REVIEW ARTICLE

Prion Disease and Dentistry

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ABSTRACT

The global annual incidence of Creutzfeldt-Jakob disease (CJD) ranges from 0.3 to 1.1 per million population.In India, Department of Neuropathology, National Institute of Mental Health and Neurosciences, Bangalore reported an incidence of 0.085 per million (8.5 cases in more than one billion population).The evidence of prion as an infectious agent is a great concern among health professionals. Importantly, PrPSc is resistant to most of the physical and chemical sterilizing procedures in normal clinical use and is only completely eliminated by incineration and also the unknown risk factors like its prevalence, altered tissue distribution and failure of sterilization technique to inactivate the prion. Nosocomial transmission of prion in the dental setting cannot be excluded.

KEYWORDS: Creutzfeldt-Jakob Disease, Prion, Dentistry

INTRODUCTION

Prion diseases are progressive neurodegenerative diseases that are rare and are characterized by long incubation period and short clinical course. A prion disease was first discovered by Stanley B. Prusiner, who won the 1997 Nobel Prize in Physiology or Medicine. Prusiner defined prion as infectious, transmissible proteinaceous particles that lack nucleic acid and are composed exclusively of a modified isoform of the non-infectious cellular prion protein (PrPC). The scrapie or PrPSc which is a pathogenic form of the prion protein (PrP) has the same amino acid content but a higher β-sheet content than PrPC. Prion is a cause of group of neurodegenerative diseases in humans and animals called transmissible spongiform encephalopathies (TSEs).[1] Human transmissible spongiform encephalopathies (TSEs) present several significant challenges to those working in health care, including neurology, surgery, and dentistry. There is still no treatment or prophylaxis for this invariably fatal disease, and no diagnostic test to identify individuals with this disease. Additionally, the agent of the disease is a protein that is remarkably resistant to inactivation by conventional methods, raising concerns about transmission among healthcare professionals.[2] TSEs were characterized by the presence of microscopic vacuoles in the brain's gray matter.[3] Globally annual incidence of CJD was reported as 0.3 to 1.1 per million population.[4] In India, Department of Neuropathology, National Institute of Mental Health and Neurosciences, Bangalore reported an incidence of 0.085 per million (8.5 cases in more than one billion population).[5] There are no published reports of the detection of prion in non-lymphoid tissues of humans with any form of Creutzfeldt-Jakob disease (CJD), but prion was detected in the oral tissues of inoculated laboratory animals. The risk of transmission of prion during dental care is not known, although on existing evidence it is likely to be very low. This article reviews current knowledge of the presence of prion in the oral cavity, discusses infection control protocol for the patients with prion disease.

CLASSIFICATION OF HUMAN TSE DISEASE

The human prion disorders were classified into CJD; Gerstmann-Straussler-Scheinker, or GSS, syndrome; and kuru. They are sub-classified into three main etiologic categories: acquired inherited, Sporadic (sCJD) as shown in Table 1. Other than the cases of vCJD in humans, there is no evidence of prion being transferred from animals to humans.[6]

Table 1: CLASSIFICATION OF HUMAN TSE DISEASE

I.	**INHERITED**
	1. Gerstmann-Straussler-Scheinker syndrome
	2. Fatal familial insomnia
	3. Other autosomal dominant families
II.	**ACQUIRED**
	1. Kuru
	2. Iatrogenic Creutzfeldt-Jacob disease
	3. Variant Creutzfeldt-Jacob disease(vCJD)
III. SPORADIC CREUTZFELDT-JACOB DISEASE (sCJD)	

I. INHERITED: Gerstmann–Sträussler–Scheinker-syndrome(GSS) and fatal familial insomnia (FFI) both occur in people with an apparent hereditary predisposition and are very rare, with an annual incidence of 1 per 10 million to 100 million people.[7] But the cause of mutation for GSS and FFI are different.[3-1]At least 20 Pathogenic Mutations of the prion protein-coding gene on chromosome 20 has been described. It is an autosomal dominant disorder, and they give rise to a spectrum of neurological features. Affected people can die from CJD-like illnesses.[6]

