NEUROPATHIC PAIN

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NEWSLETTER of the IASP Special Interest Group on Neuropathic Pain

NeuP SIG

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A NeuP SIG Speakers' Bureau?

In the next few issues of this newsletter, I would like to share with the members of NeuPSIG a number of proposals and issues that the management committee has been discussing. One very important goal that NeuPSIG has set for itself involves education. Specifically, our Constitution and Bylaws include the following two Aims and Objectives that are relevant to education: (1) "the exchange of information and experience about the assessment and treatment of neuropathic pain;" and (2) "furthering the educational objectives of the SIG via international meetings, an annual symposium, workshops at the IASP World Congress on Pain®, Congress satellite meetings, a newsletter, and the IASP Web site." To date, we have been quite successful in meeting the second of these objectives, having sponsored or co-sponsored meetings in Bermuda; Madrid; San Francisco; St. Petersburg, Russia; Sydney; and Uluru, Australia; with additional meetings being planned for Berlin; Glasgow; Guatemala; London; Snowbird, Utah; and elsewhere.

Although these meetings have differed greatly in both size and content, the impetus for them has generally come from the management committee, not the NeuPSIG membership. However, there are undoubtedly educational needs that are unknown to the management committee. We have therefore discussed the possibility of NeuPSIG supporting a program of regional or local neuropathic pain meetings. Such a program might work a bit like the speakers' bureaus developed by many pharmaceutical companies. For example, NeuPSIG could sponsor one-day "Update on Neuropathic Pain" educational meetings in locations that would be selected based on applications from local pain groups, especially from areas where such meetings are rare and where pain specialists typically have limited travel resources. NeuPSIG could solicit and then review applications from members who would like to be included in the NeuPSIG speakers' bureau, from which the speakers for these local meetings would be selected (of course, all the travel and other expenses associated with such meetings would be covered by NeuPSIG). Finally, to ensure the consistency and quality of such meetings, NeuPSIG could develop a curriculum and slides that speakers would be asked to use when presenting talks at these meetings. Such a program of NeuPSIG-sponsored local meetings would not only directly address NeuPSIG's educational objectives but would also provide opportunities for a greater number of NeuPSIG members to become involved in its activities by participating in the speakers' bureau.

We would very much like to hear your thoughts about whether this is a worthwhile initiative for NeuPSIG to undertake. Of course, this is only one example of how NeuPSIG could promote "the exchange of information and experience about the assessment and treatment of neuropathic pain," and we would also very much value your input and ideas for additional educational activities that the management committee should consider.
Bob Dworkin
Chair, Neuropathic Pain SIG

NeuPSIG Management committee met in London.
The NeuPSIG management committee met in London on April 21 and 22, 2006. The main topics covered at this meeting are summarized below. The next management committee meeting will take place in Guatemala on December 7, 2006 during the 1st Central American Congress on Pain and Palliative Care.

The 2nd International Neuropathic Pain congress will take place in Berlin 7-10, 2007.

The congress will take place at the InterContinental Berlin which is located in the heart of Berlin (please see previous newsletter at www.neupsig.org for further information about the venue and Berlin.

The Main topics of the meeting are:
- Postherpetic neuralgia
- Diabetic neuropathy
- Complex regional pain syndromes
- Central pain syndromes
- Animal models in neuropathic pain
- Mechanism-based classification and therapy
- Clinical assessment in neuropathic pain
- Quantitative sensory testing in neuropathic pain
- Genetics of neuropathic pain
- Design of clinical trials in neuropathic pain
- Novel molecular drug targets in neuropathic pain

Proposed Satellite meeting in London in 2008

The SIG is organizing a satellite meeting to the 12th IASP World Congress on Pain "Recent developments in neuropathic pain" which will take place at the Royal Society of Medicine in London August 13th - 15th 2008 immediately preceding the congress. The Scientific Program Committee under the chair of Andrew Rice has planned an exciting meeting. The proposal is awaiting approval from the IASP.

For other upcoming NeuPSIG meetings see box below.

Travel awards:

A travel grant subcommittee was struck with Geoff Gourlay as chair, and includes Gary Strichartz and Chris Wells. NeuPSIG is pleased to provide financial support for trainees to participate in our scientific meetings.

We are pleased to provide enhanced support to NeuPSIG members for the Berlin Congress as follows.

