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Clinical paper

Cardiopulmonary arrest is the most frequent cause of the unresponsive wakefulness syndrome: A prospective population-based cohort study in Austria☆

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ABSTRACT

Background: The "Unresponsive wakefulness syndrome" (UWS) or previously termed vegetative state is a possible consequence of severe brain damage where individuals just open their eyes but show no conscious behavioural reaction. While head trauma has previously been considered the prevailing cause, clinical experience suggests shows that cardiopulmonary arrest plays an increasingly important role. We therefore attempted to study this hypothesis in a well-defined region of Austria.
Methods: Prospective population-based cohort study to calculate the incidence and aetiologies of the UWS. All facilities in the state of Styria ($n = 38$), which are involved in the medical care of patients with brain damage, participated. Among the adult population of Styria ($n = 1010{,}164$) we identified all individuals who developed UWS over a one year period. The diagnosis was based on a formal neurologic evaluation at least 4 weeks after the brain damage and had to be in line with the criteria of the "Multi-society Task Force on Persistent Vegetative State".
Results: We identified 19 individual with UWS which correspond to an annual incidence of 1.88/100,000 people. Male gender predominated (78.9%) and the mean age was 57.8 years (age range 18–78 years). The most frequent cause of UWS was cerebral hypoxia in the wake of cardiopulmonary resuscitation (63%), cerebral bleeding (21%) and brain trauma (16%).
Conclusions: Cardiopulmonary resuscitation has become the major cause of UWS which leads to an increasing incidence with age. These aspects may become even more prominent with the ageing of our population and need to be considered in the organisation of care.

Introduction

Severe damage to the brain of either traumatic or non-traumatic origin may lead to a situation where patients just open their eyes over many months or years but show no other conscious behavioural reaction. Debates about how to best describe this condition have recently been settled with the suggestion to use the term "Unresponsive wakefulness syndrome" (UWS) as it alludes to the key elements of absent contact ability and existing wakefulness and avoids negative connotations associated with the earlier designation of being in a "vegetative state".[1–3] Progress has also been made by the understanding that UWS need not preclude at least some amount of functional remission in individual cases and by the need for a high sensitivity towards separating UWS from a minimally conscious state (MCS) where patients start to show more than reflex motor behaviour.[4–9] Epidemiological data for the UWS are scarce and quite variable.[10] Thus reported prevalence rates of a recent systematic review showed a wide range from 0.2 to 6.0 per 100,000 and the authors noted significant differences with regard to inclusion criteria and diagnostic verification.[11] Furthermore many studies date back to before the turn of the century and provide no insight on the likely impact of preventive measures for brain trauma and progress in intensive medical care on the frequency of UWS. While traumatic causes predominated in older studies, recent experience suggests an increasingly important role of cerebral hypoxia from cardiopulmonary arrest. The missing epidemiological data prompted us to prospectively evaluate the incidence and aetiology of UWS in adults in a well-defined region of Austria, i.e. the state of Styria.

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Methods

Study design: prospective population-based cohort study.

Study time: The study was prospectively conducted over a one year period (01.12.2011 to 30.11.2012).

Study centres: All facilities in the state of Styria ($n = 38$) that could be involved in the medical care of patients with an acute or post-acute UWS. These were intensive wards ($n = 28$), neurological departments ($n = 5$) and neurological rehabilitation clinics ($n = 5$).

Sample: To calculate incidence rates we referred to the population census of the Austrian Institute of Statistics.[12] At the time of the study 1010,164 individuals >18 years were recorded to have their main residency in the State of Styria. Of these 51.1% were women. We also extracted the population number for the following age ranges to allow for a breakdown of our results in age categories: >18–29 years: 186,205; 30–59 years: 525,029; ≥60 years: 298,930).

Case definition: Two contact persons from every facility were defined to centrally register any patient with the suspicion of possibly developing or having a UWS after an acute severe brain damage. To do so they received detailed instructions regarding the purpose and protocol of the study including the diagnostic criteria of UWS and of MCS. Other inclusion criteria were an age >18 years and current living in the State of Styria. Monthly contacts and progress updates served to reinforce active participation of all facilities throughout the entire study period.