II. ACQUIRED FORMS:

1. Kuru: Kuru is an acquired human TSE, which was geographically restricted to the Okapi area of the eastern

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highlands of Papua New Guinea. It was due to cannibalism (specifically the consumption of deceased relative's tissues as a form of respect). [8] Transmission from human to human was first in the form of kuru. While this ritualistic practice ceased over 40 years ago, occasional new cases are indicative of the lengthy incubation periods.[9]

2. Iatrogenic Creutzfeldt-Jacob disease (iCJD): It was first diagnosed in the year 1974 and describes transmission from human to human through the exposure to cadaver-derived growth hormone, pituitary Gonadotropins, dura mater homograft, corneal grafts, blood, or inadequately sterilized neurosurgical instruments.[9]iCJD varies clinically from a sCJD-type disease to a disease similar to kuru. Its incubation period and rate of progression seem to be dependent on the site of inoculation of the infectious agent. Intracerebral or optic inoculation gives rise to the more rapid onset of disease than does inoculation that is more peripheral. As a consequence of understanding iCJD's cause and the ease, its frequency has fallen considerably. It may be dependent, however, on the extent of the spread of vCJD in Europe and throughout the world.[6]

3. Variant Creutzfeldt-Jacob disease (vCJD): The National Creutzfeldt–Jakob Disease Surveillance Unit in the United Kingdom found 10 cases of CJD with a specific neuropathological profile and called them variant CJD.[10]vCJD has always affected young adults and the mean age of onset being 29 years.[9]In humans consumption of food contaminated with tissues from animals with Bovine spongiform encephalopathy (BSE) is likely to initiate vCJD.[11] In UK, vCJD is most common, and cause death in younger age group whereas in sCJD the age at the time of death is in the age group of 40-44 years. The clinical course of the variant disease is much longer with a median duration of illness of thirteen months when compared to sCJD, it was four months.[10]vCJD has been confined to a limited number of countries, with 166 definite or probable cases in the UK , with France (25 cases), Ireland (5), Italy (1), The Netherlands (2), Portugal (3), and Spain (1) having indigenous cases, plus further cases from Canada, Japan, Ireland, the USA, and Saudi Arabia, where the disease is believed to have been acquired either in the UK or from meat imported from the UK.[9]

III. SPORADIC (CLASSIC) CREUTZFELDT-JACOB DISEASE (sCJD):

Worldwide sCJD accounts for the majority of human TSEs, and it typically arises in the middle to late life.[6]These affect approximately one per million of the population per year, worldwide, and account for about 85% of all cases of CJD.[9]Sixty eight years is the mean age of patients with sCJD. The mortality rate within one year is 85% because diagnosis is best established during the final stages of the disease, at or near the time of death.[10]

ORAL MANIFESTATIONS AND INFECTED ORAL TISSUES

Oral dysphagia and dysarthria are common to all forms of CJD as a consequence of pseudo bulbar paralysis, which could be an early symptom of the disease. The infection has only been demonstrated, by human autopsies, in pulp tissue, alveolar nerves, gingiva, and salivary glands at a very low level, 100-fold lower than levels found in the brain. In some gingival and salivary gland samples levels were 1000-fold lower; however, no infection has been demonstrated in any saliva sample.[12]

For tissue infectivity concerns during oral surgical procedures in the United States, William G. Kohn, DDS, from the CDC, said there has been "nothing related to dental tissues, not root canals, tooth extractions, or periodontal bone grafting procedures".[13]