- Registration Fees of Euro 50 for bona fide graduate students and trainees. You will need to provide proof of your status. Please visit our website and download the application form.
- A number of travel grants will be available on a competitive basis to presenters of posters- first authors only. Support will include accommodation, and a grant towards verified travel expenses, these to be stated on application. A letter of support from your Chairman to verify your status and endorse your application and details of your presentation need to be provided.
- Support will also be considered for non-trainee health care professionals and researchers from developing countries.

Subcommittees updates:

Classification and taxonomy

This subcommittee, chaired by Rolf-Detlef Treede has now completed a manuscript "Redefinition of neuropathic pain and a grading system for clinical use: Consensus statement on clinical and research diagnostic criteria", which will be submitted shortly for publication.

Assessment

This subcommittee chaired by Maija Haanpaa with Ralf Baron co-chair and Rolf-Detlef Treede, Georgiou Cruccu and Jordi The committee is producing a paper on diagnosis of neuropathic pain directed for GPs. Additionally, the EFNS paper of assessment of neuropathic pain published in the European Journal of Neurology is planned to be updated in collaboration with the EFNS and the NeuPSIG Assesment committee.

Treatment

This subcommittee which is chaired by Bob Dworkin has recently completed a manuscript titled "Pharmacologic management of neuropathic pain: evidence-based clinical recommendations" which has been sent out to various national pain societies for endorsement and will be submitted shortly. The SIG has also co-sponsored treatment guidelines for herpes zoster which have recently been accepted for publication, as follows:
Dworkin RH, Johnson RW, Breuer J, Gnann JW, Levin MJ, Backonja M, Betts RF, Gershon AA, Haanpää ML, McKendrick MW, Nurmikko TJ, Oaklander AL, Oxman MN, Pavan-Langston D, Petersen KL, Rowbotham MC, Schmader KE, Stacey BR, Tyring SK, van Wijck AJM, Wallace MS, Wassilew SW, Whitley RJ. Recommendations for the management of herpes zoster. Clinical Infectious Diseases, in press.

Education

This newly formed committee is chaired by Dr Sara Bistre.
The subcommittee's objectives are to:
Disseminate information on neuropathic pain in both developed and developing countries
Provide treatment guidelines,
Elicit the interest of young health professionals in neuropathic pain
Provide /seek sponsors for travel awards and fellowships
Disseminate this information to the following groups:
1.- Medical Students
2.- Primary Care and Family Physicians
3.- Specialists
4.- Research and postgraduates

Topical Reviews

This issue of the NeuPSIG newsletter includes a review by Dr. Maija Haanpää on vaccination against herpes zoster. Other submissions are welcome

Upcoming SIG sponsored or co-sponsored meetings:

9th International Conference on the Mechanisms and Treatment of Neuropathic Pain, Bermuda, November 2-4, 2006. www.neuropathicpain.org

Neuropathic pain symposium in conjunction with the 1st Central America Congress on Pain and Palliative Care, Guatemala City, December 6, 2006. www.congresocadolorypaliativos.com

Second International Congress on Neuropathic Pain, Intercontinental Hotel, Berlin, Germany, June 7-10, 2007. www.kenes.com/neuropathic/

10th International Conference on the Mechanisms and Treatment of Neuropathic Pain will take place at Snowbird, Utah November 2-4 2007.

Satellite meeting to the 12th IASP World Congress on Pain "Recent developments in neuropathic pain" will take place in London August 13th - 15th 2008 immediately preceding the congress.

11th International Conference on the Mechanisms and Treatment of Neuropathic Pain will take place in early November 2008.

The management committee has also started initial planning for a possible meeting in Asia in 2009 and a 3rd International Neuropathic Pain Congress in 2010.

Topical Review

Vaccination Against Herpes Zoster – a New Possibility to Reduce Burden of Herpes Zoster and Postherpetic Neuralgia in Older Adults

Maija Haanpää, MD, PhD, Pain Clinic, Helsinki University Hospital, Helsinki, Finland

Introduction

Vaccination is the most effective medical intervention against diseases caused by human viral pathogens. Viral vaccines reduce the frequency of the disease and its complications and hence provide cost savings to the healthcare system. Against the varicella-zoster virus (VZV), vaccines are developed to prevent both the primary infection (varicella) and the reactivation, herpes zoster (HZ).

