



REVIEW ARTICLE

Ankylosing spondylitis: recent developments and anaesthetic implications

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Summary

Ankylosing spondylitis can present significant challenges to the anaesthetist as a consequence of the potential difficult airway, cardiovascular and respiratory complications, and the medications used to reduce pain and control the disease. There is also an increased risk of neurological complications in the peri-operative period. Awake fiberoptic intubation is the safest option in those patients with a potentially difficult airway as it allows continuous neurological monitoring while achieving a definitive airway. Neurophysiological monitoring (somatosensory and motor evoked potentials) should be considered in patients undergoing surgery for cervical spine deformity. The medical management of the disease has improved with the use of anti-tumour necrosis factor- α agents. There is potential for increased wound infection in patients taking these drugs. This article reviews the anaesthetic issues in patients with ankylosing spondylitis. The challenge to the anaesthetist is in the understanding of these issues so that appropriate management can be planned and undertaken.

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Ankylosing spondylitis (AS; also known as Bechterew disease; Marie Strumpell disease), an autoimmune seronegative spondyloarthropathy, is a painful chronic inflammatory arthritis punctuated by exacerbations ('flares') and quiescent periods. It primarily affects the spine and sacroiliac joints and eventually causes fusion and rigidity of the spine ('bamboo spine'). Ankylosing spondylitis varies widely in prognosis and outcome. It is also associated with ulcerative colitis, Crohn's disease, psoriasis and Reiter's syndrome (uveitis). Recent experience with anti-tumour necrosis factor α agents clearly indicates that these biological agents are effective in treating ankylosing spondylitis.

AS can present significant challenges to the anaesthetist as a consequence of the potential difficult airway, cardiovascular and respiratory complications, and the medications used to reduce pain and control the disease.

This article aims to provide an overview of AS and the recent advances in its management with anti-tumour necrosis factor- α (anti-TNF- α) agents and to highlight the key practical issues of relevance to the anaesthetist.

Epidemiology

Ankylosing spondylitis occurs in 1% of men and 0.5% of women in Caucasians [1–4]. It is more prevalent in males with a peak age onset of 20–30 years [5, 6]. Men tend to have more severe spinal and pelvic disease, whereas women have peripheral joint (knees, wrists, ankles, hips) involvement [7]. Symptoms develop before the third decade of life in 80% of patients with AS. Less than 5% of patients develop AS in the fourth decade. Juvenile onset (age 10–16 years) AS is a more severe disease and occurs in 4% of AS.

Pathogenesis

The initiating cause of AS is not known but environmental factors (unidentified bacterial or viral agents), susceptibility genes (HLA-B27), gender, age and ethnicity play a role [8]. Overall, sporadic AS is more severe than familial disease. Although only 5% of HLA-B27 positive individuals develop AS, 90–95% of patients with AS possess HLA-B27 alleles. HLA-B60, MHC genes

including MICA, HLADRB1/MHC Class II alleles, tumour necrosis factor- α , IL-1ra and low molecular weight proteasome are all implicated [9]. In 2007, an international collaborative research team reported the discovery of two genes (ARTS1 and IL23R) that are associated with AS. Together with HLA-B27, these two genes account for roughly 70% of the overall incidence of the disease [10]. The presence of HLA-B27 is estimated to account for no more than 50% of the genetic susceptibility to AS. One study showed that onset of symptoms of AS was earlier in HLA-B27 positive patients compared with HLA-negative patients [11, 12]. Genes in the chromosomes 18, 20 and 21 are responsible for increased severity of disease in sporadic AS, whilst susceptibility genes in chromosomes 1, 2, 9, 10, and 16 are implicated in familial AS. There are at least 23 subtypes of HLA-B27 (B*2701–B*2723). Some subtypes have a protective role, for example, HLA-B*2709 is found in healthy individuals from Sardinia, and HLA-B*2706 is negatively associated with AS [12].

