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Research

Pneumococcal Infections Pre and Post Vaccine Era in the Extreme Age in Macau

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Abstract

Objective

To analyze the effect to the inpatient with pneumococcal infection, especially extreme young and old (mainly age <10 and age >65), after introduced the pneumococcal vaccine since September 2009 in Macau.

Method

Retrospective comparison of pneumococcal infection in different age group especially to the young age <10 and elderly age >65 who hospitalized in public hospital from 2003 to 2007 that is the pre vaccine era with the 2011 to 2015 post vaccine era

Result

After the introduction of the vaccine including PCV7/PCV13 for children and PPV23 for elderly, significant decreased in total pneumococcal-related disease hospitalization rates in both age group were noticed

Conclusion

PCV for young children and PPV for elderly >65 are responsible for the reduction of pneumococcal-related disease (PD) hospitalization in Macau

Background

Streptococcus pneumoniae (pneumococcus) is a leading cause of bacterial illnesses among young and old age, co morbidities (such as splenic dysfunction, immunodeficiency's, chronic renal disease, chronic heart disease, chronic lung disease or cerebral spinal fluid leak), crowded environments or poor socioeconomic conditions. It is a *Gram-positive* coccus encapsulated with polysaccharides. The difference in the composition of capsular polysaccharides constitutes to at least 90 different serotypes of pneumococci identified thus far. Pneumococcus is responsible for invasive pneumococcal disease (IPD) (e.g. meningitis, sepsis, bacteraemic pneumonia and bacteraemia) and non-IPD (e.g. pneumonia, acute otitis media and sinusitis) [1].

The treatment of pneumococcal infections usually involves the use of antibiotic(s). The problem is the increasing resistance of the bacteria to antibiotics, which makes prevention of pneumococcal infections important. One of the most effective means of preventing pneumococcal diseases is by pneumococcal vaccination [1].

The benefit of widespread use of pneumococcal conjugate vaccine (PCV) resulted in decreased in IPD among children and elderly persons [1]. The 23-valent pneumococcal polysaccharide vaccine (PPV) provided approximately 60% protection against invasive disease in the general elderly population [2]. In recent study in Macau, after comparison pre (2001-2005) with post (2011-2015) PCV era since the introduction of vaccination in 2009, in pediatric cases, we found significant decreased in PD cases in terms of 4 IPD and 35 non-IPD in pre era to 0 IPD and 3 non-IPD post era. There was 91% drop of hospitalization rate for pneumococcal–related disease. However the impact of pneumococcal vaccine for elderly in Macau remains unknown.

Pneumococcal Disease Burden in Macau

In Macau, pneumonia is the second leading cause of death (after cancer and heart diseases) and accounted for 6.7% of total deaths in 2005. The incidence of pneumonia in adults increases with age all over the world [3]. A US study of 46,237 elderly patients reported 18.2 cases per 1,000 person-years among patients aged 65-69 years, rising to 52.3 cases per 1,000 person-years among patients aged ≥85 years [4]. Previous estimates of mortality from community acquired pneumonia range from 5.1% for hospitalized and ambulatory patients to 36.5% for patients in intensive care units [5]. It is estimated that the incidence of pneumonia in Macau under 5 year of age is similar to nearby region of Hong Kong and even US [6].

The Macau health Bureau recommends all children under 2 years of age to receive PCV under the Macau Childhood Immunization Program since September 2009. The standard regimen includes a primary series of 3 doses at 2, 4 and 6 months and a booster dose at 12-15 months. And also recommended adult age >65 at risks of chronic heart disease, chronic lung disease, chronic liver/renal

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disease, chronic metabolic disease, chronic hematologic/oncologic/immunological disease, chronic neuromuscular disease, asplenic disease, received PPV23 since September 2009.