Varicella, herpes zoster and postherpetic neuralgia

Herpes zoster (shingles) is the most common neurological disorder with cumulative life-time incidence of about 20 %. It is caused by the reactivation of VZV, which has remained dormant in the sensory ganglia since the primary infection by varicella (chickenpox). Varicella is highly communicable: approximately 90% of the cases occur by the age of ten in temperate climates, and among susceptible household contacts the attack rate is 90%. Varicella is usually benign and self-limiting, but can cause complications such as cutaneous bacterial infection, pneumonia or neurological complications. Routine childhood varicella vaccination, which was instituted in the United States in 1995, has resulted in significant savings by reducing varicella incidence, hospitalization and deaths (Banz et al. 2003, Nguyen et al. 2005). Many other countries, including Australia, Germany, Israel, Japan, and South Korea have also started mass varicella vaccination. Some studies suggest that re-exposure to VZV after primary infection may decrease the risk of HZ through immunological boosting (Brisson et al. 2002, Thomas et al. 2002). A hypothesis based on mathematical modelling suggests that in a population with high coverage of varicella vaccine, the incidence of HZ would increase for the first 20 years after transmission of varicella has been eliminated and then gradually fall (Brisson et al. 2002). The study results on this are controversial: one study reported an increase in the incidence of HZ after varicella vaccination (Yih et al. 2005), while in another study the vaccination-associated decrease in varicella did not result in an increase in the incidence of HZ (Jumaan et al. 2005).

Shingles can affect anyone who has had chickenpox. The incidence of HZ ranges from 1.2 to 3.4 per 1000 person years in community studies, but rises to 3.6 to 14.2 per 1000 person years in the oldest individuals (Thomas and Hall 2004). In the Shingles Prevention Study of people over the age of 60 years receiving a placebo vaccine the incidence of HZ was 11.1 per 1000 person years (Oxman et al. 2005). Two population-based studies from Rochester, Minnesota and Boston, Massachusetts revealed a noticeable increase in the incidence of HZ over three decades (Ragozzino et al. 1982, Donahue et al. 1995). The most obvious explanation is the increasing number of elderly and immunocompromised people in the population. The risk for HZ increases with age, paralleling the concomitant waning of cell-mediated immunity to the VZV (Miller 1980, Ragozzino et al. 1982).

Shingles is painful in most cases, but patients usually recover from it in a few weeks. About 12% of zoster patients develop at least one complication (Table 1). Of these, postherpetic neuralgia (PHN), i.e. prolonged pain after HZ, is by far the most common. Although HZ is rarely life-threatening, the effect of HZ and PHN on the quality of life is serious in many older people (Oster et al. 2005, Seventer et al. 2006). Prevention of PHN remains one of the top priorities in the field of pain medicine, because once established PHN is virtually impossible to cure, and even its symptom control is difficult. Older age and the severity of the acute pain are the most obvious risk factors for PHN. Therefore, elderly patients, especially those with severe pain, should be treated with antiviral drugs, which decrease the tissue damage caused by the virus. However, the effect of antivirals on preventing PHN is limited, owing perhaps to the fact that neural tissue involvement precedes the eruption of rash. Adequate acute pain relief is good medical practice and prevents the development of sensitisation of the nervous system. Early use of analgesics in HZ is reasonable, although no controlled studies have been published about the efficacy of analgesics in preventing PHN. One study suggests that early treatment with amitriptyline may help to prevent PHN, and tricyclics are suggested as a part of the clinical treatment of HZ in elderly patients (Bowsher 1997). Psychosocial aspects should be taken into account in the treatment of zoster, because they may contribute to the development of PHN (Dworkin et al. 1996).

Zoster vaccine

The best way to prevent PHN is to prevent zoster itself. The previous observations of the boosting of the VZV T cells by varicella exposures and subclinical reactivations suggested that exogenous boosting of VZV T cells using VZV vaccination might reduce the risk of HZ in populations at risk (Arvin and Greenberg 2006). The Shingles Prevention Study, a large, multicenter, randomized, double-blind, placebo-controlled clinical trial indicates that zoster vaccine reduces the risk of HZ in healthy older adults (Oxman et al. 2005). The study enrolled 38546 immunocompetent adults 60 years of age or older who were randomly assigned to receive one subcutaneous dose of placebo or zoster vaccine. The vaccine was a live attenuated virus vaccine, which was 10-30 times more potent than childhood varicella vaccine. Study participants were followed on a monthly basis for a mean of 3.1 years, and more than 95% of participants completed follow-up. Persons developing rashes were carefully evaluated by polymerase chain reaction assay to determine whether the zoster vaccine caused the rash. The primary endpoint was the burden of illness (BOI) due to HZ, a measure reflecting the incidence, severity and duration of the associated pain and discomfort (Coplan et al. 2004). Incidences of HZ and PHN were secondary end points. PHN was defined as pain rated as 3 or more on a 0-10 scale and persisting more than 3 months after onset of rash.

