
- ANC $<200/\text{mm}^3$ severe neutropenia
- ANC $<100/\text{mm}^3$ very severe neutropenia

Childhood ALL n=266

(June 1992 – June 2002)

MCP - 841 protocol

- Patients 266
- Mean age 6.4 yrs (range 1-12 yrs)
- Male: Female 3.8:1
- Febrile episodes 355
- Febrile neutropenic episodes 222 (62.5%)
(ANC <500)

Protocol MCP-841

Cycle	Chemotherapy drugs
Induction 1 (I_1)	Prednisolone Vincristine L-Asparaginase Daunorubicin IT-Methotrexate
Induction 2 (I_2)	Mercaptopurine Cyclophosphamide IT-Methotrexate Cranial Irradiation
Repeat Induction 1 (I_1)	Same as Induction 1

Protocol MCP-841

Cycle	Chemotherapy drugs
Consolidation (C)	Cyclophosphamide Vincristine Mercaptopurine Cytarabine
Maintenance (M) (6 Cycles)	Vincristine Prednisolone Daunorubicin L- Asparaginase Methotrexate Mercaptopurine
Total duration	- 2yrs

Fever and Neutropenia

Evaluation

- *Careful history and meticulous physical examination.*
 - Oropharynx
 - Skin
 - Venepuncture sites
 - Respiratory tract
 - Perirectal area
 - Central venous line sites and any site of recent invasive procedures

Febrile Neutropenia

Evaluation

- *Admitted to the hospital for observation and treatment*
 - CBC with differential to determine the ANC
 - Blood culture (If CVC-blood culture from all catheter lumens)
 - Urinalysis and urine culture (clean catch technique)
 - Chest radiograph
 - Culture and gram stain of the mouth, throat or skin
 - Stool culture (if diarrhoea)
 - CSF culture if indicated
 - Central line site or wound
 - Imaging studies to evaluate for sinusitis
 - Routine serum chemistries

Febrile Neutropenia

- ANC < 500 and fever require prompt evaluation and the rapid initiation of broad spectrum antibiotics
- Empiric parenteral antibiotic therapy that covers the most common infecting organisms in individuals with severe neutropenia

Febrile Neutropenic episodes

n=222

- Documented focus of infection 98 (44%) episodes
- Fever of unknown origin 124 (56%)
- 166/222 (74.7%) episodes Induction and Consolidation phase of chemotherapy
- 56/222 (25.3%) episodes Maintenance phase

Febrile Neutropenia

- Febrile neutropenic episodes - n=222
- Documented focus of infection - 98 episodes
- Documented sites of infection - 274
 - Pulmonary Infection 75 (27.3%)
 - HEENT 63 (22.9%)
 - G.I. 42 (15.3%)
 - Blood 42 (15.3%)
 - UTI 28 (10.2%)
 - Cellulitis 15 (5.4%)
 - Skin 9 (3.2%)

Febrile Neutropenic Episodes

n=222

- **Bacteria isolated** 69 (31%)
- Gram negative 46
- Gram positive 23
- **Fungal isolates** 22 (10%)

Profile of microorganisms isolated from various sites

Microorganisms	Total	Blood	Heent	Urine	Misc.
Gram-negative bacteria	46	23	6	15	2
Escherichia coli	21	8	2	11	0
Klebsiella	8	4	2	2	0
Pseudomonas	6	3	2	1	0
Acinetobacter	6	4	0	1	1
Enterobacter Species	3	3	0	0	0
Salmonella typhimurium	2	1	0	0	1

Profile of microorganisms isolated from various sites

Microorganisms	Total	Blood	Heent	Urine	Misc.
Gram-positive bacteria	23	18	2	1	2
Staphylococcus aureus	9	9	0	0	0
Staphylococcus epidermidis	6	5	0	1	0
Streptococcus fecalis	3	3	0	0	0
Streptococcus viridans	1	1	0	0	0
Clostridium difficile	1	0	0	0	1
Anaerobic streptococci	1	0	0	0	1
Gram +ve cocci unspecified	2	0	2	0	0

Profile of microorganisms isolated from various sites

Microorganisms	Total	Blood	Heent	Urine	Misc.
Fungal Organisms	22	1	9	12	0
Candida albicans	13	0	5	8	0
Candida Unspecified	3	0	0	3	0
Mucor	2	0	2	0	0
Penicillium	1	1	0	0	0
Trichosporon	1	0	0	1	0
Zygomycetes	1	0	1	0	0
Aseptate fungi unspecified	1	0	1	0	0

Therapy and outcome of febrile neutropenia

- 95/222 (42.8%) febrile neutropenic episodes improved with first line antibiotic therapy.
- Modification of antibiotics required in 127/222 (57.2%) episodes.
- Anti-fungal therapy was used in 86(38.7%) episodes.

Febrile Neutropnic Episodes n=222

Mortality **13/222 (6%)**

12 Deaths **Induction and consolidation
phase of chemotherapy**

1 Death **Maintenance phase**

Febrile Neutropenia

Mortality 13/222 (6%)

- **Pneumonia** 10 (76.9%)
- **Bacteremia** 8 (61.5%)
- **UTI** 5 (38.5%)
- **HEENT** 4 (30.8%)
- **G.I. Infection** 4 (30.8%)
- **7/13 (53.8%) had documented fungal infection (5 in urine, 1 each in blood and HEENT)**

Conclusion

- Gram negative bacterial infections were the commonest infections.
- Most common site of isolation for gram-negative bacteria was blood (50%) followed by urine (32.6%)
- Blood (78.3%) was the predominant site of isolation of gram-positive bacteria.
- The majority of fungal infections 19/22 were detected during induction chemotherapy.
- These results stress the need to treat fungal infections early as this was a major cause of mortality in our patients.



Thank You