Two hypotheses, the arthrogenic peptide hypothesis and the HLA-B27 folding hypothesis have been proposed [9]. The arthrogenic peptide hypothesis postulates that when an individual with HLA-B27 is exposed to an antigenic pathogen (e.g. Epstein–Barr virus protein, human vasoactive intestinal peptide receptor-1 and a peptide derived from type VI collagen), a cytotoxic T cell mediated autoimmune response occurs in the joints [13]. The HLA-B27 folding hypothesis suggests that abnormal conformation or misfolding of the HLA-B27 heavy chains results in the accumulation of unfolded proteins in the endoplasmic reticulum. This generates pro-inflammatory cytokines and chemokines that activate nuclear factor $\kappa\beta$, resulting in transcription of genes encoding cytokines, tumour necrosis factor α , and interleukins IL-1 and IL-6, that are responsible for the inflammation in the joints. Synovial fluid mononuclear cells of patients with spondyloarthropathy provide evidence of this process [14].

Gram negative bacteria such as *Campylobacter*, *Salmonella*, *Shigella flexneri* and *Yersinia* cause reactive arthropathy. Of these patients who have reactive arthritis and possess HLA-B27, approximately 10–20% develop AS 10–20 years later. In patients with Crohn's disease, 54% of HLA positive patients develop AS whilst only 2–6% of HLA negative patients develop AS. It is postulated that leakage of gut mucosa causes an interaction between the immune system with gut bacteria [15]. However, there is no clear evidence as to the role of bacteria in development of AS.

Both innate and adaptive immune responses play a role in spondyloarthritis. CD4+ and CD8+ T cell infiltrates are found in synovial fluid, sacroiliac joint biopsies and in

peripheral blood of patients with AS. TNF- α is over-expressed in sacroiliac joints of patients with AS and this provides the basis of the use of anti TNF- α agents in the treatment of AS [16].

Clinical features

Ankylosing spondylitis is characterised by sacroilitis, peripheral arthropathy, enthesopathy (pathological changes at the sites of insertion of ligaments and tendons), and the absence of rheumatoid factor. The symptoms of AS usually begin between the ages of 15 and 40 years with persistent pain and morning stiffness (worse at rest but improves with exercise) in the lower spine and the sacroiliac joints. The mortality of patients with AS is 1.5–4 times higher than the general population [17].

Histologically, granulomatous inflammatory tissues in the affected joints are infiltrated by plasma cells, lymphocytes, mast cells, macrophages and chondrocytes. These are gradually replaced by fibrocartilage and progress to bony fusion in about 70% of patients. The absence of any specific pathognomonic clinical feature or laboratory test tends to delay the diagnosis by 7–10 years from onset of symptoms. Extensive ectopic bone formation occurs within the inflamed vertebral ligaments, leading to syndesmophyte formation. This is compounded further by the increased incidence of osteoporosis in patients with AS, which, in the long term, can lead to compression fractures resulting in a rigid hyperkyphotic deformity ('hump'). This greatly increases the iatrogenic risk of spinal cord injury when transferring patients or performing fracture reduction manoeuvres. The rigid, kyphotic spinal deformity and peripheral arthritis cause an unsteady gait, and an increased susceptibility to falls leading to fracture.

Complications of severe spinal disease include fractures with little or no history of trauma, collapse of vertebral end-plates (spondylodiscitis) and spinal nerve root compression. Cervical fractures which occur commonly at C5–6 are often overlooked because they occur with minimal trauma or hyperextension. Clinically significant atlanto-axial subluxation occurs in 21% of patients with AS. About 47% of AS patients with vertebral compression fractures have a neurological complication ranging from paraesthesia to loss of muscle strength [17–19].

The most common joints affected are the hips and shoulders. End stage hip disease requiring hip replacements occurs in 20% of patients with juvenile onset AS, in about 10% of patients with onset in late teens, and rare when the onset is in the late 20–30s. Peripheral joint involvement occurs in 50% of patients and is more common in patients with concomitant psoriasis [12].

Temporomandibular joint involvement causes limited mouth opening in 10% of patients and this increases to 30–40% patients with long standing disease. The disease rarely causes arthritis of the cricoarytenoid joint, but can lead to dyspnoea, hoarseness and vocal cord fixation. AS often affects costovertebral and costo-transverse joints (less commonly the manubriosternal and costochondral joints) causing local tenderness and pain on coughing or sneezing. Other features include plantar fasciitis and Achilles tendonitis [7].