The vaccine was associated with a 51% reduction in the incidence of HZ, a 67% reduction in the incidence of PHN, and a 61% reduction in the BOI caused by HZ in vaccine recipients compared with placebo recipients. Of note, the FDA's review report concluded that the efficacy of the vaccine on the BOI of HZ and on the PHN incidence beyond the efficacy of the vaccine on the HZ incidence is minimal (FDA 2005). The vaccine effect on the incidence of zoster was highest at 64% in people between the ages 60-69, but its effectiveness declined with increasing age, to 41% for the 70-79 age group, and 18% for those 80 years of age and older (FDA 2006a). In those who were vaccinated with zoster vaccine, but still developed shingles, the pain lasted on average 20 days, whereas the pain lasted about 22 days in those who received placebo. The vaccine was safe, had few adverse events, and was associated with only mild local reactions at the injection site. Based on PCR analysis, all episodes of HZ were wild type VZV, indicating that zoster vaccine did not cause HZ. Over the 3.1 years of study, the number needed to treat (NNT) to prevent one case of HZ was 59 and the NNT to prevent one case of PHN was 353.

The Shingles Prevention Study showed the efficacy and safety of the zoster vaccine (ZostavaxTM, Merck). However, some questions remained open. First, the duration of protection and the need for revaccination needs to be tested. Second, the risks and benefits of zoster vaccine in people younger than 60 years of age are not known. Third, due to the small sample size of the people aged 80 or older (less than 7 % of the study population), the efficacy of the vaccine on them needs to be confirmed.

On 23 March 2006 the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMEA) adopted a positive opinion, recommending to grant a marketing authorisation for Zostavax for prevention of HZ and PHN for individuals 60 years of age and older (EMEA 2006). The Food and Drug Administration (FDA) licensed Zostavax on May 25 2006 to reduce the risk of HZ for use in people 60 years of age and older (FDA 2006b). Four post-marketing studies will be conducted: (1) a randomized, placebo-controlled general safety study to assess the rates of serious adverse experiences in 6000 Zostavax recipients and 6000 placebo recipients; (2) a large-scale (20 000 vaccinated subjects) observational post-licensure safety study; (3) an observational study of the safety of a high-potency dose of Zostavax in 5000 subjects; and (4) a randomized, placebo-controlled, double-blind study to assess the safety of Zostavax in subjects receiving low-to moderate maintenance doses of corticosteroids (FDA 2006c).

The potential cost-effectiveness of vaccination against HZ has been previously assessed in the United Kingdom for a theoretical vaccine (Edmunds et al. 2001). The first estimation of the cost-effectiveness has been recently published (Hornberger and Robertus 2006). Because of the unknown duration of the vaccination efficacy no definitive conclusions could be drawn. The cost for a single-dose vaccine is $ 150, and the vaccination is estimated to be in an intermediate cost-effectiveness category (Koplan and Harpaz 2006). When the authorities decide on the reimbursement of Zostavax, they consider efficacy, safety, cost-effectiveness and the health care priorities. The pivotal question is whether the societal investment in zoster vaccine gives better gain in health and well-being than the other possible uses of that money. In those countries in which varicella vaccination in not instituted, it is likely to be prioritized over zoster vaccination in the battle against VZV.

Table 1. Complications of herpes zoster in three studies.

Complication	Galil 1997[1]	Ragozzino 1982[2]	Burgoon 1957[3]
Any complication	11,6 %	12,0 %	17,0 %
Postherpetic neuralgia*	7,9 %	9,3 %	9,7 %
Skin superinfection	2,3 %	Not assessed	
Herpes gangrenosum	Not assessed	0,5 %	1,0 %
Ocular complications	2,2 %	1,9 %	5,8 %
Motor deficit	0,9 %	1,0 %	
Meningitis, encephalitis or CNS vasculitis	0,5 %	0,2 %	0,5 %
Herpes zoster oticus	0,2 %	0,2 %	
Pneumonia		0,2 %	

* defined as pain continuing after healing of rash

1 population-based study from Boston, Massachusetts

2 population-based study from Rochester, Minnesota

3 clinic-based study from Philadelphia, Pennsylvania

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MARK YOUR CALENDARS! June 7-10, 2007, Berlin

Current SIG information

As of October 24, 2006, the NeuP SIG has 771 members in 55 countries representing 37 specialties.

The SIG Web site is: www.neupsig.org

Please submit your contributions, ideas and comments for the NeuP SIG newsletter to the SIG Secretary/ Newsletter Editor:

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