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Scientific Review

Autonomic dysreflexia

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Autonomic dysreflexia (AD) may complicate spinal cord injured (SCI) subjects with a lesion level above the sixth thoracic level. There are several ways to remove triggering factors and, furthermore, new trigger mechanisms may be added by the introduction of new treatments. New data about the pathogenic mechanisms have been suggested in recent years as well as signs of metabolic effects associated with the reaction. This review of the syndrome includes clinical aspects of the AD reaction; the known pathogenic mechanisms, the incidence and prevalence and triggering factors. AD is associated with some cases of severe morbidity, including cerebral haemorrhage, seizures and pulmonary oedema. Symptomatic as well as specific treatments are discussed. Finally, some further questions are raised by the necessity of a proper definition of the syndrome, the revealing of the underlying pathophysiology, and new investigations concerning incidence and prevalence.

Keywords: autonomic dysreflexia; spinal cord injury; paraplegia; sympathetic nervous system

Introduction

Spinal cord injury affecting the cord above the fifth to sixth thoracic levels is sometimes complicated by an autonomic dysreflexia (AD) reaction. The reaction has a rapid onset, is often dramatic with a huge increase in blood pressure and is triggered by stimuli arising below the lesion level. AD may be an important clinical sign of underlying morbidity in a body deprived of normal sensation but may in itself be dangerous and associated with morbidity. Furthermore, when introducing new treatments affecting the paralysed part of the body an awareness of the risk of provoking the AD syndrome is needed.

There are several ways to remove triggering factors, and the introduction of new treatments may introduce new triggering factors, therefore a review of the literature concerning these aspects is needed. Furthermore, in recent years further elucidation of the pathogenic mechanisms as well as signs of metabolic effects associated with the reaction have been reported. Against this background, a review of the clinical aspects of AD is presented.

Symptoms and signs

The presenting symptoms of the AD reaction are diverse and include pounding headache, cutis anserina (goose flesh), paresthesias, shivering, flushing and sweating of the head, nasal obstruction, desire to void, anxiety, malaise and nausea. There may be a feeling of dullness in the head and blurring of vision is not uncommon. Severe headache, usually of occipital, bitemporal and bifrontal location is noted in more than half of the patients.[1] A sensation of precordial pressure is sometimes reported.

The main objective sign of the reaction is a huge increase in systolic and diastolic blood pressure. Systolic blood pressure of 250–300 mm Hg and diastolic of 200–220 mm Hg have been reported.[1–3] In the able-bodied, such hypertension would be counteracted by a baro-receptor induced vasodilatation and a slowing of heart rate. In SCI subjects, where the connection between the baroreceptor and the main part of the body is broken, the only remaining way to centrally counteract the hypertension is vasodilatation above the lesion level and a baroreceptor mediated decrease in heart rate. The vasodilatation above the lesion level explains the flushing, sweating and stiffness in the nose and probably also the pounding headache. The baroreceptor-mediated increase in vagal activity above the lesion level explains the bradycardia. However, even though bradycardia is considered to be one of the main signs of AD this is far from always the case. A survey of 40 medical records by Kewalramani[1] found only 10% of true bradycardia, whereas tachycardia was reported in 38% of the cases.[1,4] It may be that the spinal reflex arc that induces a vasoconstriction below the lesion level also involves the sympathetic nerve

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fibres supplying the heart, thereby inducing an increase in heart rate by activating these fibres. If this is the case then there would be a difference in reaction between SCI subjects with a lesion level of T1–T5 exhibiting an intact connection between the brain and the sympathetic nerve fibres of the heart and SCI subjects with a cervical level of lesion with a disrupted connection. Whether this is the case deserves further investigation.