Extra-articular manifestations are associated with more severe AS and those relevant to anaesthesia involve the cardiovascular system, lungs and skin. Cardiovascular complications associated with AS are seen infrequently. Fibrous proliferation of the intima of the aorta can result in aortic insufficiency. It occasionally affects the mitral valve [20]. Involvement of the Purkinje fibres causes conduction defects and there is an increased risk of myocardial infarction. Respiratory complications include upper lobe fibrosis and reduced chest expansion due to involvement of the costovertebral joints. In patients with restricted chest movement, vital capacity and functional residual capacity are decreased. Owing to lung fibrosis, chest X-rays may show apical fibrosis while pulmonary function testing may reveal a restrictive lung defect. Anterior uveitis (iridocyclitis) occurs in 20–40% of AS patients, psoriasis in 9% and inflammatory bowel disease in up to 6% of patients with AS. Anterior uveitis classically presents with sudden onset of blurred vision associated with eye pain, redness and photophobia. Some can progress to become chronic uveitis with permanent visual impairment [21]. Neurological effects include spinal cord compression, cauda equina syndrome, cervical spine fracture, focal epilepsy, vertebrobasilar insufficiency and peripheral nerve lesions. Spinal fractures can lead to acute epidural haematoma. Other systemic effects include fatigue, weight loss and fever. Most (85%) male patients complain of symptoms of prostatitis at some point in the disease [22].

Diagnosis

The diagnosis of AS is made on clinical and radiological criteria [23]. Radiological evidence of sacroiliitis is a late feature of the disease. Earlier diagnosis and treatment may reduce the severity of the effects of the disease [24]. In 2006, Rudwaleit et al. [25] proposed diagnostic criteria for inflammatory back pain in patients < 50 years with chronic back pain that may lead to an earlier diagnosis of AS. These included morning stiffness > 30 min, improvement in back pain with exercise but not rest, awakening because of back pain during the second half of the night only, and alternating buttock pain. The criteria

Table 1 Modified New York criteria for AS [23]. Diagnosis of AS requires one radiological criterion with at least one clinical criterion. Probable AS > 3 clinical criteria present or radiological criteria.

Clinical criteria	
Low back pain > 3 months duration, improves with exercise and is not relieved by rest	
Limitation of motion of the lumbar spine in sagittal and coronal planes	
Limitation of chest expansion relative to normal values corrected for age and sex	
Radiological criteria	
Bilateral sacroiliitis – grade 2 (sclerosis with some erosions) or higher	
Unilateral sacroiliitis – grade 3 (severe erosions, pseudodilatation of joint space and partial ankylosis) or grade 4 (complete ankylosis)	

required for diagnosis of AS are summarised in Table 1. Mild normochromic anaemia and raised IgA serum levels may be present. ESR is elevated in 50% of patients but may be normal even in severe disease. A raised alkaline phosphatase is found in severe disease. The correlation between inflammatory markers and AS is poor with only half of patients with AS having a raised CRP [26]. HLA-B27 may be useful in diagnosis of early spondyloarthritis. Most patients with AS are HLA-B27 positive with a 50% chance of transmitting the antigen to their children. Children who are HLA-B27 positive have a 33% risk of developing AS.

Radiographs of the sacroiliac spines appear normal in the early phase of the disease and structural changes only become apparent after many years. As the disease progresses, interspinous ligaments become ossified and bony bridges form between the vertebrae of the lumbar spine giving the classic bamboo spine appearance on X-ray. The characteristic bamboo spine and fused sacroiliac joints on radiographs are a late presentation. Magnetic resonance imaging (MRI) is useful in the early diagnosis of AS because it can show inflammation, bone marrow oedema and erosions at the sacroiliac joints and at cartilage/bone interphase before they can be observed on plain radiographs. It is a highly specific and sensitive tool that can detect active inflammatory axial disease, especially in combination with scintigraphy used to screen for other affected sites. MRI is useful for monitoring the progression of the disease and can predict the development of structural radiographic change 3 years before they occur (positive predictive value of 60%). In a prospective study of the role of MRI, quantitative sacroiliac scintigraphy and plain radiography in detecting active sacroiliitis in 44 patients, MRI was found to be the most sensitive imaging technique (95% sensitive vs 48% sensitive for scintigraphy and 19% sensitive for plain radiographs) [27, 28].

