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Autonomic Dysreflexia (AD): A serious, rather underestimated condition, a review based on Workshop 11, held on ICS Vienna 2022



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ABSTRACT

Autonomic Dysreflexia (AD) is a common complication among patients with a Spinal Cord Lesion (SCL) located above the T6 level. Various stimuli below the spinal cord lesion may initiate the onset of AD. In most cases, the phenomenon subsides after the removal of the initial stimuli but sometimes is rapidly reactivated and progressively overexpressed causing uncontrolled blood hypertension with the severe danger of stroke or other cardiovascular accidents (CVAs).

The establishment of adequate awareness among the health care providers and individuals with SCL is our main goal which may occur through a deep understanding of the pathophysiology of AD. The proper prevention and management of the syndrome are essential for our patient's life.

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1. Introduction

In this manuscript, we present the proceedings of workshop 11, held at the ICS annual meeting in Vienna in 2022. The structure of the manuscript is serving the understanding of the pathophysiology of AD in order to reveal the severity of this condition, highlight iatrogenic causes of AD and increase relative awareness among healthcare professionals.

2. Cardiovascular system and autonomic function

The cardiovascular system is under the control of complex regulation by the autonomic system. The heart receives innervation from both the parasympathetic and sympathetic systems and blood vessels

receive predominantly sympathetic innervation. This regulation is not under our voluntary control. The cardiac muscle has an automatic function that permits to have a rhythmic contraction. Both sinoatrial and atrioventricular nodes are responsible for this rhythmic automatic activity. But in another hand sympathetic and parasympathetic systems can modulate the contractility of the cardiac muscle and the frequency of heart rate to adapt the cardiac activity to various behaviours such as standing, physical activity, or sleeping. Sympathetic nervous stimulation increases cardiac rhythm and vascular contractility leading to an increase in blood pressure. Parasympathetic stimulation decreases heart rate and cardiomyocyte contractility with limited peripheral vascular effect except in some specific regions (brain, genitals).

This complex regulation involves multiple sites of the central and peripheral nervous system and various reflexes. Neurological disorders

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and spinal cord injury may modify cardiovascular regulation that is severe enough to increase the risk of cardiac arrest, rhythmic abnormalities, hypotension or AD.

Cardiovascular dysregulation is an important topic to understand and consider for all physicians in charge of such patients. Depending on the level and the extent of the lesion the type and severity of cardiovascular symptoms are predictable and accessible for treatment and prevention.

3. Pathophysiology of Autonomic Dysreflexia

AD is often triggered by unperceived noxious visceral or somatic stimuli below the injury level in high-level spinal cord injury patients and if severe enough can develop dangerous hypertension that requires immediate medical attention. The pathophysiologic mechanisms that are contributing to the development of AD, are focused on the maladaptive plasticity of neural circuits mediating abnormal sympathetic reflexes and hypersensitization of peripheral vasculature that collectively contribute to abnormal hemodynamics after SCL. The phenomenon is initiated by a sympathetic response to the triggering stimuli below the level of the lesion. The activation of the sympathetic system causes vessel contraction resulting in a blood pressure incision. Baroreceptors in the carotid sinus detect the hypertension episode and give signals to the brain to deactivate the sympathetic response. This is feasible through the cranial nerves IX and X (Glossopharyngeal nerve and Vagus nerve) that contain autonomic fibres but is impossible to control the sympathetic center in the Spinal Cord, which extends below the T6 level, as this connection has been interrupted due to SCL. The clinical signs and symptoms of the syndrome contain vasoconstriction in the lower part of the body which supports and maintain hypertension and vasodilation in the upper part of the body which causes headache and nasal congestion. The legs and the body are getting “blue” and the upper thoracic part of the body, the arms and the head are getting “red”. As the phenomenon goes on, parasympathetic activation through the vagus nerve causes bradycardia. Uncontrolled hypertension and low heart rate can be a lethal combination that can cause stroke or myocardial infarction.

4. Iatrogenic Autonomic Dysreflexia

Urological procedures and bowel investigations or evacuation management can cause Autonomic Dysreflexia (AD) in individuals who are candidates for AD.