Symptoms and signs are diversified, and in order to compare the figures of incidence, prevalence and morbidity as well as evaluation of different treatments some major criteria need to be defined. The first descriptions of the syndrome involved profuse sweating and rash of the head and neck[5,6] and it was not until 1947 that paroxysmal hypertension was included in the description of the syndrome.[7] Today, most authors seem to include a blood pressure rise in the inclusion criteria, but the level of increase varies, some state 30 mm Hg others 40 mm Hg. In a treatment evaluation an AD severity score was used. Systolic blood pressure, sweating, spasm, headache, heart rate decrease and duration were evaluated on a five-graded scale, and treatment efficacy was evaluated by this score.[8] This seems to be an attractive way to evaluate the syndrome since several aspects are included. However, some objections may be risen: the evaluation of heart rate decrease seems to be inappropriate, since even heart rate increase may be seen during AD. Furthermore, muscle spasm is probably more a coexisting phenomenon than a symptom of AD. However, it is an important task for the international association to establish some common criteria for the AD reaction and to construct a severity score in order to be able to compare incidence and prevalence between different centres and over time as well as to be able to evaluate new treatments. For clinical use the following criteria can be suggested: Increase in systolic blood pressure by at least 20%, combined with at least one of the following symptoms: sweating or chills or cutis anserina or headache or flushing. For scientific use the increase in blood pressure of at least 20% ought to be combined with a visualised vasoconstriction below lesion level, illustrated by, for example, laser doppler flowmetry of skin blood flow or occlusion plethysmography.

Incidence and prevalence

The AD reaction is seen in paraplegics and tetraplegics with a level of lesion above the fifth to sixth thoracic segment. It is reported among complete lesions as well as among incomplete lesions,[1,9] although the reaction seems to be milder in subjects with incomplete lesions.[1] However, AD is also reported among paraplegics with a level of lesion below T6 although the reported reaction seems to be milder.[10] This indicates that a spinal reflex arc activates vasoconstrictor fibres below lesion level also in lower lesions, but that the full-blown reaction requires involvement of the splanchnic vascular bed. Furthermore, causes of spinal cord lesions other than traumatic have been reported to give rise to AD, eg. intramedullary haemorrhage caused by a spinal hemangioma[11] or astrocytoma mimicking a pheochromocytoma.[12] AD has also been reported after a brainstem tumour resection in area postrema.[13]

SCI subjects with lesions at or above T6 may exhibit AD, but how frequently is the syndrome actually seen? In a survey of 213 patients with complete lesions at T6 or above admitted to a spinal cord injury centre, 48% exhibited AD.[2] When taking the whole group into account that figure may be an underestimation since incomplete lesions may also exhibit AD, as found when evaluating the incidence of AD during urodynamic examinations, where a total of 59% (13/22) showed signs of AD.[14] Others have reported 70%[15] of a population of 20 subjects exhibiting dysreflexia. A field investigation of out-patients at the Spinal Injury Unit in Göteborg showed that 48 out of 76 (67%) SCI subjects stated that they sometimes suffered from AD. Thirty subjects graded the frequency as more than one occasion *versus* occasionally in the rest of the group (personal comm. M. Kreuter). In a survey of current treatment carried out in the USA in 1991, 86 physicians estimated the percentage of patients with symptomatic AD and the mean result was 19%.[16] 71% of the physicians stated that they felt that the incidence was lower than 10 years earlier. This lower incidence was thought to be due to fewer patients showing symptoms as well as milder symptoms in the patients exhibiting the reaction. Even though the incidence may decline we are facing a syndrome with a capacity to affect all SCI subjects with lesions above T6 and in fact affecting half to three quarter of that SCI population. The postulated decline in incidence may be due to improved awareness of the syndrome, new treatments of the urinary bladder as well as heightened attention to prevention.

Pathogenic mechanisms

It is impossible to understand the puzzling and diverse components of this huge reaction without consideration of the pathogenic mechanisms. Several mechanisms underlying the blood pressure increase have been proposed. Vasoconstriction below the lesion level in skin and skeletal muscle vascular bed[17–19] are manifested but the amplitude of the reaction indicates involvement of a large vascular bed, and the splanchnic vascular bed is a major candidate. A lesion level above the sixth thoracic segment involves an interruption of the connection between the brain and the splanchnic vascular bed, entailing an inability to dilate the vascular bed by central command when needed. Whether this inability to dilate explains the full-blown reaction is not known; there may be an active vasoconstriction also in the splanchnic vascular bed.

