A Decade after the Tokyo Sarin Attack: A Review of Neurological Follow-Up of the Victims

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Objective: On March 20, 1995, sarin gas was used in Tokyo by members of the Japanese “Uhm-Shirikku” cult, killing 12 and injuring >5,500 innocent people. Most of the casualties were mildly injured. This article reviews the neurological follow-up data for some of the victims over the past decade. Methods: We reviewed the published literature regarding neurological follow-up of the victims, dividing the data according to the time elapsed after the attack. Results: The digit span test, finger-tapping test, and computerized posturography were the only performance tests that showed statistically significant differences between the victims and the control groups in some of the surveys. The main sequela 7 years after the attack was post-traumatic stress disorder. Conclusions: The results emphasize the need for a national preparedness program for such mass casualty events, led by national health systems. This should include long-term, neurological, follow-up monitoring with performance tests and a post-traumatic stress disorder screening test.

Introduction

More than a decade ago, on March 20, 1995, the nerve agent sarin was used in a terror attack in Tokyo by members of the Japanese “Uhm-Shirikku” cult. Sarin, a potent inhibitor of the enzyme acetylcholinesterase, causes a prompt flux of the neurotransmitter acetylcholine, resulting in a variety of peripheral and central neurological symptoms. The attack took place during the morning rush hour, in several subway stations simultaneously. More than 5,500 civilians, including members of the rescue teams, were injured. Most of them (4,073) suffered only mild symptoms (mainly ocular) and were dismissed from hospital after a few hours; 984 victims suffered moderate injuries, without the need for mechanical ventilation; 50 victims had severe injuries and needed mechanical ventilation and resuscitation, and 12 people died as a result of the attack.

The international St. Luke’s Hospital, which was closest to the scene, received 640 of the casualties, of whom two died shortly after their arrival. The Japanese Sendai army hospital reported treating 62 casualties, all of whom were sent home 1 week after the attack with only ocular complaints.

The Tokyo sarin attack is actually the largest nerve agent exposure of a civilian population to date. Since this terror attack, both governments and health organizations are taking steps to prepare themselves for the possibility of a nonconventional terror attack.

In this article, we summarize a decade of neurological follow-up for some of the victims of the Tokyo sarin attack. In most of the studies, information was gathered in the early years following the attack, because of increased medical and public interest, as well as relatively accessible data.

Methods

We reviewed the data of the studies published to date on the victims, focusing on neuropsychological performance, memory tests, balance tests, and signs of post-traumatic stress disorder (PTSD). We divided the studies into three subgroups, based on the time that elapsed from the terror attack to the time the study was carried out, i.e., (1) studies carried out up to 1 year after the attack, (2) studies carried out up to 3 years after the attack, and (3) studies carried out >3 years after the terror attack.

Studies Carried Out Up to 1 Year after the Attack

A group of 18 victims was admitted to St. Luke’s Hospital after the attack. They were discharged after being diagnosed as suffering from mild sarin intoxication. This group underwent neuropsychological follow-up examinations 6 to 8 months after the event. After completion of a questionnaire aimed at diagnosing PTSD, the neurophysiological effects were evaluated by using electroencephalography and event-related potential, visual evoked potential, and brainstem auditory evoked potential monitoring. The patients did not suffer from any other diseases and did not express any signs of organophosphate intoxication at the time the study was conducted.

In another study, questionnaires were sent to victims treated at St. Luke’s Hospital 1 month after the attack. The questionnaires were PTSD oriented, dealing with fear, avoidance of trains, sleep disorders, and mood changes. Approximately 80% of the victims complied and filled out the questionnaires.

Yokoyama et al. conducted balance performance tests, memory tests, and neurobehavioral tests, looking for signs of PTSD in a group of 18 victims suffering from mild organophosphate intoxication. The tests were performed 6 to 8 months after the attack and included computerized posturography, the Wechsler Adult Intelligence Scale, the digit symbol test, the picture completion test, and the digit span test. Computerized tests for neurobehavioral assessment (finger-tapping, stimulation reaction time, and continuous function tests) and self-evaluation questionnaires (general screening, mood profile, and PTSD questionnaires) were also performed.

