Low doses of ionizing radiation as a treatment for Alzheimer's disease*

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Abstract

Background: In 2015, a patient in hospice with Alzheimer disease was treated with ionizing radiation to her brain using repeated CT scans. Improvement in cognition, speech, movement, and appetite was observed. These improvements were so momentous that she was discharged from the hospice to a long-term care home. Based on this case, we conducted a pilot clinical trial to examine the effect of low-dose ionizing radiation (LDIR) in severe Alzheimer disease (AD).

Objective: To determine whether the previously reported benefits of LDIR in a single case with AD could be observed again in other cases with AD when the same treatments are given.

Methods: In this single-arm study, four patients were treated with three consecutive treatments of LDIR, each spaced two weeks apart. Qualitative changes in communication and behaviour with close relatives were observed and recorded. Quantitative measures of cognition and behaviour were administered pre and post treatments.

Results: Minor improvements on quantitative measures were noted in three of the four patients following treatment. However, the qualitative observations of cognition and behaviour suggested remarkable improvements within days post-treatment, including greater overall alertness. One patient showed no change.

Conclusion: LDIR may be a promising, albeit controversial therapy for AD. Trials of patients with less severe AD, double-blind and placebo-controlled, should be carried out to determine the benefits of LDIR. Quantitative measures are needed that are sensitive to the remarkable changes induced by LDIR, such as biological markers of oxidative stress that are associated with AD.

Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder affecting older adults. It is a leading source of morbidity and mortality in the aging population. While treatments can ameliorate some symptoms of the illness, there is no cure or disease-modifying therapy. It inevitably progresses in all patients. Survival after diagnosis ranges from 3 to 20 years; average life expectancy is 8 to 10 years. Patients with advanced AD enter hospice as their end-of-life approaches. The changes in the brain are associated with the accumulation of amyloid-plaques and tau protein. Clinical trials are evaluating anti-amyloid therapies; however, autopsy data suggest AD will not occur in every patient with amyloid.

The **primary goal of a therapy** for old adults with AD should be to improve the quality of their lives by optimizing their well-being, staying brain health, and restoring communication with family and friends to avoid social isolation, loneliness, and under stimulation. Old adults should recognize their spouse, children, and grandchildren.

The **pilot clinical trial** in this paper was different from trials that will remove amyloid plaque. It repeated low dose treatments in 2015 to a patient with severe AD. Remarkably improved cognition, speech, movement, and appetite were observed after CT scans of the brain. Each scan gave a dose of 40 mGy in 10 s. Two were given on July 23, and the surprising changes were observed on the next day. Additional scans, to amplify and prolong the recovery, led to the patient's transfer from hospice to a home for seniors. A neuropsychological examination found the patient completely nonresponsive prior to treatment. After, she gave verbal responses to simple questions. She received a booster treatment on February 24, and others in 2016 and 2017, to enhance and prolong the changes. Living in a seniors home contributed to her improved state. In 2017, her condition began to decline. On March 6, 2017, she was returned to hospice care, and she died on May 18, 2018.

The **objective of this study** was to determine whether the benefits of this therapy in 2015 could be observed in others with severe AD when the same treatments are repeated. The data collected were qualitative observations of patient communication and behavior with relatives. In addition, quantitative measures of cognition and behavior were carried out, pre and post LDIR treatments.

LDIR therapy is controversial because it is generally accepted that ionizing radiation is a significant cause of DNA mutations and cancer risk. People are unaware that the rate of DNA damage due to natural background radiation is negligible compared to the high rate of DNA alterations caused by the endogenous production of reactive oxygen species. Oxidative stress is a common denominator in the pathology of neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, multiple sclerosis, and traumatic brain injury. The brain is highly vulnerable to oxidative damage due to high metabolic demand. However, therapies attempting to scavenge free radicals have shown little success.

Organisms require redox cell-signaling agents in order to function and have multiple sources of these vital agents. To cope with oxidative and all other causes of damage, organisms have enormously powerful innate adaptive protection systems (APS), which produce antioxidant enzymes, repair DNA breaks and other molecular damage, kill and scavenge unrepaired cells, and restore good health (Fig. 1). However, APS potency progressively weakens with age, becoming less capable in remediating the damaging effects of ongoing oxidative distress.

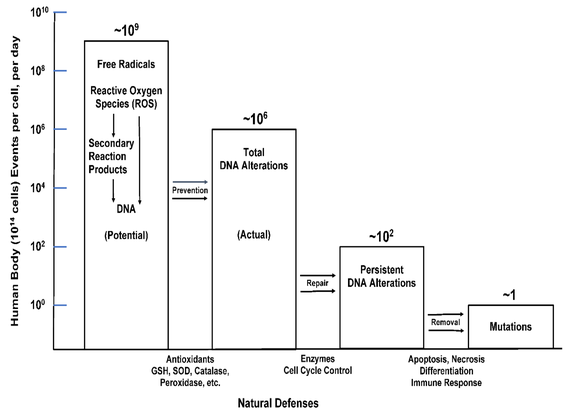

Fig. 1. Natural defenses act against endogenous DNA damage. Free radical production would cause ~ 10^9 DNA alterations per cell per day; however, antioxidant production lowers the actual rate to ~ 10^6 DNA alterations per cell per day. Damage-repair lowers the incidence of alterations to ~ 10^2 per cell per day, and damaged removal results in the natural occurrence of about one mutation per cell per day.