Animal research has shown an increase in renal sympathetic activity during induced dysreflexia, indicating an active vasoconstriction in the kidney.[20] Furthermore, the sympathetic innervation of the kidney leaves the spinal cord at the same level as the splanchnic outflow.

Most authors agree that the sympathetic nervous system is involved. However, microneurographic investigation of sympathetic nerve fibre activity below the lesion level were not able to demonstrate a significant increase in sympathetic nerve activity during induced dysreflexia,[21] in spite of a visualised decrease in muscle and skin blood flow. Endorgan supersensitivity has therefore been proposed.[21,22] However, platelet alpha-adrenoceptor density is normal in tetraplegic subjects.[23] in contrast to other autonomic deficiencies presenting denervation supersensitivity.[24] Furthermore, recent investigations of noradrenaline spillover below the lesion level exhibit a huge increase in spillover during induced dysreflexia.[19] This establishes that the peripheral sympathetic nerves are intact and readily activated. In contrast, there was no reaction in the plasma adrenaline level, or in the adrenaline spillover, showing that the adrenal medulla is not activated by this spinal reflex arc. The discrepancy between the microneurographic registrations of nerve activity and the spillover of neurogenically released transmitter to blood stream, may indicate an alteration in the intermediate region that is not visualized by either method. There may, for example, be an increased transmitter release per nerve impulse.

Furthermore, there are signs that the AD reaction is not an all or none reaction but rather the most severe form of a continuum. The finding of signs of AD also in SCI subjects with a lesion level below T6 indicate this. Recently, a continuous evaluation of p-noradrenaline by 30 min sampling during a period of 24 h showed episodes of elevation through the registration time that were mostly asymptomatic.[25] This indicates an ongoing activity in the isolated sympathetic nervous system below the lesion level. Another interesting feature of the sympathetic nervous system function after a spinal cord injury is the finding of signs of increased reactivity also above the lesion level.[19,20]

It may be that the AD reaction is an unmasked spinal reflex arc that is found also in the able-bodied but out of central control. However, some recent animal and human findings indicate a spinal remodelling below, as well as above, the lesion level after a spinal cord lesion. It is known that experimental spinal cord injury is associated with a remodelling involving a dendrite degradation of sympathetic preganglionic neurones post-injury, followed by signs of new synapse formation in the injured medulla above as well as below lesion level.[20,26–28] Recently, a study was published showing the same alterations also in humans.[29] Such a remodelling together with the inability to regulate the answer by central command may underlie the marked capacity for peripheral afferent stimulation of the sympathetic nervous system arising after spinal cord injury.

Triggering factors

Underlying disease

The AD reaction is provoked by peripheral afferent stimulation below the lesion level reaching the isolated spinal cord. The stimuli may arise from distension or contraction of hollow organs or from activation of pain receptors. If more than one peripheral stimuli is present simultaneously, it seems that the reaction is more severe and more readily activated. The AD reaction may be triggered by underlying disease but may also be caused by iatrogenic actions. Distension of hollow organs such as the bladder and the bowel are perhaps the most common causes. Catheterisation and manipulation of an indwelling catheter, urinary tract infection, detrusor sphincter dyssynergia[30] cystoscopy[15] cystometry and bladder percussion are all well-known precipitating factors. Among the 48 patients in Göteborg reporting an AD reaction some stated more than one triggering factor. Half of the patients mentioned problems with the urinary bladder, such as urinary tract infection or overfilling of the bladder. Eight subjects mentioned the bowel as a triggering factor, whereas seven subjects mentioned sexual activity including ejaculation, vibrator stimulation or sexual intercourse. Four patients related their AD to painful stimuli. Disease of the upper gastrointestinal tract such as gastric ulcer[13] and gastro-eosophagal reflux[31] may present as an AD reaction. Acute abdomen[32] and disease of the lower gastrointestinal tract eg. colorectal disease[33] and haemorrhoidal disease[34] may induce an AD reaction as well as faecal impaction. Syringomyelia usually presents with pain, motor weakness, sensory changes and/or increasing spasticity. However, the presenting symptom may be hyperhidrosis or other symptoms of AD.[35–37] Increasing spasticity is often seen during AD reactions, but whether spasticity in itself may trigger a dysreflexia reaction is not known. More likely the two symptoms are parallel and induced by the same triggering mechanism.