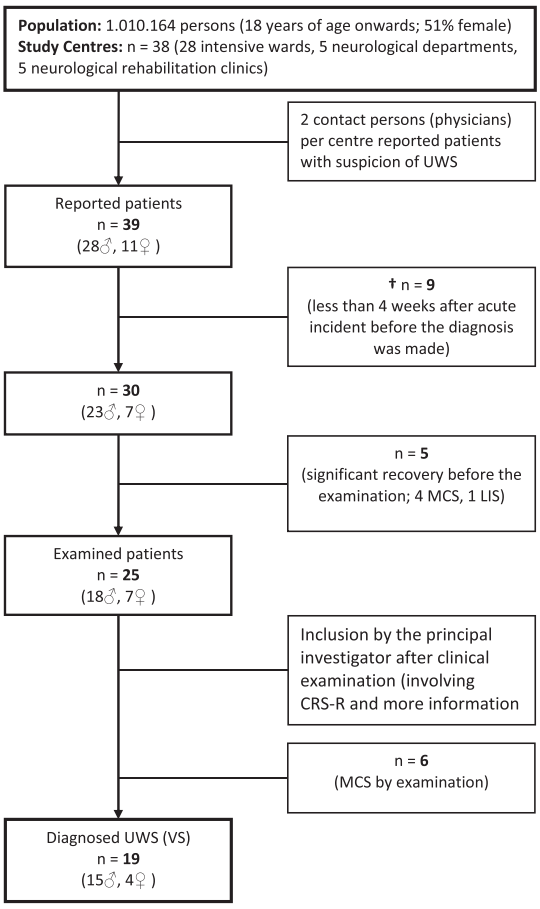
Following the registration a single senior neurologist experienced in this field (GP) visited the patients to verify the suspicion. This was done not before 4 weeks after the acute incident to allow for a certain stabilisation of the situation and repeated in case of factors possibly still interfering with the evaluation such as the necessity to continue sedation or high fever. The neurologist reviewed all relevant documents, collected information from responsible doctors and nursing staff and when possible also talked with the patients relatives. The neurological exam focused especially on the criteria of the "Multi-Society Task Force on PVS" and a diagnosis of UWS was given if all of the following criteria were fulfilled: (1) no evidence of awareness of self or environment and an inability to interact with others; (2) no evidence of sustained, reproducible, purposeful, or voluntary behavioural responses to visual, auditory, tactile, or noxious stimuli; (3) no evidence of language comprehension or expression; (4) intermittent wakefulness manifested by the presence of sleep-wake cycles; (5) sufficiently preserved hypothalamic and brainstem autonomic functions to permit survival with medical and nursing care; (6) bowel and bladder incontinence; and (7) variably preserved cranial-nerve reflexes (pupillary, oculocephalic, corneal, vestibulo-ocular, and gag) and spinal reflexes.[4] He also took great care to search for an evidence of a "Minimally conscious state," and applied the "Coma-Recovery-Scale revised" (CRS-R).[13,14] All examinations were done only after relevant sedation had been stopped for an adequate time interval. Data on the aetiology of UWS were also collected. Patients with a progressive degenerative disease as the cause of UWS were not considered in this study.

Statistical analysis was done in a descriptive manner.

Ethics: The study protocol was reviewed and approved by the Ethics Committee of the Medical University of Graz, Austria (Number 24-027 ex 11/12).

Results

During the one year study period a total of 39 patients were registered with suspicion of UWS from overall 14 facilities (Fig. 1). Nine patients died within the first 4 weeks after the acute brain damage. Five more patients were excluded before the examination as they showed noticeable improvement compatible with MCS



† = dead; MCS = Minimally conscious state; LIS = Locked-In syndrome; UWS = Unresponsive wakefulness syndrome; VS = Vegetative state

Fig. 1. Research design and ascertainment.

($n = 4$) or had developed into a locked-in syndrome ($n = 1$). All these 5 patients had been registered within the first week after the acute event.

Thus 25 patients were formally evaluated between 30 and 50 days (mean 35.2 ± 4.5) after acute severe brain damage. The diagnosis of a UWS was confirmed in 19 (76%) of them. In 6 (24%) patients findings were compatible with a MCS. This clinical separation was supported by the ratings on the CRS-R which ranged from 2 to 6 (mean 3.5) in UWS and 10–15 (mean 12.5) in MCS. The demographic data, aetiology of brain damage and individual CRS-R scores at examination are listed in Table 1.

In relation to the entire population the number of patients with UWS observed in our study thus corresponds to an incidence rate of 1.88/100,000/year for the state of Styria.

The age of our patients with a UWS at the time of the acute event ranged from 18 to 78 years (mean 57.8 years) and 15 (78.9%) were men. There was a clear increase in the incidence of UWS with increasing age (Table 2).

Global cerebral hypoxia was the most frequent aetiology of a UWS ($n = 12$) in our series which was of cardiac origin, i.e. following cardiopulmonary resuscitation in more than half of our patients. Brain trauma and intracranial bleedings were more rare causes (Table 1, Fig. 2).

Discussion

This prospective study evaluated the incidence of UWS following acute severe brain damage in the adult population of a well