Management

The main aims of the management of AS patients are to relieve pain, reduce inflammation and maintain good posture and function. Early diagnosis and treatment may prevent spinal deformity. Traditionally, non-steroidal-anti-inflammatory-drugs (NSAIDs), education, exercise and physical therapy are the cornerstones of management for AS. Anti-TNF- α agents are novel drugs that are relatively efficacious in the management of patients who have failed conventional treatment. Joint replacement and spinal surgery is considered in patients with severe advanced disease associated with refractory pain and disability. Daily hydrotherapy and swimming can improve general fitness while protecting the joints. Although a Cochrane review concluded that there is little evidence for the effectiveness of non-pharmacological management, expert opinion and clinical experience suggest that individuals benefit from intensive physiotherapy [29].

Conventional drug therapy

Randomised controlled trials demonstrated that NSAIDs and cyclooxygenase-2 specific inhibitors were useful in controlling spinal pain [30]. In addition, NSAIDs may have a protective role against structural damage in the spine because they inhibit the synthesis of prostaglandin E2 which promotes bone growth.

Disease-modifying antirheumatic drugs such as methotrexate, sulfasalazine and leflunomide may provide symptomatic relief of symptoms of synovitis in peripheral joints but not spinal pain (caused by enthesitis) in axial joints [22]. Bisphosphonates may have a beneficial effect on underlying osteoporosis, the inflammatory process and spinal symptoms [31]. Thalidomide has also been used with some success but its toxic side effects has prevented its widespread use.

Intra-articular corticosteroid injection (guided by arthrography, CT or MRI) of an inflamed joint is safe and can provide rapid and long-lasting relief. Oral steroid therapy is less effective in patients with AS compared to patients with rheumatoid arthritis [32]. Pulsed intravenous methylprednisolone (0.5 mg) may provide short-term benefits by enabling the patient to obtain more benefit from physiotherapy [12].

Novel drugs

Anti-TNF- α drugs are the first drugs that have been shown in large randomised, placebo controlled, double blind trials to benefit patients with AS. Other cytokine based therapies in various stages of clinical development include PEG-sTNFR1 and CDP-870 [33]. TNF- α is a multifunctional cytokine involved in acute and chronic inflammation, antitumour responses and infection. TNF

messenger RNA is found in synovial biopsies of sacroiliac joints of patients with AS. TNF- α binds to cell membrane receptors and this results in adhesion molecule expression for leucocytes and vascular cell adhesion, chemoattraction, monocyte chemotactic protein and tissue degradation. It also promotes the generation of T cells and plays an important role in antigen presenting cell function and in regulating apoptosis of T cells. TNF- α increases inflammation in AS as well as other related spondyloarthropathies, psoriasis, and inflammatory bowel disease. Anti-TNF- α agents render TNF- α biologically inactive and diminish their biological responses. These drugs are also approved for severe and active rheumatoid arthritis that is refractory to conventional treatment, active juvenile idiopathic arthritis, psoriatic arthritis, severe Crohn's disease with inadequate response to conventional therapies, and severe psoriasis.

The three anti TNF α agents available for clinical use are infliximab (RemicadeTM; Centocor Inc., Malvern, PA, USA), adalimumab (HumiraTM; Abbott Laboratories, Abbott Park, IL, USA) and etanercept (EnbrelTM; Immunex Corporation, Seattle, WA, USA). Infliximab and adalimumab are monoclonal antibodies that bind specifically to human TNF- α and inhibit it binding to its receptors, neutralising its biological activity. These two monoclonal antibodies also inhibit TNF- α production by binding to TNF expressing cells such as macrophages. Etanercept is a fusion protein that binds to TNF- α and TNF- β and neutralises these two cytokines but does not inhibit production from the cells. Patients usually improve within 2 weeks of commencing therapy [33].

Large-scale randomised, double blind, placebo controlled trials demonstrated that the TNF- α blockers suppress disease activity, improve physical function, slow disease progression and may achieve remission of the disease. MRI studies showed reduced spinal inflammation [34]. The erythrocyte sedimentation rate and C-reactive protein levels decrease following treatment with anti-TNF- α agents. Symptoms relapse when treatment with infliximab and adalimumab is ceased. Unlike infliximab and adalimumab, etanercept is not effective for the treatment of gastrointestinal symptoms and uveitis associated with AS. Recent international experience with anti-TNF- α agents suggests that these drugs are effective in treating patients with AS. Short term benefits include significant improvements in the control of the disease, function and quality of life. Younger patients with a shorter disease duration respond better to anti-TNF- α agents [35]. The pharmacological properties of the anti-TNF- α agents are summarised in Table 2 [36–39].