A brief radiation exposure damages biomolecules, including DNA, directly by "hits" on atoms and indirectly by the ROS from radiolysis of water. The burst of damage events triggers an APS response that is biphasic (Fig. 2). A *high dose*, above the threshold for lasting harmful effects, inhibits or damages the APS. From cancer radiotherapy, this threshold is about 3 Gy. A *low dose*, below 3 Gy, stimulates the APS to overrespond (Fig. 3). After a low dose, there is remediation not only of the radiation-induced damage but also damage resulting from both endogenous and exogenous factors such as natural oxidative stress, pathogens, toxins, and injuries. There is an immediate response and a delayed response because of cellular signaling.

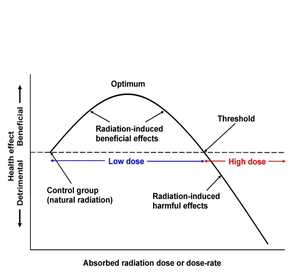

Fig. 2. Biphasic dose-response model and definition of low dose

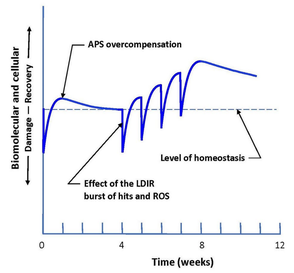

Fig. 3. Response to a single and to repeated LDIR treatments

LDIR therapy of AD is based on the hypotheses that oxidative stress is a major factor in the development of AD and that stimulation of the APS in the brain by a low radiation dose, e.g., the X-rays of a CT scan, will reverse or delay progression of this disorder.

Methods

The study was approved by the Research Ethics Board at Baycrest and at Sunnybrook and registered at ClinicalTrials.gov. Informed consent was obtained from the substitute decision makers, who accompanied the Baycrest residents for their treatments at Sunnybrook Hospital. CT was performed on a General Electric Light Speed VCT 64 detector scanner. Speed was 19.37 mm per rotation. Rotation time was 1.0 second. kV was 120. Patients received standard CT brain scans; each scan delivered a $CTDI_{vol}$ dose of 40 mGy. The first treatment was a double scan (80 mGy) because the original case received a second scan after moving her head during the first scan.

Four participants with advanced dementia were studied (MMSE < 12; ages 81-90; males/females = 3/1). All were clinically stable for at least 3 months. Exclusion criteria were history of malignancy, radiotherapy, neurological disorder other than AD, stroke, active major depression, bipolar affective disorder, or psychosis within the previous 90 days.

As in the case report, qualitative data on patient communication and interaction with family members and caregivers were obtained, verbal and written feedback, and by careful observation during their visits.

In addition, the following quantitative outcome measures were administered to assess neurocognitive capacity, behavioral symptoms, and functional ability: Severe Impairment Battery, Cohen-Mansfield Agitation Index and the Alzheimer Disease Functional Assessment and Change Scale.

Table 1. LDIR treatment dates (2019) and $CTDI_{vol}$ doses (mGy)

	1st Treatment	2nd Treatment	3rd Treatment
Case 1 (88 yrs)	Feb 8	Feb 22	Mar 8
Dose	81.0	41.0	43.0
Case 2 (90 yrs)	Jul 16	Jul 30	Aug 13
Dose	89.0	46.0	40.0
Case 3 (84 yrs)	Sep 10	Sep 24	Oct 8
Dose	79.0	40.0	43.0
Case 4 (82 yrs)	Dec 17	Dec 31	Jan 14
Dose	80.0	40.3	40.4

Results

As in the case report, qualitive data on the interactions of the patients with their relatives and friends revealed remarkable improvements in cognition and behaviour. However, results from the three quantitative outcome measures showed few indications of improvement. Months after the treatments, there was no evidence of deterioration in any of the cases. Case 2 showed no improvements following the treatments.

The other cases became more alert. Case 1, hours after first treatment, participated strongly in a Shabbat service. Days later, he recognized and talked with a granddaughter by video cell phone, walked with the aid of his son, spoke about his surroundings, sang and applauded at a concert. Case 3, mostly non-verbal, recognized, moved and interacted much better with his wife and children. He responded in short words and began eating independently. The family requested more CT scans. Case 4 recognized all her children better and started speaking to them. During a visit, the children talked about the memorable events of her life. She remarked jokingly, "Don't give away all the family secrets." They asked whether she was in pain or upset, when she cried several times. She replied, "No, I'm very happy." Normally, she needed help to walk; however, after treatment, she could stand and walk away from the table. Two months after her final treatment, caregivers stated that she was still improved over her condition before the treatments.

Discussion

Improvement in cognition and behavior was already apparent within a day of treatment. Although the observed recoveries from symptoms of Alzheimer's were quite small, a therapy of multiple treatments of the optimal X-ray dose, separated by the optimal time interval, may yield significantly greater and longer lasting benefits (Fig. 3). Although the results of this pilot study support the biological hypothesis, adequately powered double-blind placebo-controlled trials will determine efficacy and limitations of this therapy. Trials with less advanced cases should be carried out. It is essential to identify and employ objective measures that are sensitive to the changes induced in cognition and behavior.

If future studies establish that this novel therapy is effective, a mobile radiation device will replace the CT scanner. Based on evidence from low-dose studies on mice and patients, the optimal dose to upregulate the innate adaptive protection systems will likely be in the 100 to 500 mGy range. This dose will be about the same for all humans; however, the amount of benefit will depend on the individual's genetics, age and health status. The dose will be far below the 3 Gy threshold for lasting harmful effects. The biological damage caused by each treatment dose is repaired or removed by the APS, and the patient's health is restored.

This pilot study indicated that low doses of ionizing radiation may be a promising mode of treatment for Alzheimer's disease. Moreover, the rationale for this therapy, stimulation of the innate adaptive protection systems against oxidative distress, suggests that it might be effective in treating other neurodegenerative diseases.