Already in 1996, Linsenmeyer et al. found urodynamics as an excellent tool for detecting both symptomatic and silent AD in men with SCI above T6 [1]. Research activities in the last years yielded important new insights about the frequency and severity of AD triggered by diagnostic and therapeutic interventions in the Lower Urinary Tract (LUT) and the bowels such as urodynamics, cystoscopy, transurethral lithotripsy, Extracorporeal Shock Wave Lithotripsy (ESWL), sperm retrieval, bowel evacuation by digital rectal stimulation, and transanal irrigation. The incidence of AD varies mainly according to the density of receptors stimulated. The receptor density is high in the area of the bladder neck, prostate, posterior urethra and anal canal, but less in the bladder and the colon.

Regarding the level of the Spinal Cord Lesion, AD is more prevalent and more severe in cervical SCI than in thoracic one (above Th6 level). Among cervical lesions, there was found no difference in AD prevalence and severity between C1–C5 and C6–C7 lesions. During Urodynamics, AD may occur in 37%–78% of tetraplegics and 24%–77% of paraplegics with lesions upper to Th6 level. During cystoscopy, AD may occur in 80% of tetraplegics and 10%–40% of SCI individuals with upper thoracic lesions [2].

In AD candidates, monitoring of the BP is recommended during urological interventions. If AD occurs the procedure should be terminated immediately, the bladder should be evacuated and the patient should

be placed in an upright position (in a wheelchair). The monitoring should be continued, so as to assure that AD is subsided [3]. Clinicians should initiate pharmacologic management in those with persistent AD following bladder decompression. Patients with systolic blood pressure greater than 150 mm Hg and/or 20 mm Hg above baseline who exhibit persistent classic symptoms (flushing, sweating, headache, blurry vision) should be treated. In general, nitrates are the most commonly used medication to manage refractory AD-associated blood pressure elevation: the topical application of a nitroglycerine paste on the skin, above the level of the spinal cord lesion, is effective and can be easily removed in order to reduce the subsequent risk of hypotension. Alternatively, nifedipine, a calcium channel blocker, can be used. Nifedipine can rapidly and precipitously lower blood pressure well below baseline values and its effects may not be rapidly reversed in the clinic setting, as can be done with wiping topical nitroglycerine off, so it should be used with caution. If such antihypertensive compounds do not alleviate symptoms, then escalating care to an intensively monitored setting may be appropriate [3].

As urodynamics are performed more often than cystoscopies in SCI patients, they are an important screening tool for AD. Curt et al. (1997) reported that urodynamic examination may be an effective and standardized diagnostic procedure for provoking signs of AD [4]. In their study only half of the patients, who showed signs of AD during an examination, presented also with clinical symptoms, the other half had “silent” AD, only diagnosed based on systolic blood pressure (sBP) increase. Therefore, cardiovascular monitoring is mandatory to detect AD using urodynamics as a screening test.

The increase in sBP was also used to compare the severity of AD between urodynamics and cystoscopy. The sBP change was greater during cystoscopy than in urodynamics, indicating that stimulation of the bladder neck, urethra, and prostate area is more potent than just bladder filling. On the other side, if urodynamics causes a severe increase in sBP, the risk for AD in other situations is high.

Bowel management may cause AD, as well. The increase in sBP is low with transanal irrigation compared to evacuation by digital rectal assistance in which the increase in sBP is comparable to that with cystoscopy [5]. As 60%–70% of SCI patients use digital anorectal stimulation for bowel evacuation, at least those with significant AD should use transanal irrigation instead [6]. The occurrence of AD episodes in connection with diagnostic and therapeutic procedures in the LUT and the bowels can be used as an excellent tool in detecting both symptomatic and silent AD in patients with SCI above T6. Recent studies in this field allow nowadays better interpretation of these findings regarding the risk for AD, thus also counselling of the patient is improved.

5. Prevention — Treatment and awareness programs

Prevention of AD is a major challenge for patients with a high thoracic or cervical SCL. AD can cause major acute cardiovascular complications, such as transient aphasia, stroke, retinal haemorrhage, pulmonary oedema, and myocardial infarction [7]. In another hand cardiovascular complications are a major cause of death in the SCI population [8], as example, it increases the risk of stroke by 3 to 4 fold according to the nationwide database from two different countries [9,10]. There is some evidence from the literature to support the idea that AD is an independent risk factor that increases cardiovascular risk in association with numerous others risk factors. Animal models of cervical SCL with blood pressure instability show more arterial stiffness and impaired cardiac function. Those findings are confirmed in humans in small cohorts [11,12]. The impact of AD on cardiovascular function and risk of major cardiovascular events (mortality and morbidity) deserve larger prospective cohort studies to be finally demonstrated. Altogether it reinforces the necessity of an appropriate prevention strategy both to reduce the acute risk of severe AD and a long-term prevention management plan taking into account the specific risk of chronic AD.