Studies Carried Out Up to 3 Years after the Attack

Fifty-six matched, control, police and rescue team personnel involved in the rescue efforts had medical follow-up assess-
ments, including neurobehavioral tests, balance test, vibration threshold test, and psychomotor tests, 3 years after the attack. The study group was divided into two subgroups, that is, individuals who were treated in an outpatient clinic and probably were exposed to low doses of sarin and individuals who were hospitalized after exposure to high doses of sarin. The latter group was further divided into those who lost consciousness or had signs of hypoxia and those who did not. The information gathered included results of psychomotor performance tests (finger-tapping, simple reaction time, and choice reaction time tests), memory tests (digit span test and Benton visual retention test), balance tests, and questionnaires, including the Impact of Event Scale (IES) questionnaire and a general health questionnaire (GHQ).

In an attempt to follow up on the psychophysiological effects of the St. Luke’s Hospital patients, 2, 3, and 5 years after the event a specially written symptom questionnaire (St. Luke’s questionnaire) was sent to some of the casualties. The survey included 582 patients who arrived at the emergency department on the day of the attack. The questionnaire, developed by the researchers, included 33 questions with a scale of 1 to 5. Fourteen of the questions referred to physical complaints, eight to ocular symptoms, and 11 to psychological symptoms (avoidance, hyperarousal, and reliving the event) as representative signs of PTSD. Of the 582 patients, ~44% answered after 2 years, ~35% after 3 years, and ~33% after 5 years.

Studies Carried Out >3 Years after the Event

In a study, aimed at locating PTSD patients, 5 years after the attack, among casualties treated in an outpatient clinic at St. Luke’s Hospital, 34 people were given several questionnaires, including (1) a 34-question, self-grading questionnaire aimed at locating somatic and emotional symptoms; each question was rated 0 (‘not at all’) to 2 (‘severe’); (2) IES-Revised, a self-grading questionnaire in psychiatric use aimed at identifying PTSD, including 22 questions aimed at finding major symptoms of PTSD (flashbacks, avoidance/desensitization, and hyperarousal) in the week before filling out the questionnaire; each question was graded 0 (‘not at all’) to 4 (‘very high’), and each patient received a grade of 0 to 88; (3) State Trait Anxiety Inventory questionnaire, which included questions about current medical status and general emotional stress; (4) Mini International Neuropsychiatric Interview, a standard interview designed to diagnose mental problems according to the Diagnostic and Statis
tical Manual of Mental Disorders, Fourth Edition, and the International Classification of Diseases, 10th Revision; and (5) Clinician-Administered PTSD Scale, an evaluation of symptoms by a psychiatrist to diagnose PTSD in the past month or at any time in the past; the questionnaire evaluates the frequency and severity of PTSD signs and their effects on the subject’s daily function; and (6) Wechsler Memory Scale-Revised, aimed to examine each subject’s memory abilities.

Results

We divided the reviewed data into three groups, that is (1) neuropsychological and memory tests, (2) balance tests, and (3) PTSD tests. In each group, we summarized the relevant tests and organized them chronologically. The data are summarized in Tables I–III.

Discussion

The neurological follow-up surveys that included up to 7 years of follow-up monitoring after the attack showed that the main neurological symptoms were neuropsychiatric and PTSD

<table>
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<td>Murata et al. 1997</td>
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ERP, event-related potential; VEP, visual evoked potential; BAEP, brainstem auditory evoked potential.
related. These findings are not significantly different from what is known from surveys following agricultural organophosphate poisoning.\(^3\) Most of the studies described tried to quantify the amount of damage to different neurological pathways, using various research and laboratory means. There are many differences in the methods used by the different researchers. This is more obvious when looking into the performance tests used in each survey. The causes of these variations are the different preferences of each research group and the tests chosen to identify organophosphate poisoning, highlighting the need for standard tests based on a clear policy and previous experience. The exception is the diagnosis of PTSD, which was based on rich experience and validation tests present in the psychiatric literature.

