A survey of the “medical” articles in the European Spine Journal, 2006

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Received: 7 November 2006 / Accepted: 7 November 2006 / Published online: 3 January 2007
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Introduction

It has been a pleasure to do this overview of the 2006 issues of European Spine Journal (ESJ). ESJ is obviously in good health, considering the number of excellent papers coming from all parts of the world. Thanks to the remarkable and professional efforts of the Editors, much has been accomplished since the founding of the Journal, fifteen years ago by M. Aebi. At that time, and as is the case for most new publications, the immediate future of the Journal was not assured. Very rapidly, however, ESJ became the official

publication of the original European Spine Society, created in Brussels at approximately the same time. This association has proven to be successful.

Because of the multiplicity of high-quality papers, the “readers’ digest” task assigned to Bob Mulholland and me was not easy; moreover, this past year, in addition to an abundance of original papers and case reports, three excellent supplements were published. Two of them concern the evidence-based effectiveness and cost effectiveness of various treatments of spinal disorders. Efforts in this direction tend to lead to the development of appropriate guidelines. This clearly indicates the wishes of the Editors to take a leading role in this important matter.

Among the wealth of information, I have tried to select the most medically oriented papers which would primarily interest non-surgical readers of ESJ. I am convinced that ESJ will continue to be the expression of the multi-disciplinary commitment of all of us to the care of patients with spinal diseases.

Senescence and regeneration of the intervertebral disc

Biochemical and biomechanical changes implicated or resulting from disc degeneration may lead to nociception and pain production. For this reason, treatment strategies are being tested and developed experimentally in attempts to restore discs or retard disc degeneration. The August supplement of ESJ is devoted to updating current knowledge of the various strategies of discal regeneration.

Because matrix degradation results from failure of the disc cells to maintain and repair the matrix, one approach has been to inject cells into the disc. The

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article by Leung et al. [18] reviews the state of the art in this field and discusses the difficulty in obtaining appropriate cells and scaffolds. Another strategy is to deliver therapeutic molecules directly to the cells. Molecular therapy is updated by Yoon [30], a pioneer in this field. The article summarizes the *in vivo* and *in vitro* experimental studies and the various molecules under investigation which could be effective in disc repair. Although still in infancy, biologic therapy is a fascinating approach for the future.

Osteoporosis

The December issue has provided more information on diagnosis and treatment of osteoporosis. Friedrich et al. [8] have investigated the associations between the location of osteoporotic vertebral fractures between T8 and L2 and the patients' localization of pain in 51 consecutive patients. Pain location was divided into thoracic, lumbar and thoraco-lumbar area and was assessed by pain drawing. Pain intensity and the role of a trigger event at the onset of pain were also analyzed. Results of this study show that the location of the pain described by the patients is not accurate in determining the site of the compression fracture. For example, only 4 of the 20 patients with thoracic fractures reported thoracic pain, the other 16 reporting lumbar pain. These findings which need to be confirmed in a larger population should from now on prompt clinicians to obtain thoracic X-rays in LBP patients at risk for osteoporosis.

Several medications with a demonstrated efficacy are now currently used in the treatment of osteoporosis. These include estrogens, raloxifene, bisphosphonates and strontium. Calcitonin has also been used because of its anti-resorptive effect as well as its analgesic action in various pain syndromes. Papadokostakis et al. [22] have studied this latter effect on chronic back pain in post-menopausal women with osteoporosis as reported in the March issue. Forty women with osteoporotic vertebral fractures were compared with 30 women with degenerative disorders and 40 women with non-specific low-back pain. The three groups of post-menopausal women were randomly assigned to either nasal calcitonin and calcium daily, or only calcium daily. No effect on chronic back pain and functional capacity, evaluated by numerical rating scale and Oswestry questionnaire was observed in any of the three groups. The article contains a good discussion of the mechanisms of the analgesic effect of calcitonin, with an adequate review of the literature. It is important to know about the negative results of a

medication; they may prompt further studies and sometimes put an end to the use of ineffective, costly procedures.