Table 1: PPV23 coverage in adult age>65 population in Macau

year	total population in Macau (x1000)	age>65 population (x1000)	age>65 with PPV23	age>65 with PPV23 coverage
2011	557.4	40.9	15833	38%
2012	582.0	44.6	15971	35%
2013	607.5	48.7	16142	33%
2014	636.2	53.6	16279	30%
2015	646.8	58.1	16557	28%

Pneumococcal Vaccination

Polysaccharide Vaccines

The 23-valent pneumococcal polysaccharide vaccine (PPSV23, PPV23), available since the 1980s, effectiveness has ranged from 43%–81% [7]. PPSV23 has been found to be effective in healthy individuals <75 years of age, but protection wanes after 5 years. Unlike conjugate vaccines, PPSVs have not been shown to interrupt carriage and therefore do not have the potential for herd effects [8]. There is no discernible impact of PPSV23 on population incidence of IPD, and the older and high-risk individuals are less likely to benefit. However, based on vaccine efficacy estimates, PPSV23 is still considered a cost-effective intervention for the low-risk elderly.

Conjugate Vaccine

In an effort to improve the immunogenicity of vaccines, pneumococcal conjugate vaccines (PCVs) were developed. The advantages of the conjugate vaccines are related to the way the antibodies are produced by the body. PCV induces a T-cell-dependent response which results in plasma cells producing immunoglobulin G but also produces memory B-cells. This T-cell-dependent response elicits immunological memory, and therefore primes the immune system for either natural exposure or subsequent booster vaccination. The latter observation may be considered a surrogate for exposure to the polysaccharide during a "natural" infection [9]. There is no decrease in the immune response seen with revaccination with conjugate vaccines, as they produce immunoglobulin G rather than just immunoglobulin M [10]. Memory B-cells ensure boosting of the effect with revaccination. Memory B-cells are not produced in response to most free polysaccharide vaccines and, in fact, may be depleted post-vaccination, resulting in hypo responsiveness [11].

Seven-valent PCV (PCV7), which included the purified capsular polysaccharides of seven serotypes conjugated to a nontoxic variant of diphtheria toxin known as CRM197, was developed in 2000 [12]. After PCV7 was introduced in the US, rates of IPD caused by the seven serotypes have decreased substantially even among the unvaccinated population [13]. The indirect benefits of vaccination, or herd effects, likely result from reduced nasopharyngeal carriage of pneumococcus in PCV7-vaccinated children and reduced transmission from children to unvaccinated children and adults [14]. Surveillance data has shown reduction in IPD, pneumonia, and acute otitis media in young children after the introduction of PCV7 in many different geographic locations .In order to provide improvements in serotype coverage and potentially reduce the remaining IPD burden, further improvements in conjugate vaccines were released. PCV13 comprises "13" *S. pneumoniae* polysaccharide serotypes, including the existing seven in PCV7 and six additional serotypes. The immunogenicity of PCV13 has been evaluated in a number of trials in healthy infants in comparator studies versus PCV7 and when co administered with other vaccines [15]. Non inferiority in terms of the proportion of responders 1 month after the final dose of the primary series of PCV13 versus PCV7 has been demonstrated for six of the seven common serotypes in one pivotal study [16]. and in five of the seven in another [17]. The remaining six serotypes in PCV13 also demonstrated robust immune responses. Importantly, functional antibodies were elicited against all 13 serotypes contained in PCV13 after primary vaccination. Recently, the results of first randomized PCV13 versus PCV7 pediatric trial results were published. PCV13 resulted in lower acquisition and prevalence of nasopharyngeal colonization than PCV7 for four additional PCV13 serotypes, and serotypes 6C and 19F. It was comparable with PCV7 for all other common serotypes. Evidence for PCV13 protective effectiveness against IPD is also beginning to emerge in many industrialized countries such as England, Wales, Germany, and the US [17]. These findings predict vaccine effectiveness through both direct and indirect protection. PCV13 immunogenicity and safety was also demonstrated either alone or with concomitant administration of a trivalent inactivated influenza vaccine in adults aged ≥65 years who were naive to PPSV23 [18].

A meta-analysis of all available published data from controlled clinical trials of PCV found the efficacy of PCV in the reduction of IPD was 89% for disease due to vaccine serotypes and 63%–74% for disease due to all serotypes. The efficacy to prevent acute otitis media by vaccine serotypes was 55%–57% and 29% to prevent otitis media involving all serotypes. However, the efficacy to prevent clinical pneumonia was only 6%–7%, although it was 29%–32% to prevent radiograph-confirmed pneumonia [19].