There is a twofold increase in the risk of bacterial infections in patients taking TNF- α blockers especially

Table 2 Anti TNF- α agents [49, 52].

Drug	Comments
Infliximab	Chimeric monoclonal antibody (human and murine proteins) Dose: 5 mg.kg ⁻¹ intravenous infusion every 6–8 weeks Half life: 8–10 days Effective in AS and concomitant IBD, uveitis and psoriasis
Adalimumab	Human monoclonal antibody Dose: 40 mg subcutaneous injection every other week Half life: 10–20 days Effective in AS, psoriasis and IBD
Etanercept	Human fusion protein Dose: Subcutaneous injection weekly (50 mg) or biweekly (25 mg) Half life: 5 days Effective in psoriasis but less efficacious for uveitis and IBD

IBD, immune bowel disease.

with adalimumab, which causes a longer period of immunosuppression. *Mycobacterium tuberculosis* (TB) is reported most frequently, with a preponderance of extrapulmonary tuberculosis. Patients should therefore be screened (Mantoux test and chest X-ray) for tuberculosis before starting treatment. Active or latent TB must be treated prior to commencing a TNF- α blocker. TNF- α blockers can reactivate chronic hepatitis B if concurrent antiviral therapy is not administered. Preliminary data suggest it may be safe and even beneficial in patients with chronic hepatitis C. The increased risk of serious infection in patients taking TNF- α blockers has implications for those patients undergoing surgery.

The most common side effects are injection site reactions to drugs administered subcutaneously and infusion reactions with infliximab. TNF- α blockers can induce a range of autoimmune neurological diseases such as Guillain–Barre syndrome and multifocal motor neuropathy. These drugs should be avoided in patients with pre-existing demyelinating diseases such as multiple sclerosis because of a risk of exacerbating demyelination in these patients. Vasculitis (a type III hypersensitivity reaction) is a very rare but serious complication associated with TNF- α targeted therapies. Paradoxically, anecdotal reports suggest that TNF- α blockers may be effective in the treatment of various types of vasculitis [40–42]. Large phase II and III trials have shown that TNF- α blockers should be avoided in patients with advanced cardiac failure (New York Heart Association class III–IV) because they may worsen the prognosis. The role of the anti-TNF agents in the incidence of lymphoma is debatable. The only study to investigate the rate of lymphoma in

Table 3 Contraindications for the use of TNF- α blockers [49].

Absolute contraindications	Active infections (including joint infections, infected prosthesis within previous 12 months) or severe sepsis Indwelling catheter Previous, untreated tuberculosis Moderate to severe congestive heart failure Multiple sclerosis or optic neuritis Combination treatment with anakinra (IL-1 receptor antagonist) Active or history of malignancy in the last 10 years (except basal cell carcinoma)
Relative contraindications	Pregnancy Lactation HIV, hepatitis B, hepatitis C infection

Table 4 Criteria for initiating anti-TNF therapy in ankylosing spondylitis [44].

Diagnosis	Modified New York criteria for definitive AS fulfilled
Active disease	Active disease > 4 weeks BASDAI \geq 4 (range 0–10) and an expert opinion
Treatment failure after trial of:	Non steroidal anti-inflammatory drugs (NSAIDs) \geq 2 NSAIDs for a minimum of 3 months at maximum recommended or tolerated dose or < 3 months if treatment withdrawal because of intolerance/toxicity/contraindications Disease Modifying Anti-rheumatic Drugs – no response to sulfasalazine in patients with persistent peripheral arthritis Corticosteroid injection – no response to at least one local corticosteroid injection in patients with symptomatic peripheral arthritis

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index.

If there are no contraindications, all three sections have to be fulfilled before treatment with TNF blockers is commenced.

rheumatoid arthritis patients on TNF- α blockers found no increased risk [43]. The contraindications for the use of TNF- α blockers are summarised in Table 3 [42].

Guidelines for the use of anti TNF agents in the management of patients with AS are summarised in the international assessment in ankylosing spondylitis consensus (Table 4) [44].

Anakinra is a recombinant human interleukin-1 receptor antagonist that has been investigated in the treatment of AS. Two open trials have reported conflicting results [45, 46].