Glucocorticosteroid-induced osteoporosis

Risk factors of osteoporosis are numerous. They include for example alcohol, tobacco, and medications. Among the latter, cortico-steroid treatment is the most frequent cause of secondary types of osteoporosis. Spine specialists, both medical and surgical, are prescribers of cortico-steroids for various vertebral disorders. Studies have shown that physicians do not always correctly consider the iatrogenic effect on bone. For this reason, the excellent review by Popp et al. [25], published in July, is a useful reminder of this complication. There is a good and clear overview of the pathophysiology of GIOP, resulting from a low activity of the osteoblast, and increased bone resorption due to a prolonged life span of osteoclasts. A detailed analysis of steroid-induced bone loss indicates that the risk factor varies according to age and to the pathology for which the treatment has been prescribed. It also shows that the risk is rapidly established after initiation of treatment, is cumulative dose-dependent and can be observed at low doses. The risks of fractures are discussed as well as the indications of vertebroplasty. There is a good update of treatment and of prevention. Bisphosphonates (risedronate and alendronate) are the current gold standard medications, in addition to calcium and vitamin D. Strontium ranelate is not discussed by the authors. This latter therapeutic class could however be used in the future because of its bone formation and anti-resorptive effects. I strongly recommend that all clinicians interested in spine care read this review.

Vertebroplasty

In the December issue of ESJ, the reader will find a well-conducted, systematic review by Ploeg et al. [24] of percutaneous vertebroplasty for treatment of osteoporotic vertebral fractures in order to assess the efficacy and safety of the procedure. Selection and methodological assessment followed the guidelines for systematic review developed by the Cochrane Collaboration Group. The article contains a good description of the 23 selected studies. Most of the papers are case-series studies with only one control trial. Most of the open studies report good results on pain, functional activity and quality of life, persisting for one or two

years. However the beneficial outcome could only be demonstrated in the controlled trial by Diamond et al. [5], showing a clear superiority of vertebroplasty over the classical conservative treatment. The authors conclude that evidence-based assessment of vertebroplasty requires future controlled trials. Complications of the procedures at short and long term are tabulated, including cement leakage and odds ratio of a vertebral fracture in the vicinity of a cemented vertebra, 2.27, compared with 1.44 in an uncemented fractured vertebra. There are a number of risk factors of symptomatic vertebral compression fractures. These factors principally include the bone mineral density and other variables such as familial or personal previous fractures, use of steroids and of tobacco, the body mass index, and perturbation in equilibrium in the elderly.

The paper by Lee et al. [17] investigates the factors related to the development of new symptomatic vertebral compression fractures after percutaneous vertebroplasty in osteoporotic patients. A retrospective review of 244 cases of PVP was performed. Numerous clinical, socio-demographic and procedural data were analyzed and compared between two groups: the first one with no further OCVF during the follow-up period (mean 52.5 months) and the second group with newly developed fractures which were observed in 38 out of 244 (15.6%) treated patients. Old age and the multiplicity of treated fractures during the initial procedures were strong predictors of new fractures. A mild wedge deformity of the treated vertebra was also a parameter of increased risk. Unlike observations of previous studies, location of the new fractures was adjacent to the treated fracture in 122 patients (58%) and remote in 42%. Half of the fractures developed within the first post-operative year.

Spinal tumors

The article by Janson and Bauer [12] published in the February issue reports a prospective study of 282 patients operated for spinal metastases at the thoracolumbar level. All patients had a neurological deficit due to epidural compression, evaluated according to the Frankel classification. Approximately two-thirds of the patients could not walk preoperatively. No surgery was performed for pain alone. This series confirms the usual sites of the primary tumor: prostate, breast, lung, and kidney. Most patients operated by posterior decompression and stabilization improved their motor function. The ability to walk was retained post-operatively in 80% of patients. However, this improvement is counter balanced by the high rate of complications,

the slow recovery of the motor deficit, and the fact that many patients died within the first months after surgery. The authors stress the difficulty of identifying the patients who will die early. The survival depends on several interrelated factors: primary site of the tumor, general condition, extra-spinal bone metastases, number of spinal metastases and metastases to other organs. Series such as this one based on a large number of patients are rare. This paper is of high quality and provides extremely useful information.