Methods

Retrospectively rates of inpatient with laboratory positive result of growth with streptococcus pneumonia in any culture specimen were compared before (2003-2007) and after (2011-2015) pneumococcal vaccine introduction in September 2009 in governmental hospital in Macau. To evaluate vaccine effects in the pneumococcal-related disease rates who admitted in public hospital especially in the view of extreme young and old as group age 0-10 and age >65.

Results

After introduced the pneumococcal vaccine since September 2009, there were significant decreased in total pneumococcal-related disease (PD) hospitalization rates, absolute IPD rates and mortality rates, especially in extreme age group.

In pre era, total 92 cases found with PD, 57(61%) of them in age group 0-10, 26(28%) of them in age >65, and 21% of total case suffered from IPD, with mortality rate about 9.7%.

In post era, there were significant dropping cases from 92 to 23 cases with PD, only 8(34%) of them in age group 0-10, 6(26%) of them in age >65, and 14% suffered from IPD, with mortality rate about 13%.

Discussion

After pneumococcal vaccination introduced in Macau since September 2009, pneumococcal infection hospitalization rates in public hospital decreased significantly. Majority drop being found in extreme age group as shown in this study. No matter overall age group or age 0-10 and age >65, all dropped significantly. But in this study, it is difficult to distinguish the impact of decreasing PD inpatient requirement from the direct protection by the vaccination itself or by the indirect effect from the contact with other vaccine as both group of inpatient receiving certain level of vaccination coverage.

Also as the data collection is limited as we only encountered cases

Table 2: the age distribution of total inpatient with PD in different age group in pre era (2003-2007):

case	57	1	1	0	1	3	10	8	9	2
age	0-10	11-20	21-30	31-40	41-50	50-60	61-70	71-80	81-90	>90

Table 3: the age distribution of total inpatient with PD in different age group in post era (2011-2015):

case	8	0	0	3	0	2	6	1	2	1
age	0-10	11-20	21-30	31-40	41-50	50-60	61-70	71-80	81-90	>90

Table 4: characteristic of total inpatients of PD during pre/post era

	total cases	sex(M:F)	ave. age	IPD	non-IPD	Mortality
Pre era	92	60:32	45.7	20 (21%)	72	9/92 (9.7%)
Post era	23	13:10	78.3	13 (14%)	10	3/23 (13%)

Table 5: characteristic of total mortality cases of PD during pre/post era

	Mortality	sex(M:F)	average age	IPD	Non-IPD
Pre era	9/92 (9.7%)	9:0	71.4	8/9 (88%)	1
Post era	3/23 (13%)	2:1	74.3	3/3(100%)	0

Table 6: cases of PD in age 0-10 during pre/post era

	total case	sex(M:F)	ave. age	IPD	non-IPD	mortality
Pre era	57	32:25	2.0	3/57(5.2%)	54	0/57 (0%)
Post era	8	4:4	2.6	1(12.5%)	1	0/8 (0%)

Table 7: cases of PD in age >65 during pre/post era

	total case	sex(M:F)	ave. age	IPD	non-IPD	mortality
Pre era	26	11:2	78.5	7 (26%)	19	6/26 (23%)
Post era	6	4:2	76	5 (83%)	1	2/6 (33%)

Table 8: characteristic of mortality cases of PD in age >65during pre/post era

	Mortality	sex(M:F)	average age	IPD	Non-IPD
Pre era	6/26 (23%)	6:0	73.8	3/6(50%)	3
Post era	2/6 (33%)	1:1	80.5	2/2(100%)	0

in public hospital. The number of cases might be underestimated no matter pre or post vaccine era.

For the time being, it is recommended that PCV for young children, and PPV23 is still the best anti-pneumococcal vaccine options to be used for high-risk adults and all elderly people (with or without additional high-risk conditions) [20].

According to the record from Macau health Bureau, there were average only 33% of PPV23 coverage rate in elderly age>65 since the launch of vaccination from 2009 and seems the coverage rates was dropping gradually. Besides to keep on the children vaccination plan for PCV used in infants and young children, it should be advised to enhance the vaccination coverage in elderly group in Macau for increasing the protection from pneumococcal-related disease.