Other pathological conditions that in the able-bodied is associated with pain may induce an AD reaction. Skeletal fractures below the lesion level may present as an AD reaction.[38,39] Furthermore, three cases of hip dislocation have been reported to be associated with AD reaction.[40]

Sexual activity in both sexes may induce a dysreflexia reaction. Manipulation of the vagina during investigations may be a triggering factor and induction of AD by ovarian cysts have been reported.[41] Pregnancy[42,43] has been reported with increased frequency of AD attacks. More serious is the AD occurring during labour, which has been

reported in two-thirds of women with lesions above T6.[44] The blood pressure increase may be very large and two cases of intraventricular haemorrhage during labour induced AD have been reported.[44] It is of great importance that the staff is skilled and familiar with this reaction when treating spinal cord injured women.

Iatrogenic causes

The risk of inducing a dysreflexia reaction during urodynamic evaluation is well known and blood pressure monitoring during the investigations is recommended.[30] Invasive treatment of the urinary tract bears the risk of inducing a dysreflexia reaction. Therefore efforts have been made to reduce the risk by using flexible cytoscopes. An evaluation of this use was reported in 1993.[45] Of 39 patients previously exhibiting a dysreflexia reaction during cystoscopy only six subjects suffered from AD during flexible cystoscopy, thus emphasising that this technique is safer.

SCI subjects are at increased risk for urolithiasis. There are several possible treatments. One way to treat it is extracorporeal shock wave lithotropsy. In 1988 a paper reported five tetraplegic subjects who underwent the procedure following either a local field block or no anaesthesia. Significant hypertension occurred in two patients. In a report of 20 consecutive cases in 1993 treated without anaesthesia all but one (a T12 lesion level) experienced autonomic dysreflexia[46] with a mean increase of 44 mm Hg systolic blood pressure. However, in 1995 15 SCI subjects were reported. Eight subjects had a cervical lesion level, six a thoracic and one subject had a lumbar level of lesion. All underwent the procedure without autonomic dysreflexia reaction.[47] As seen, the majority of the subjects were at risk of developing the reaction with respect to lesion level. In a case report of another way to treat renal stones, percutaneous nehrolithotomy, a dysreflexia reaction was found during the operation.[48] The discrepancy between the studies is hard to explain, but one possibility is differences in definition of the syndrome. However, the main conclusion is that awareness of the risk is needed.

Electrostimulation

In an attempt to increase fertility in SCI men, electro-ejaculation and vibrator stimulation is used. These procedures have been reported to be associated with increased blood pressure assumed to be part of a dysreflexia reaction.[49–52]

Recently functional electrical stimulation of the legs has been used in an attempt to increase muscle size and improve metabolism. Stimulation of paralysed legs may be associated with AD reactions.[53–55] The increase in blood pressure is sometimes reported at the beginning of the procedure and is sometimes transitory[55] but more protracted reactions are also found, lasting during the whole stimulation period.[54]

A new way to increase arm and hand function is functional electrical stimulation with the stimulating electrodes applied directly on the muscles. Interestingly, the use of electrical stimulation in the arms has not been found to be associated with AD symptoms, even though the stimulation is performed below the lesion level (personal communication). In summary, electrical stimulation of legs and visceral organs may act as triggering factors and blood pressure monitoring is needed.

Stimuli that do not induce an AD reaction

Theoretically it is possible that all afferent stimuli below the lesion level may induce a dysreflexia reaction. However, there are, as far as known to the author, no reports in the literature of stimuli from the bronchio-pulmonary system that have been associated with an AD reaction. In the cervical lesioned SCI subjects the sympathetic outflow to the lungs are decentralised. As mentioned above, electrical stimulation of the muscles in the legs may provoke a dysreflexia reaction whereas the same stimuli applied to the arms do not seem to provoke a reaction. It might thus be suggested that it is afferent stimuli arising below the sixth thoracic segments that may trigger a dysreflexia reaction, not all stimuli below lesion level. Whether this is true needs to be tested experimentally.