Infection

In an experimental study on sheep, Walters et al. [28] have assessed the efficacy of cephalozin in preventing and treating infection of the disc. This paper consists of two studies. The first study describes the effect of a prophylactic injection of cephalozin in normal and degenerated discs prior to intra-discal injection of a suspension of *S. aureus*. Discitis was disclosed in all non-treated sheep, and in 7 out of 24 treated sheep, indicating that infectious discitis cannot be eliminated by broad-spectrum antibiotic such as cephazolin. The second study demonstrates that cephazolin enters the disc but is unable to prevent endplate destruction if infection is established. This study, published in September, shows the importance of choosing an appropriate antibiotic for prophylactic as well as for treatment in infectious discitis.

In the same issue of the Journal, there is an interesting report by Khazim et al. [14] of three cases of fungal osteomyelitis (*Candida albicans*) of the spine, with an extensive review of the literature. *C. albicans* is a rare cause of vertebral osteomyelitis. It affects the spine through hematogenous dissemination, and leads to vertebral destruction with neurologic complications in the absence of antifungal treatment. In the cases described by the authors, the long delay in diagnosis made by MRI findings and percutaneous biopsy necessitated a combined medical treatment and surgical debridement.

Imaging

In the September issue an interesting study by Kjaer et al. [15] has attempted to determine whether people with low-back pain and Modic changes on MRI have specific clinical findings. Four hundred and twelve individuals extracted from the general population underwent extensive history and clinical examination tests which were compared with lumbar MRI findings.

The study sample was divided into three groups: the first consisted of people with discal degeneration (DD) and Modic changes (MC). The second group consisted of individuals with DD but no MC. The third group consisted of persons without DD and MC. A specific clinical profile for individuals with both DD and MC was observed, including for example a higher prevalence of LBP, more reduced activities and sick leave for LBP, more heavy smokers, and more pain on movement. This study, published in the September issue, confirms the prevalence and clinical relevance of end plate changes in patients with discogenic pain. As suggested by the authors, more studies are needed to look at the factors that initiate the development of MC, and investigate whether the presence of Modic 1 changes could identify the LBP patients for whom fusion or disc replacement is indicated.

Since the first description by Aprill and Bogduk [2] of a high-intensity zone within the posterior annulus on T2 MRI, the value of this finding in the diagnosis of low-back pain has been a subject of controversy. In the May issue, the paper by Peng et al. [23], coming from China, somewhat relaunches the discussion on this controversial issue. Fifty-two patients with low-back pain without radiculopathy and disc herniation were studied. Discs with HIZ were correlated with a concordant pain response at discography and grading of annular disruption according to the Dallas discogram scale. HIZ was detected in 17 discograms and all had a concordant pain response at discography and grade 2 or 3 of annular disruption. Moreover, 11 patients with high-intensity zone on MRI underwent a posterior interbody fusion, allowing a histologic examination of the HIZ lesion, showing vascularized granulation tissue. Despite the fact that pain response of the discs without HIZ has not been recorded, and considering the usual discussion of the value of discography, this paper is worth reading as it contains a good review of the literature and might stimulate further studies.

Disc herniation

Dealing with patients who have a lumbar disc herniation with predominantly controlateral symptoms is not exceptional. It creates a difficult therapeutic strategy when a surgical treatment is considered, the question being whether the disc herniation is really the cause of the symptoms. The paper by Sucu and Gelal [26], published in the May issue, raises an interesting discussion. Five patients with disc herniation and controlateral symptoms were operated at the side of the disc herniation without exploring the symptomatic side. All

patients had a wide broad-based paracentral disc herniation with an apex inclined away from the symptomatic side. Partial unilateral discectomy and removal of the disc herniation was followed by immediate resolution of the symptoms. For the authors, the explanation of this paradoxical situation relies on the lateral deviation of the apex of the herniation which generates a traction force on the controlateral nerve root.

This explanation is discussed in the reviewer's comment by Balague and Gunzburg [3]. Aside from a critic of the methodology and validity of the reported outcomes and the absence of follow-up imaging, there is an interesting discussion on the etiology of sciatica which is worth reading. The commentators briefly state that inflammatory irritation of the nerve root may be more important than the mechanical compression. Some references are cited to reinforce their point of view.

