

Role of Pneumococcal Vaccination in Oncology Patients

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Disease Burden

It is estimated that in 2015, the age standardized incidence rate and the crude mortality rate of cancer in India will be 104.2 and 49.1 per 100000 population respectively.¹ Such figures are partly indicative of low rates of early-stage detection and poor treatment outcomes in India.

Infectious Complications in Oncology Patients

Infections represent an important cause of morbidity and mortality in oncology patients, especially those patients receiving intensive chemotherapy or undergoing stem cell transplant. Infectious complications are common in patients with hematological malignancies. They develop not only because of the immune deficiency that is intrinsic to hematological disease, but also because of the treatments used that cause immunosuppression or aplasia.² Around 50% of patients with a hematological malignancy will present a pulmonary infection during their management.³ The chemotherapy induced neutropenia and the deficiencies in antibody-mediated immunity (splenectomy, hypo/ergammaglobulinemia and myeloma) are usually associated with bacterial infections especially *S pneumoniae*.⁴ High incidence of gram-positive infections, particularly recurrent pneumococcal pneumonia, was recognized in Multiple Myeloma.^{5,6}

Lymphoproliferative malignancies such as chronic lymphocytic leukaemia, myeloma, and low grade non-Hodgkin's lymphoma are associated with

immune paresis. Such patients are often treated with corticosteroids, and a combination of these two factors renders them vulnerable to infections with encapsulated organisms such as *S pneumoniae*. These infections have high morbidity and mortality.⁷ A prospective observational study in Spain showed that in adults with cancer the presence of pneumococcal bacteremia was particularly frequent in men with co-morbidities, and mainly occurs as a complication of pneumonia.⁸ In CLL patients treated with conventional alkylator-based regimens, the respiratory tract is, and remains, the most common site of bacterial infection especially with *S aureus*, *S pneumoniae*, *H influenzae* etc.⁹ In prospective, observational single-institutional study to describe the profile of infections in febrile neutropenia (FN) in acute leukemia and hematopoietic stem cell transplant (HSCT) in Delhi, gram positive bacteria were isolated from 44.3% of all bacterial isolates.¹⁰ Splenectomy performed for hematologic malignancies for diagnostic and therapeutic indications also increases the risk of overwhelming sepsis by encapsulated bacteria. Pulmonary complications were the most common morbidity seen in such patients.¹¹

Clinical and immunogenicity data of pneumococcal vaccines in oncology patients

In a study with 27 CLL patients aged 66 years (median, range 48 ± 80 years), plain polysaccharide vaccine (PPV23) seemed to be ineffective in

mounting a protective antibody response.¹² Similar observations were found in the patients with CLL and multiple myeloma in other studies.^{13,14} Conjugate T-cell dependent pneumococcal vaccines in combination with polysaccharide vaccines have shown promising results in inducing booster responses in patients previously treated for Hodgkin's disease¹⁵. In this study the responses to 39 patients who had received PCV7 followed by PPV23 a year later to those of the 57 patients who were randomized to receive PPV23 only. The geometric mean antibody concentrations after immunization with PPV23 vaccine were significantly higher for five of the six measured serotypes in HD patients primed with PCV7 compared with responses in patients who received PPV23 only.

Most HCT patients respond poorly to immunization with unconjugated polysaccharide vaccines, because immune responses to T cell-independent antigens are slow to mature after transplantation even when immunization is delayed until 12 months.¹⁶⁻¹⁹ A study on 61 patients scheduled for auto HCT assessed the effect of immunization with PCV7 before stem cell collection on patients' ability to respond to PCV7 administered at 3, 6, and 12 months after auto HCT. Patients who received PCV7 before stem cell collection had significantly higher antibody concentrations to 6 of the 7 vaccine serotypes at 3 and 6 months after auto HCT compared with patients who received vaccine after

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transplantation only beginning at 3 months.²⁰

National and global recommendations for pneumococcal vaccination in oncology patients

The National Comprehensive Cancer Network (NCCN 2013) Clinical Practice Guidelines and European Society for Medical Oncology (ESMO 2013) recommend pneumococcal vaccination in splenectomy, HSCT and other cancer patients on immunosuppressive therapy.^{21,22} The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP 2014) recommends the sequential use of PCV13 and PPV23 in adults with splenectomy, Leukemia, Lymphoma, Hodgkin disease, generalized malignancy and Multiple Myeloma.²³ The recent guidelines of German AGIHO recommend the use of PCV13 and PPV23 in hematology and oncology patients in adulthood.²⁴ The American Society for Blood and Marrow Transplantation (ASBMT 2011)²⁵ and The Fred Hutchinson Cancer Research Center and Seattle Cancer Care Alliance (HCRC / SCCA 2014)²⁶ guidelines recommends the use of PCV in hematopoietic stem cell transplant patients.