An advantageous reaction?

Intentional induction of AD, so called boosting, is used among athletes for performance enhancement. A study of eight tetraplegic elite athletic subjects was performed in order to compare 7.5 km races during boosted and un-boosted conditions.[56,57] Blood pressure and the O_2 utilisation were higher during boosted conditions, whereas cardiac output was unaffected. There was an increase in noradrenaline levels, whereas adrenaline showed no difference. The intentional induction of AD was successful since there was a decrease in race time by almost 10%. Metabolic parameters were investigated. Glucose decreased during exercise and lactate increased, whereas the level of free fatty acids (FFA) was unchanged, and no difference was found between the boosted and unboosted condition. It is unlikely that a higher blood pressure or p-noradrenaline *per se* may increase performance. The higher O_2 utilisation indicates alterations in metabolism during boosted conditions. This was, however, not visualised by this study, maybe because the investigated parameters, especially FFA is difficult to interpret since released FFA is subject to re-esterification. A study of lipolysis during induced AD found an increase in glycerol release below the lesion level. The lipolysis was measured by microdialysis in the subcutaneous adipose tissue above and below the lesion level.[25] This

suggests that an increased supply of substrates during boosted conditions may explain the increased performance rate. If there is an increase in lipolysis during AD reaction, what is then the long-term effect? The previous mentioned continuous p-noradrenaline monitoring revealed a level sufficient to induce lipolysis in 20% of the registration periods. That study was done during 24 h of normal living in SCI subjects without urinary tract infections, pressure ulcers or other known triggering factors. This way to activate lipolysis may play the role of a compensating mechanism for the inability to activate lipolysis by central activation, as proposed during boosted conditions in athletics. However, the extra supply of glycerol and FFA during one fifth of the 24 h without any increased metabolic requirements may be pathogenic. It is known that SCI subjects exhibit decreased glucose tolerance, insulin resistance, and diabetes mellitus.[58,59] Furthermore, the group show alterations in body composition with an increased fat tissue mass below the lesion level.[60] A frequent peripheral activation of lipolysis in this increased fat tissue mass may be one pathogenic factor in the insulin resistance syndrome.

Morbidity

The AD reaction may be severe and constitute an acute condition. The increase in blood pressure is huge and is associated with neurological symptoms such as blurring of vision and headache. However, more serious events are reported including seizures,[61,62] intracerebral[63] and subarachnoid haemorrhage.[62] Seizures have been reported as secondary to subarachnoid haemorrhage[62] but are also reported in three patients that had no intracerebral pathology. However, a spinal cord injury is often part of a multitrauma and slight intracerebral lesions may be present, thereby increasing the risk for seizures during extreme conditions such as the blood pressure increase during AD.

Furthermore, spontaneous intracerebral haemorrhage leading to death[44,62,63] has been described. This may be an increasing problem since we are facing a growing population of ageing spinal cord injured, facing the same risk factors for cerebrovascular disease as the able-bodied, but with the additional risk of huge and abrupt increase in blood pressure during AD episodes.

Another serious complication associated with AD was described in a case report of a prolonged AD in a C6 tetraplegic patient, where the AD reaction was complicated by neurogenic pulmonary oedema.[64] The patient underwent sphincterotomy and was left with an overinflated Foley catheter balloon inducing an AD reaction. The patient became dyspnoeic, coughed pink frothy sputum, showed central and peripheral cyanosis, respiration rate was 44 and bilateral moist pulmonary rates were present. Chest X-ray showed pulmonary oedema. The oedema was resolved when the catheter balloon was deflated. The oedema was thought to be caused by a massive sympathetic discharge in the same way as may be seen in patients with pheochromocytoma.[65] The intense prolonged vasoconstriction shifted blood from the systemic vascular bed to the lower resistance pulmonary vascular bed. This case report emphasises the importance of a rapid recognition and immediate action to remove the triggering factors.