Transforaminal injections

Transforaminal injections of steroids and/or local anesthetic are now commonly used as treatment for patients with radicular pain in the lumbar and cervical spine. Two interesting papers published in the October issue deal with this subject.

The article by Faraj and Mulholland [7] demonstrates the value of guiding the nerve root infiltration by a neurostimulator. This is a prospective study of 96 patients with radicular leg pain. Patients were divided into two groups. In the first group consisting of 39 patients, the nerve infiltration was performed without the help of the stimulator. In the second group consisting of 57 patients, the procedure was done with guidance of the nerve stimulator. Results were assessed using the Oswestry questionnaire. The response to NRI was statistically better when the stimulator was used: 96% as compared with 79% with no stimulator. In addition to a better placement of the needle with the stimulator, the authors also point out and comment on the variation of the responses according to the pathology, the best responses coming from patients with lateral stenosis.

Transforaminal injections are also used at the cervical level. In a very useful paper, Andeberg et al. [1] have studied the distribution patterns of cervical transforaminal injections evaluated by CT. Distribution of contrast media injected prior to carbocain and depomedrol was classified as epidural/intraspinal, intra-foraminal and periarterial with contrast around/along the vertebral artery. The length of the perineural distribution and the presence of contrast media at the level above or below the injected level were also studied. Three different volumes were injected in three

groups of patients (0.6, 1.1, 1.7 ml). In all patients the injected mixture had perineural, intra-foraminal, and extra-foraminal distribution. The spread of the injected product (carbocain for selective diagnostic root block or steroid) was related to the size of the foraminal area and to the injected volume. In patients with a narrowed foramen, the space may be too small to contain the injected product and spread along the vertebral artery may occur at adjacent levels. At larger volume there is an increasing distribution in the epidural area and at levels away from the injected foramen. The authors also review the neurological complications of the procedure, including the risk of penetrating the radicular artery, the vertebral artery, and the sub-dural space. References of these complications are updated. Although preliminary, this paper should be read carefully by radiologists performing therapeutic transforaminal injections.

Synovial lumbar cysts

Due to progress in imaging, there is an increasing frequency of reported synovial cysts in routine clinical practice. An interesting article by Khan and Girardi [13] in the August issue reviews the clinical symptoms, diagnosis imaging and therapeutic management. Although the etiology is not clear the authors confirm the frequent association of the cysts with facet arthropathy, instability, and degenerative spondylolisthesis. This explains the high rate of failure of conservative treatment, including steroid injections, in the series reviewed by the authors. Surgical treatment is often necessary, the technique depending on the size of the cyst, its location, and associated comorbidity. The article contains an adequate review of the literature with outcome of treatments.

Epidural lipomatosis

Maillot et al. [19] present an interesting case report of epidural lipomatosis in the January issue. The 63-year old patient presented with LBP and sciatica with neurogenic claudication. CT myelography revealed a voluminous epidural lipomatosis at L4 L5 and L5 S1 levels. The patient was obese, with heavy absorption of alcohol, glucose intolerance, and mixed hyperlipidemia. Reduction in alcohol intake and a restrictive diet obtained a loss of weight and a dramatic improvement in pain and walking distance, with a marked reduction of lipomatosis on the imaging studies. In the discussion the authors establish a relationship between epidural

lipomatosis and central obesity phenotype. They also suggest the possibility of a specific insulin resistance treatment for this category of patients in order to avoid laminectomy, sometimes required in idiopathic forms of the disease.

Atlanto-axial osteoarthritis

Atlanto-axial osteoarthritis is a distinct clinical syndrome, characterized by uni- or bilateral upper cervical pain, irradiating in the occipital area. It is a rather frequent condition in older patients, often neglected if a plain radiograph trans-oral view of the C1–C2 joint is not obtained. The paper by Grob et al. [9] which appeared in the March issue is a good reminder of the syndrome and of its difficult and often resistant conservative treatment. Thirty-five patients with a severe intractable pain were operated by trans-articular screw fixation. Self-rated outcome measures were obtained in 29 patients (83%) with a mean follow up of 6.5 years. A great majority (85%) declared to be satisfied with the procedure and would do it again in spite of the restriction in overall head rotation. A low rate of serious complications was observed. This surgical paper based on a large series should be of interest to clinicians dealing with neck-pain patients.