When comparing this review with a comprehensive study conducted among 4,022 U.S. army volunteers who participated in experiments in the United States during the years 1955 to 1975,\(^4\) we found that, in the present study, there were higher rates of concentration and sleep disorders. The U.S. study used a self-grading questionnaire, which was especially developed. No statistically significant differences were found in memory tests, signs of peripheral neuropathy, balance tests, signs of depression, or congenital defects. According to the author, because of the method that was used to gather the information, the participants had a higher tendency to report illnesses. The questionnaires in that study were different from those sent to the Tokyo casualties and included more-general questions concerning overall medical state and less-specific questions dealing with neuropsychiatric disturbances. Additionally, the U.S. survey did not include questions aimed toward PTSD detection.

Most of the studies of the Tokyo attack casualties examined the frequency of stress reactions that developed in the affected population, an understandable objective of a post-chemical terrorism survey. The methods used to diagnose stress reactions differed between the studies. Some used self-grading questionnaires, including general health questions. Most of the questionnaires were developed by the researchers, based on the abundant information available (although less for unconv-
tional scenarios), but were not validated to ascertain their accuracy. The only validated PTSD questionnaires were the IES questionnaire, which was developed to evaluate emotional stress and to locate symptoms of PTSD, and the GHQ, which evaluated general mental health and not specifically PTSD.\(^9,11\) Ohtani et al.\(^11\) examined the casualties 5 years after the attack by using screening questionnaires and structured validated interviews by a psychiatrist (Mini International Neuropsychiatric Interview and Clinician-Administered PTSD Scale questionnaires). Although 40 to 65% of the subjects showed signs of stress, memories of the event, and avoidance in the screening questionnaire (IES), only one-third of the subjects (11 of 34 subjects) showed it in the personal interviews. This combination achieved its purpose, with a questionnaire used for screening that was sensitive enough to ensure that no casualty was overlooked and a complementary psychiatric interview for suspected PTSD patients among casualties who were found by using the questionnaires.

When assessing the methods used to evaluate the effects on the casualties’ nervous system in Tokyo, no uniformity is found. The neurophysiological and memory tests chosen were generally used to examine agricultural organophosphate poisoning. The majority of the tests did not find statistically significant differences, compared with control findings, with the exception of the majority of the tests did not find statistically significant differences, compared with control findings, with the exception of the finger-tapping test and the digit span test.\(^7,12\) Performance tests for clinically poisoned patients exposed to a single dose of agricultural organophosphate showed a difference in the digit-tapping test, as well as in other neurological tests.\(^3\) The meaning of these differences is still unclear. On the basis of the data, it is difficult to define neurological pathways that may be responsible for the clinical signs when damaged.

There were no clear differences in memory tests for the victims. The memory tests were not validated and therefore might not be sensitive enough to detect slight memory reduction after low-dose exposure to sarin, if present. In contrast, when results of the computerized balance tests are examined, it is reasonable to assume that these tests are sensitive enough to locate slight neurological changes caused by sarin.\(^7,12\) However, the latest study, performed 7 years after the attack, did not indicate significant changes in the same balance tests.\(^12\) A central issue remains whether we should perform a very sensitive neurological test capable of detecting even minor changes in a heterogeneous civilian population that is influenced by many other environmental and genetic factors. These influences could bias the test results if we are not able to recognize the direct effect of organophosphate poisoning. Therefore, the interesting posturography test finding should be addressed carefully when considering adding it to a practical follow-up program.

A case of possible damage to the peripheral nervous system, which is more common in agricultural poisonings, was described for a 51-year-old victim of the sarin attack.\(^13\) He died 15 months after the attack. In a neuropathological inquiry that was conducted, decreased numbers of nerve fibers in his sciatic and sural nerves were found, without any change in ganglions of the spinal cord. In light of missing information regarding the activity of neural cell esterase, which probably causes this phenomenon, it is hard to connect it to the sarin exposure.

In conclusion, this article summarizes the data concerning the Tokyo sarin attack casualties. It strengthens the understanding that a plan is needed for long-term follow-up monitoring and treatment of victims following such an event. It is evident that most of the results of the long-term follow-up monitoring of the Tokyo casualties could be predicted, but their extended presence was surprising at the time. Most of the studies in recent years focused mainly on diagnosing PTSD.\(^11\) Recent function tests performed in a group of 56 rescue team members found only slight decreases in balance and finger-tapping tests.\(^9,12\) Those tests were not repeated in other groups of victims, a fact that supports the need to validate the function tests and to build a follow-up program for organophosphate casualties.

**References**