Anaesthetic considerations

In severe AS, knee and hip joint replacements and corrective spinal surgery for severe flexion deformities may be required to improve function and quality of life. Fixed cervical flexion resulting in chin on chest deformity

leads to difficulty with forward vision, swallowing and hygiene. Treatment of severe cervical kyphosis may ultimately require surgical correction. These surgical procedures present a wide range of challenges to the anaesthetist [47].

A thorough pre-operative assessment is essential to evaluate the severity of the disease, in particular airway involvement and the extra-articular manifestations of the disease. Peri-operative neurological deficits should be documented. The range of movement of all joints should be assessed to plan optimal positioning of the patient. The extent of pre-operative investigations depends on the severity of the disease and these include echocardiography, lung function tests, imaging of the cervical spine and arterial blood gas analysis. In view of the potential for conduction defects, a pre-operative ECG is mandatory. An echocardiogram is required to assess the severity of valvular disease associated with AS.

There is no clear consensus regarding the management of anti-TNF- α blockers in the peri-operative period. Giles et al. [48] showed a significant association between infectious complications following orthopaedic surgery and treatment with anti-TNF- α agents. Chang et al. [49] suggested that TNF- α blocker should be stopped pre-operatively in patients undergoing abdominal surgery to reduce the risk of infection and restarted when postoperative healing is established. The Dutch Society for Rheumatology advocated stopping the anti-TNF- α agents to allow the washout of the drug by the time of operation, i.e. 4.5 times the half-life of the particular agent. This recommendation is currently under debate [50]. However, in a retrospective study, den Broeder et al. [51] concluded that the peri-operative continuation of anti-TNF- α agents was not a significant risk factor for surgical wound infections. Other authors have also suggested that the infection risk is no reason to withhold therapy [52]. Prospective studies are needed to address this issue.

Airway management

Difficult intubation is associated with AS involving the cervical spine and can be compounded further when the temporomandibular joint is involved. Neck movements in extension and flexion should be assessed by radiological screening. Pre-operative indirect laryngoscopy can be invaluable in assessing a patient to predict difficult intubation. There is significant risk of neurological injury with any excessive neck extension in patients with chronic cervical kyphosis. Neck extension can cause vertebral artery insufficiency as a result of bony encroachment on the vertebral artery. Injuries to the cervical spine and spinal cord such as dislocation of C6 vertebra and quadriplegia after an emergency intubation have been reported. Fixed cervical flexion deformities limit access to

the trachea and tracheostomy may be impossible. Neck supports should be used during anaesthesia and forcible movements of the neck in the presence of neuromuscular blockade avoided.

Death from a retropharyngeal abscess that resulted from multiple attempts at blind intubation has been reported [53]. Awake fibreoptic intubation is the safest option, especially in those patients where it is not possible to visualise the larynx on indirect laryngoscopy or those with severe chin on chest deformity. It also allows for constant neurological monitoring during placement of the tracheal tube. Retrograde intubation may also be considered.

The intubating laryngeal mask (ILM) and the classic laryngeal mask have been used during failed intubations in AS patients as alternatives or aids to tracheal intubation in the anaesthetised patient, and for awake insertion. An advantage of this technique is that the trachea can be intubated without head and neck movement or direct laryngoscopy and ventilation of the patient's lungs can be maintained during the procedure. However, it may be impossible to insert a laryngeal mask in patients with severe flexion deformities because the angle of the oropharynx axis can cause it to kink and hinder its placement over the trachea.

In elective surgical patients who refuse an awake fibreoptic intubation, the ILM may be a useful device in managing the airway in an anaesthetised patient. One case series demonstrated successful blind intubation through the ILM in 11 of the 12 patients with severe AS. The ILM was inserted and manual ventilation was achieved at first attempt in all 12 patients. The authors suggested that a precurved PVC tracheal tube in the reverse direction enabled higher success with a lower complication rate compared to the straight silicone tube [54]. The ILM may also be easier to insert in patients with an immobile neck and is a superior aid for fibreoptic intubations compared with a laryngeal mask [54–56].

The laryngeal mask is more appropriate in patients with restricted mouth opening of < 2 cm or in patients who do not require intubation. It may not be possible to place a laryngeal mask in patients with AS when the mouth opening is < 1.2 cm and if a fixed extension deformity and large cervical osteophytes are present [54].