RISK OF TRANSMISSION THROUGH DENTISTRY

All the standard procedure of infection control and surface disinfection are followed the risk of transmission of prion through dental treatment can be reduced to minimum.[14]The vCJD transmission through re-use of instruments in dental surgery is very low, as reported by the UK Department of Health. Even in the most cynical clinical scenario of infectivity of dental pulp, risk of transmission of vCJD is 10 times lower than that of tonsillectomy and also lower when comparing surgeries involving the central nervous system.[15]

Case–control studies have found no relationship between tooth extraction, dental surgery or major dental work and human TSEs.[16]

Infection Control in Dentistry: The treatment of TSE patients with procedures not involving neurovascular tissue, the general infection control practices recommended by World Health Organization (WHO) are sufficient. The WHO guideline for infection control guidelines transmissible spongiform encephalopathies.[17] (Table 2)

ORAL HEALTH CARE MANAGEMENT OF PATIENTS WITH PRION DISEASE

For patients with prion disease there was lack of guidelines in clinical dentistry for the management. The suggested infection control procedures for the dental management of patients with known prion disease are similar to those of all other patients, with certain important modifications. The current United Kingdom guidance is that all health care instruments employed in the treatment of a patient with known prion disease

Category	Methods
Incineration	•For all disposable instruments, materials, and wastes. •The Preferred method for all instruments exposed to high infectivity tissues.
Autoclave and chemical technique for heat-resistant instruments	• Put in sodium hydroxide (1 N NaOH) and heat in a gravity displacement autoclave at 121°C for 30 minutes; clean; rinse in water and follow routine sterilization. • Put in NaOH or sodium hypochlorite solution (20 000 ppm available chlorine) for 1 hour; clean it with water; heat in a gravity displacement autoclave at 121°C for one hour; clean and follow routine sterilization. • Put in NaOH or sodium hypochlorite for one hour; rinse in water, then put it to open pan and heat in a gravity displacement (121°C) or porous load (134°C) autoclave for 1 hour; clean and follow routine sterilization. • Put in NaOH and boil for 10 minutes at atmospheric pressure; clean, rinse in water and follow routine sterilization. • Put in sodium hypochlorite (preferred) or NaOH (alternative) at ambient temperature for one hour; clean; rinse in water and follow routine sterilization. • Autoclave at 134°C for 18 min (to be used for the cases i.e.,brain tissue bake-dried on surfaces).
Chemical methods for surfaces and heat-sensitive instruments	Flood with 2 N NaOH or undiluted sodium hypochlorite; let stand for one hour; mop up and clean with water. • For surfaces that cannot tolerate NaOH or hypochlorite, cleaning will remove most infective agents by dilution, and additional benefit may be derived from the use of one or another of the partially effective methods like chlorine dioxide glutaraldehyde, guanidinium thiocyanate [4 mol/L], iodophors, sodium dichloro-isocyanurate, sodium metaperiodate, urea [6 mol/L]).
Autoclave or chemical technique for dry goods	• Small dry goods that can withstand either NaOH or sodium hypochlorite should first be put in one or the other solution (as described above) and then heated in a porous load autoclave at ≥ 121°C for one hour. • Dry goods of any size that cannot withstand exposure to NaOH or sodium hypochlorite should be heated in a porous load autoclave at 134°C for one hour.

Table 2: Methods of Sterilization

should be discarded. Single-use instruments are preferred.[6] PrPSc is resistant to most of the physical and chemical sterilizing procedures in normal clinical use and is only completely eliminated by incineration. Instruments such as endodontic files should never be re-used since their complete sterilization is impossible.[12]

CONCLUSION

There appears to be a very low potential risk of CJD transmission, account must be taken of this possibility. There is no scientific basis for refusing treatment to patients with CJD or referring them elsewhere. Since there is no evidence of transmission by direct contact between people or via air or saliva, the only special requirement in the dental office is for measures to be taken to inactivate prion on instruments which should be done following the recommendations that has been explained before. The rapid progress of the disease and the physical and psychological dependency of these patients may mean that they require special dental treatments.

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