The increase in blood pressure is accompanied by alterations in heart rate, that may in some cases be pathological. Pulse rate may sometimes be irregular and arrhythmias such as premature ventricular contractions, bigeminy and second degree A-V block have been reported.[66] An ischaemic pattern may be seen on ECG recording[10] and episodes of atrial fibrillation are reported following AD episodes among SCI subjects without other risk factors for heart disease.[67,68] Again, this may be of importance in the ageing SCI population, facing other cardiovascular risk factors together with the risk of arrhythmia associated with the AD reaction.

Treatment

Acute treatment

In order to prevent further blood pressure increase the patient needs to be placed in the upright, sitting position. The next measure is a rapid survey of possible triggering factors such as an obstruction of urinary outlet or a faecal mass. If the elevated blood pressure does not start to decline after 1 min or if the cause can not be determined, then medical treatment is essential. The choice of medical treatment is commented on later in the review.

Remove triggering factors – urinary bladder

The most common triggering factor for AD is problems related to the urinary tract. In order to permanently remove triggering factors it is therefore important to reduce any irritating factors in the urinary bladder. The goal in all bladder treatment is the creation of a balanced bladder, with low intravesical pressure that is drained totally at regular intervals and is free of urinary tract infections. There are several ways to empty the neurogenic bladder. Suprapubic percussion sometimes combined with sphincterotomy is a possible way to empty the reflexogenic bladder. The method was more common earlier but is still used by high tetraplegic patients with poor handfunction. The method does not fulfil the goal of a low-pressure bladder and the procedure itself induces an AD reaction. The use of sphincterotomy and its outcome has been evaluated in several studies. A prospective study of 92 patients undergoing sphincterotomy was followed for 20 months and found that subjective AD resolved in 93% of the patients.[69] Other studies of 26 subjects and 16 subjects respectively[30,70] undergoing a modified transurethral spincterotomy found a significant reduction of blood

pressure during urodynamic studies following the sphincterotomy. However, long-term follow-up indicates problems. Eleven patients who underwent sphincterotomy due to AD symptoms were followed for almost 10 years. Nine of eleven patients were re-sphincterotomized (82%). The AD symptoms were controlled in ten of 11 patients.[71] Another retrospective study of 37 SCI subjects undergoing sphincterotomy found failure in 18 operations, and reoperation in 32% of the subjects.[72] These findings, together with the almost total risk of retrograde ejaculation following sphincterotomy, have resulted in reduced rates of sphincterotomies.

There are alternative methods to decrease detrusor sphincter dyssynergia and AD symptoms by manipulating the external sphincter, such as balloon dilatation, injection of botulinum A toxin or insertion of a transurethral prosthetic stent. A study of 61 SCI subjects treated with balloon dilatation (20 patients), internal stent prosthesis (26 patients) and external sphincterotomy (15 patients) were followed for a mean of 15 months. There was a reduction of AD symptoms in all subjects.[73] 25 SCI subjects were treated with a stent and followed for a year. All reported decreased AD symptoms.[74] Device migration was, however reported (3/26 patients)[73] and insertion of the stent may be associated by transient AD reactions.[75] Injection of botulinum A toxin in the sphincter was performed in 11 SCI subjects. The method seems to be less successful since AD symptoms were reduced in only five subjects and, due to the pharmacological effect of the substance, the effect lasted for no more than 50 days.

Clean intermittent catheterisation is today the gold standard for drainage of the bladder. The method is often combined with anticholinergic treatment in order to increase bladder capacity and reduce leakage. The method has been evaluated with respect to urinary tract infections, urethral strictures and genital infections[76–78] but little or nothing is written about the frequency of AD reactions during this regimen. Urinary tract infections and bacteriuria are rather common among subjects on clean intermittent catheterisation and an incidence of 32–55%[76–78] of UTI were found during long term follow up studies. These infections have the capacity to provoke a dysreflexia reaction, but the cited authors do not comment on the issue.