Lai et al. [57] reported that the Glidescope[®] (GS) (Saturn Biomedical System Inc., Burnaby, BC, Canada) was a useful device that improved visualisation of the larynx and facilitated naso-tracheal intubation in anaesthetised patients with AS. In this study of 11 AS patients who were assessed to have difficult airways, the GS improved the laryngoscopic view in all patients and nasal intubation was successful in eight of the 11 patients. Awake fibreoptic intubation was performed in the other three patients who could not be intubated using the GS.

The main limitation of the GS is the resistance encountered during advancement of the tracheal tube.

Regional or local anaesthesia

Spinal and epidural anaesthesia is technically difficult and may result in an increased risk of complications. Convulsions secondary to accidental intra-osseous injection of bupivacaine during a caudal block and spinal haematomas following insertion of an epidural anaesthetic have been reported. Subarachnoid block using a lateral approach has been advocated as an alternative when general anaesthesia is contraindicated [58].

The placement of epidural anaesthesia is technically difficult and is associated with an increased risk of an epidural haematoma. In a comprehensive review of spinal haematoma associated with epidural anaesthesia over a 30-year period (1966–1995), Wulf reported five out of 51 patients with spinal haematoma occurred in patients with AS. These were related to difficult or traumatic insertion [59]. Other predisposing factors included concurrent NSAID therapy and a narrow epidural space. Pre-operative coagulation studies may be prudent in these patients. Repeated neurological examination in these patients after neuraxial anaesthesia should be undertaken because they have an increased risk of developing a spinal haematoma [60].

The epidural space is narrow in AS patients and local anaesthetic solutions should be administered slowly in small doses to avoid total spinal anaesthesia. A recent case report described a total spinal anaesthetic following epidural test dose in an AS patient with anticipated difficult airway for a total hip replacement. Technical difficulty and multiple attempts of a combined spinal epidural were possible contributory causes [61].

Corrective spinal surgery

Surgical correction of severe cervical spine deformity can significantly improve a patient's functional and psychological status. Airway problems and potential neurological injury are the main issues. A fixed thoracic deformity causes restrictive pulmonary function. The patient may be malnourished due to swallowing difficulties and may need pre-operative supplementation or parenteral nutrition. The surgical procedure itself is technically demanding and carries a potential risk of significant neurological injury. Peri-operative mortality as a result of pulmonary, cardiac and intestinal problems is approximately 4% [62]. Important anaesthetic considerations include neurophysiological monitoring, patient positioning, surgical approach and spinal instrumentation. The prone position allows surgical access for multilevel decompression and internal fixation.

General anaesthesia with controlled ventilation via tracheal intubation affords a secure airway, facilitates

cervical spine surgery by allowing a patient to be prone, eases placement of instrumentation, and reduces the risk of air embolism. Neurological function monitoring is essential because spinal cord injury can result from direct translational injury or from impingement from osseous compression. A wake-up test can allow assessment of patient's neurological function.

Motor evoked potentials (MEPs) and somatosensory evoked potentials (SSEPs) are used to monitor neurological function intra-operatively [63]. SSEPs primarily evaluate sensory function mediated by the dorsal columns of the spinal cord. Unlike intravenous anaesthetic agents, inhalational anaesthetics cause a dose related increase in latency and a decrease in the amplitude of SSEP. Several case reports of significant postoperative neurological deficits associated with normal intra-operative SSEPs have been published. [47]. MEPs are used to complement SSEP monitoring to detect potential damage to the corticospinal (motor) tracts of the spinal cord. The relatively large voltage of MEP enables instantaneous monitoring because signal averaging is not required. Following extension of the neck during corrective surgery decreases in the amplitude of MEPs actuates immediate corrective measures [47].

Anaesthetic management of the parturient with AS

Most pregnant patients with AS have normal vaginal deliveries. However, manifestations of AS can interfere with labour, delivery and the administration of regional and general anaesthesia. Awake fiberoptic intubation in the left lateral position has been reported in a parturient with a history of a failed intubation at previous surgery [64]. These patients should be referred early on in the pregnancy to the obstetrician and anaesthetist so that together they can prepare a management plan.

Postoperative management

The same precautions regarding patient positioning and neck movement apply at emergence from anaesthesia as with intubation. Physiotherapy, breathing exercises and early mobilisation should be instituted early because patients are at increased risk of respiratory complications. The effects of fluid shifts and the effects of medications on peri-operative fluid balance should be monitored.

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