Conclusion

This study provides a comprehensive assessment of changes in pneumococcal disease after pneumococcal vaccine immunization program began in Macau. Results from this study contribute to the evidence supporting the overall nationwide beneficial effects of pneumococcal vaccine on pneumococcal infection, the most common cause of community-acquired bacteria.

References

1. Hicks LA (2007) Incidence of pneumococcal disease due to non-pneumococcal conjugate vaccine (PCV7) serotypes in the United States during the era of widespread PCV7 vaccination, 1998–2004. J Infect Dis 196: 1346-1354.
2. Vila-Corcoles A (2007) Advances in pneumococcal vaccines: what are the advantages for the elderly? Drugs Aging 24(10): 791-800.
3. Nuorti JP (2008) Uptake of pneumococcal conjugate vaccine among children in the 1998-2002 United States birth cohorts. Am J Prev Med 34: 46-53.
4. G rijalva CG (2006) National impact of universal childhood immunization with pneumococcal conjugate vaccine on outpatient medical care visits in the United States. Pediatrics 118: 865-873.
5. Thompson WW (2004) Influenza-associated hospitalizations in the United States. JAMA 292: 1333-1340.
6. Lee Yan, Lao U Lei, Leong Iek Hou, Chan Soi Fan, Lam Kuo, et al. (2009) Pneumococcal infection in Macau. Health Science Journal of Macao 9(4).
7. Fedson DS, Guppy MJ (2013) Pneumococcal vaccination of older adults: conjugate or polysaccharide? Hum Vaccin Immunother 9(6): 1382-1384.
8. Fletcher MA, Laufer DS, McIntosh ED, Cimino C, Malinoski FJ, et al. (2006) Controlling invasive pneumococcal disease: is vaccination of at-risk groups sufficient? Int J Clin Pract 60(4): 450-456.
9. Paradiso PR (2012) Pneumococcal conjugate vaccine for adults: a new paradigm. Clin Infect Dis 55(2): 259-264.
10. Richmond P, Borrow R, Miller E (1999) Meningococcal serogroup C conjugate vaccine is immunogenic in infancy and primes for memory. J Infect Dis 179(6): 1569-1572.
11. Torling J, Hedlund J, Konradsen HB, Ortqvist A (2003) Revaccination with the 23-valent pneumococcal polysaccharide vaccine in middle-aged and elderly persons previously treated for pneumonia. Vaccine 22(1): 96-103.
12. Black S, Shinefield H, Fireman B (2000) Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. Northern California Kaiser Permanente Vaccine Study Center Group. Pediatr Infect Dis J 19(3): 187-195.
13. Millar EV, Watt JP, Bronsdon MA (2008) indirect effect of 7-valent pneumococcal conjugate vaccine on pneumococcal colonization among unvaccinated household members. Clin Infect Dis 47(8): 989-996.
14. Whitney CG, Farley MM, Hadler J (2003) Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. N Engl J Med 348(18):1737-1746.
15. Duggan ST (2010) Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) (Prevenar 13®) Drugs. 70(15):1973-1986.
16. Kieninger DM, Kueper K, Steul K (2010) Safety, tolerability, and immunologic noninferiority of a 13-valent pneumococcal conjugate vaccine compared to a 7-valent pneumococcal conjugate vaccine given with routine pediatric vaccinations in Germany. Vaccine 28(25): 4192-4203.
17. Plosker GL (2013) 13-valent pneumococcal conjugate vaccine: a review of its use in infants, children, and adolescents. Paediatr Drugs 15(5): 403-423.
18. Schwarz TF, Flamaring J, Rumke HC (2011) A randomized, double-blind trial to evaluate immunogenicity and safety of 13-valent pneumococcal conjugate vaccine given concomitantly with trivalent influenza vaccine in adults ageds>=65years. Vaccine 29(32): 5195-5202.
19. Pavia M, Bianco A, Nobile CG, Marinelli P, Agnelillo IF, et al. (2009) Efficacy of pneumococcal vaccination in children younger than 24 months: a meta-analysis. Pediatrics 123(6): e1103-e1110.
20. Vila-Corcoles A (2013) Preventing pneumococcal disease in the elderly: recent advcances in vaccines and implications for clinical practice. Drugs Aging 30(5): 263-276.