Whiplash-associated disorders

Factors predicting outcome after whiplash injury in patients pursuing litigations have been studied in a large cohort of patients by Lankester et al. [16], published in the August issue. This is a retrospective study of 277 patients pursuing compensation, representing a selective group, commonly encountered in clinical practice. Pre-accident, accident, and ensuing symptoms and signs variables were recorded. A multivariate analysis determined the individual variables that predict a poor outcome, evaluated on three scoring systems. Many of these factors, whether physical or psychological, were present before the accident. This interesting article indicates a physical and psychological vulnerability in this group of patients, thus explaining the wide variety of response to whiplash injury.

Medical treatment

An evidence-based review of the outcome of non-invasive treatment modalities for back pain appeared in the January supplement. This huge piece of work by

van Tulder et al. [27] updates the present available evidence of the efficacy of interventions currently used in treating LBP patients. Reading this article is recommended. It shows that many of these interventions are effective at short term for acute and chronic LBP. However, there is still no evidence of long-term effects on pain and function for chronic LBP. Another interesting systematic review paper by Wessels et al. [29] has attempted to determine whether changes in treatment variables of the three non-operative treatments of chronic LBP proven to be effective (exercise, behavioral, and multimodal therapy) could improve outcome. Although not conclusive, this review suggests that changes in behavioral variables and reduction of disability may be more important than physical performance factors, underlining the role of social and psychological factors.

Outcome assessment

Existing scientific evidence of efficacy or inefficacy has been obtained for various treatments, medical or surgical, such as, for example, surgical discectomy for disc herniation or advice to stay active for acute LBP. Randomized controlled trials are at the present time the gold standard for determining the evidence-based efficacy of a treatment modality. However, as emphasized by van Tulder et al. [27], no clear evidence has been obtained for many interventions because many trials show methodological weaknesses. The January supplement contains some very good papers in the field of outcome assessment and documentation.

The excellent editorial by Boos [4] summarizes the basics of a comprehensive outcome assessment, pointing out the necessity of an adequate economic evaluation by health-care providers. The author very wisely reminds us that the golden rule of “less is more” also applies in spinal disorders, calling for simplification and for what is really needed for the patient’s care. The paper by Hiebert and Nordin [11] provides a checklist of the key methodological issues to look for when evaluating a research paper. This review paper should be read carefully by researchers as well as by manuscript reviewers. In addition, the article reminds us that synthesizing conclusions on treatment efficacy come from systematic literature reviews, which unfortunately do not necessarily provide scientific evidence and consensus, the other approach being the best synthesis evidence. The authors clearly explain these two categories of conclusions.

An excellent review on pain assessment is provided by Haefeli and Elfering [10] who discuss the various

instruments to assess pain intensity and pain effect. The authors stress the importance of pain history in evaluating back-pain patients, pain being the main complaint of this category of patients.

Self-administered, condition-specific questionnaires are now widely used to assess outcomes in low-back therapies. Advantages and disadvantages of the five most frequently used questionnaires (Oswestry Disability Index, Roland Morris Disability Questionnaire, Low-back Outcome Score, Nass Lumbar Spine Outcome Instrument, and The Quebec Back-Pain Disability Scale) are thoroughly discussed in the paper by Müller et al. [20] who also provide some recommendations.

Two other basics of assessment i.e. world-related outcome and health-related quality-of-life outcome instruments are discussed in depth, respectively by Elfering [6] and Nemeth [21] in the same supplement which is full of important information.

Conclusion

My selection of the papers presented in ESJ during the past year has been based not only on their scientific quality but also on their diagnostic and/or therapeutic interest in clinical practice. Many other excellent review or original articles and research papers can be found in the 2006 issues. They open a wide field of discussion and controversies. To quote Alf Nachemson, it is still “springtime for low-back pain”.

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