A prevention strategy requires appropriate diagnostic and follow-up tools. At least 40% of AD events are clinically silent. Silent AD is an increase in blood pressure without any symptoms and is more dangerous because nothing is done to adapt the current management to this potentially acute and chronic cause of severe complications. 24-hour blood pressure monitoring is required to establish the diagnosis. It means that blood pressure instability must be researched in every patient at risk and not only during the acute phase but also during the chronic follow-up where the prevalence of AD increase [13].

The best way to prevent this is to have proper management of SCL to reduce the incidence of the usual risk factors. Most of the precipitating factors are pelvic-perineal complications such as urinary tract infection, acute urinary retention, foley catheter, haemorrhoids, and rectal prolapse. But attention must also be paid to skin lesions, such as pressure ulcers and ingrown toenails, and bone-related defects, such as undiagnosed fractures or severe arthritis under the level of the SCL. A specific caution has to be paid in iatrogenic AD that takes place during specific diagnostic and/or therapeutic invasive procedures.

Prevention is also education, of patients but also of family and caregivers and professionals that may be in charge of patients for example during a visit to emergency care. This education is based on how and why it is so important to make the diagnosis, how to prevent AD for example during a procedure and finally how to treat acute and severe AD. Some patient associations in cooperation with scientific societies have developed pocket cards that the patient may demonstrate in case of unplanned visits or emergencies. This education is a major challenge, even patients and their families have gaps in their knowledge [14], and it is even more the case for nurses, physiotherapists, radiologists, gynaecologists, urologists and other health care providers who are in contact with SCL individuals. New methods of education such as online training improve short- and long-term knowledge and attitudes regarding diagnostic and management [15] and must be developed worldwide in local languages.

The treatment of the acute crisis is very well described and follows a step-by-step management plan beginning with undressing and setting up followed by bladder catheterization, and other steps finishing with pharmacological treatment if the previous interventions failed to control the AD [3,16]. This algorithm of treatment is adopted worldwide.

Prevention is also, based on evidence, making the best choice of bladder and bowel management considering the impact on the severity and frequency of AD. Very few studies are looking at this. AD frequency and severity are significantly reduced after sacral anterior roots stimulator [17] and after intradetrusor botulinum toxin injections associated with clean intermittent catheterization [18,19].

6. Conclusion

AD is a common complication among patients with a SCL located above the T6 level. Noxious or even not noxious stimuli below the spinal cord lesion may initiate the onset of AD. Bladder distention or bowel impaction, are the most common stimuli which may result in AD. Pressure ulcers, toenails into the skin or other wounds may be the responsible factors for AD, as well. In the majority of these cases, the phenomenon is self-limited and subsides after the removal of the initial stimuli. On the other hand, in some cases, the phenomenon is rapidly reactivated and progressively overexpressed causing uncontrolled blood hypertension with the severe danger of stroke or other CVAs. The syndrome is not well known among physicians and other healthcare professionals unless they are working in a spinal cord unit.

On the other hand, these individuals (with SCL), are not institutionalized or hospitalized, they stay at home and may contact any healthcare unit for any medical reason. Physicians, nurses, and other therapists who deal with incontinence are likely that they will be asked to manage these patients with paraplegia or tetraplegia. Under these circumstances, a deep knowledge of AD is essential for early detection,

adequate treatment and sometimes even for the life support of these patients.

Additionally, simple urologic procedures such as urodynamics, cystoscopy or sperm retrieval by vibration may lead to uncontrolled AD episodes. Awareness of the syndrome is crucial for the prevention, early detection, and proper management of AD.

The establishment of adequate awareness among the health care providers and individuals with SCL is our main goal which may occur through a deep understanding of the pathophysiology of AD. The proper prevention and management of the syndrome are essential for our patient's life.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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