For some years, denervation of the bladder, sometimes combined with electrical stimulation, has been used in order to create a low-pressure system with good capacity and safe emptying of the bladder. A study compared different methods of denervation:[79] intrathecal phenol or alcohol injection, complete sacral rhizotomy and dorsal root ganglionectomy. The number of patients was small, 3 in each group but follow-up ranged from 2–10 years. The authors found that phenol or alcohol blockade was insufficient in reducing detrusor sphincter dyssynergia and to resolve AD attacks. Complete sacral rhizotomy was complicated by incontinence. Dorsal root ganglionectomy proved to be more successful, the patients were continent and previous problems with AD were resolved. GS Brindley reported a general description of the first 500 patients with sacral anterior root stimulator implants.[80] The description was based on a questionnaire and the existence of AD during stimulation is not described. In another report on the same procedure 52 patients were reported.[81] Seven of the patients presented signs of severe AD preoperatively. In four patients the AD resolved but in two patients the stimulation induced a limited dysreflexia reaction. Another study of ten SCI subjects showed that all the subjects who suffered from AD prior to denervation still showed an AD reaction during stimulation induced micturition in spite of denervation.[82] Sacral anterior root stimulation is used both to control micturition and defecation. In two reports detailed data about the intracolonic and anal sphincter tonus are given[83,84] but nothing is commented about blood pressure reaction or other symptoms of AD during stimulation. Since distension of the colon and rectum is a potent triggering factor for AD it seems proper to make an evaluation of the occurrence of AD during stimulation of the sacral anterior roots. The above data points to the need of being aware of the risk and to evaluate the existence of AD reaction in the introduction of new treatments.

Symptomatic treatment

The symptomatic treatment of AD has a dual direction. It is partly directed to reduce triggering factors and partly to reduce hypertension. There has been a shift in the choice of drugs from alpha-receptor blocking agents to calcium channel antagonists. In the seventies, some work dealt with the effect of phenoxybenzamine, an alpha-receptor blocker[4,33] and found a good effect on internal sphincter function as well as AD symptoms. A study in 1985 compared the use of phenoxybenzamine with nifedipine, a calcium-channel blocker[85] during cystometry. Nifedipine was found to be capable of preventing an attack if given shortly before the stimulation. The same was found in a study from 1994, when four patients were evaluated during cystometry without and with nifedipine. In a comprehensive survey of the current treatment of AD published in 1991 nifedipine was the most common choice when treating minor as well as severe symptoms of AD. The results were based on a questionnaire to members of the American Spinal Injury Association, answered by 86 physicians. When treating minor symptoms, phenoxybenzamine was the second most common choice, whereas nitrates were the second most common in severe attacks. In a small survey of the present choice of medical treatment, five answers from SCI units in Europe and Australia were given. The answers showed that nifedipine was still among the first choice, but in Australia as well as in

Sweden the capsular form of nifedipine is no longer available, and there has therefore been a change towards glyceryl trinitrate as the first choice, since the effect is more prompt. However, there are some problems associated with the use of nitrates. The use of sildenafil (Viagra) in the treatment of erectile dysfunction may change this choice since the use of nitrates is contra-indicated in treatment with sildenafil. The resulting decrease in blood pressure may be huge and dangerous. This might be a problem in the future since sexual activity may induce an AD attack.

Summary

The AD reaction is a potent reaction sometimes associated with severe morbidity that asks for prompt relief of the afferent stimulation inducing the reaction. It also constitutes an important clinical sign of underlying disease in a body deprived of normal sensation and is by this means valuable for the spinal cord injured as well as for the treating physician. The AD reaction is the full-blown answer to a peripheral stimuli activating sympathetic fibres below lesion level; milder forms of activation are common. The reaction may in part be advantageous since it is possible to activate lipolysis below the lesion level by the reaction. This may act as a compensating mechanism for the inability to activate lipolysis by central command, and may explain the increased performances during boosted conditions in athletics. However, a pathogenic role may be suspected in the insulin resistance syndrome. When introducing new treatments affecting the paralysed part of the body it is necessary to evaluate the existence of symptoms and signs of AD. The review of the literature has raised some questions. The underlying pathophysiology is not totally clear and further investigations are needed. Furthermore, there are stimuli arising below the lesion level that do not induce an AD reaction, indicating an upper level of reactivity. In order to compare treatments, incidence and prevalence and morbidity associated with the reaction some common criteria need to be established. There are signs in the literature of decreasing prevalence of the AD reaction. This needs to be established by retrospective and/or prospective investigations.

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