References

- Nair MK, Varghese C, Swaminathan R. Cancer: Current scenario, intervention strategies and projections for 2015. NCMH Background Papers- Burden of Disease in India. Available from www.searo.who.int/india Accessed on 7 October 2014
- Franquet T. High-resolution computed tomography (HRCT) of lung infections in non-AIDS immunocompromised patients. *Eur Radiol* 2006;16:707-18.
- Morrison VA. Infectious complications in patients with chronic lymphocytic leukemia: pathogenesis, spectrum of infection, and approaches to prophylaxis. *Clin Lymphoma Myeloma* 2009;9:365-70.
- S. Bommarta, A. Bourdin, A. Makinson, G. Durand, A. Micheau, V. Monnin-Bares et al. Infectious chest complications in haematological malignancies. *Diagnostic and Interventional Imaging* 2013;94:193-201.
- Clenchur H, Zinneman HH & Hall WH. A review of 51 cases of multiple myeloma: emphasis on pneumonia and other infections as complications. *Arch Intern Med* 1959;103:173-183.
- Zinneman HH & Hall WH. Recurrent pneumonia in multiple myeloma and some observations on immunological response. *Ann Intern Med* 1954;41:1152-1163.
- R Gowda, FMRazvi, G P Summerfield. Risk of pneumococcal septicaemia in patients with chronic lymphoproliferative malignancies. *BMJ* 1995;311:26-7.
- Garcia-Vidal C, Ardanuy C, Gudiol C, Cuervo G, Calatayud L, Bodro M et al. Clinical and microbiological epidemiology of Streptococcus pneumoniae bacteremia in cancer patients. *J Infect* (2012), <http://dx.doi.org/10.1016/j.jinf.2012.08.015>
- Vicki A. Morrison. Management of Infectious Complications in Patients with Chronic Lymphocytic Leukemia. *Hematology Am Soc Hematol Educ Program* 2007:332-8.
- Ghosh I, Raina V, Kumar L, Sharma A, Bakhshi S, Thulker S et al. Profile of infections and outcome in high-risk febrile neutropenia: experience from a tertiary care cancer center in India. *Med Oncol* 2012;29:1354-1360
- J Horowitz, J L Smith, T K Weber, M A Rodriguez-Bigas, and N J Petrelli. Postoperative complications after splenectomy for hematologic malignancies. *Ann Surg* 1996;223:290-296.
- Sinisalo M, Aittoniemi J, Oivanen P, Kayhty H, Olander RM and Vilpo J. Response to vaccination against different types of antigens in patients with chronic lymphocytic leukaemia. *British Journal of Haematology* 2001;114:107-110
- Robertson JD, et al. Immunogenicity of vaccination against influenza, Streptococcus pneumoniae and Haemophilus influenzae type B in patients with multiple myeloma. *Br J Cancer* 2000;82:1261-1265.
- Hartkamp A, Mulder AHL, Rijkers GT, van Velzen-Blad H, Biesma DH. Antibody responses to pneumococcal and haemophilus vaccinations in patients with B-cell chronic lymphocytic leukemia. *Vaccine* 19:1671-1677.
- Chan CY, Molrine DC, George S, Tarbell NJ, Mauch P, Diller L et al. Pneumococcal Conjugate Vaccine Primes for Antibody Responses to Polysaccharide Pneumococcal Vaccine after Treatment of Hodgkin's Disease. *The Journal of Infectious Diseases* 1996; 173:256-8.
- Winston DJ, Ho WG, Schiffman G, Champlin RE, Feig SA, Gale RP. Pneumococcal vaccination of recipients of bone marrow transplants. *Arch Intern Med* 1983; 143:1735-1737.
- Guinan EC, Molrine DC, Antin JH, et al. Polysaccharide conjugate vaccine responses in bone marrow transplant patients. *Transplantation* 1994;57:677-684.
- Avanzini MA, Carra AM, Maccario R, et al. Antibody response to pneumococcal vaccine in children receiving bone marrow transplantation. *J Clin Immunol* 1995;15:137-144.
- Spoulou V, Victoratos P, Ioannidis J, Grafakos S. Kinetics of antibody concentration and avidity for the assessment of immune response to pneumococcal vaccine among children with bone marrow transplants. *J Infect Dis* 2000;182:965-969.
- Antin JH, Guinan EC, Avigan D, Soiffer RJ, Joyce RM, Martin VJ et al. Protective Antibody Responses to Pneumococcal Conjugate Vaccine after Autologous Hematopoietic Stem Cell Transplantation. *Biology of Blood and Marrow Transplantation* 2005;11:213-222.
- The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology™ for Prevention and Treatment of Cancer-Related Infections, 2013. Available from http://www.nccn.org/professionals/physician_gls/f_guidelines.asp Accessed on 7 October 2014.
- European Society for Medical Oncology (ESMO) Handbook of Cancer Treatments in Special Clinical Situations 2013, ESMO Press; ISBN: 978-88-906359-3-9.
- Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report (MMWR)* 2012;61:816-819.
- Recommendation of the AGIHO Pneumococcal Vaccination in hematology and oncology patients in adulthood. Available from http://www.dghoinfektion.de/agiho/content/e2735/e15963/e19600/Datei19601/AGIHO_Pneumokokkenimpfung_13MAR14_Master.pdf. Accessed on 7 October 2014.
- Majhail NS, Rizzo JD, Lee SJ, Aljurf M, Atsuta Y, Bonfim C et al. Recommended Screening and Preventive Practices for Long-Term Survivors after Hematopoietic Cell Transplantation. *Biol Blood Marrow Transplant* 2012; 18:348-371.
- Fred Hutchinson Cancer Research Center/ Seattle Cancer Care Alliance Version April 02, 2014 long-term follow-up after hematopoietic stem cell transplant general guidelines for referring physicians. Available from www.fhcrc.org/content/.../Long-Term-Follow-Up/LTFU_Guidelines.pdf. Accessed on 7 October 2014.