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REVIEW ARTICLE

Oral Medicine

Prion diseases: risks, characteristics, and infection control considerations in dentistry

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Abstract

Prion diseases are a group of fatal neurodegenerative diseases that are rapidly progressive and fatal, with no definite cure. There are no reported cases of prion disease transmission arising from dental procedures. Nevertheless, there is a theoretical but real risk of transmission of prion disease from dental instruments. A review was made of studies up to 2008 to provide an update of the characteristics, risk of transmission, and the infection-control implications of prions in the field of dentistry. As the prions are resistant to conventional sterilization methods, highly-specific, cross-infection control measures are required when managing patients infected with these.

Introduction

The term prion has been used since 1982 to differentiate it from infectious agents that contain nucleic acids (e.g. viruses and bacteria). Prion diseases are caused by the transformation of normal cell glycoprotein into a conformationally-altered isoform (PrP) that is infectious in the absence of nucleic acid. This transition confers PrP with partial resistance to proteolytic degradation and detergent insolubility.[1]

The potential for onward transmission of prions via instruments used in dental surgery has raised the possibility of transmission in that setting. This article provides an overview of the characteristics, risks of transmission, and infection-control considerations of prions in dentistry.

Materials and methods

Search strategy for the identification of studies

A literature search for relevant articles was performed using Science Direct, Hinari, Pubmed Ovid Medline, In-Process & Other Non-Indexed Citations, and, Cochrane Database of Systematic Reviews.

Methods of the review

Approximately 215 articles up to 2008 were identified in the English language literature using the search strategy. Article title duplicates were removed, and 90 articles were searched for relevancy of contents. Articles that did not address the characteristics, the risk of transmission, and infection-control considerations in dentistry for prions were excluded. Further articles were identified by reviewing the references and bibliographies of articles obtained by the search strategy.

General clinical aspects of prion disease

One of the most peculiar features of prion disease is the co-existence of infectious, genetic, and sporadic forms. According to the Creutzfeldt–Jakob disease (CJD) surveillance unit, UK, up to May 2010, a total of 2617 cases of

CJD were reported, with 1494 deaths.[2] Scrapie affecting sheep and goats was the first prion disease to be described. Other animal prion diseases are now known. Human prion disorders are classified into CJD, Gerstmann–Sträussler–Scheinker (GSS) syndrome, and kuru, and subclassified into two main etiologic categories: inherited and acquired.

Inherited prion diseases

Inherited prion diseases account for approximately 15% of all human prion diseases, and they comprise GSS syndrome and a group of other familial human prion diseases.

At least 30 pathogenic mutations of the prion protein-coding gene have been described. All of the mutations are inherited in an autosomal dominant manner, and they give rise to a spectrum of neurological features. Affected people can die from CJD-like illnesses.[1]

Acquired prion diseases

Kuru is an incurable, degenerative, neurological disorder (brain disease) that is a type of transmissible spongiform encephalopathy found in humans. Kuru is believed to be caused by prions and is related to CJD. It is best known for the epidemic that occurred in Papua New Guinea in the middle of the 20th century.[1] Kuru has a long incubation period, and causes physiological as well as neurological effects that ultimately lead to death. It is characterized by cerebellar ataxia, preceded by headaches, joint pains, and shaking of the limbs, with the clinical stage lasting an average of 12 months.[1,3]

Classic CJD is a human prion disease. It is a neurodegenerative disorder with characteristic clinical and diagnostic features. This disease is rapidly progressive and is always fatal. Infection with this disease leads to death, usually within 1 year of the onset of illness. Classical CJD is also referred to as sporadic CJD (sCJD).[4] The most common form of classic CJD is believed to occur sporadically, caused by the spontaneous transformation of normal prion proteins into abnormal prions. This sporadic disease occurs worldwide, at a rate of approximately 0.50–0.68 cases per 1 million people per year in Europe.[5] It is most common in the 45–75 age group, with the peak age of onset being 60–65.[6] The inherited forms include GSS syndrome and fatal familial insomnia.[1]

Variant CJD (vCJD) is a rare and fatal human neurodegenerative condition first described in 1996 in the UK.[3] As with CJD, vCJD is classified as a transmissible spongiform encephalopathy (TSE) because of its characteristic spongy degeneration of the brain and its ability to be transmitted.

Before the identification of vCJD, CJD was recognized to exist in only three forms. Sporadic cases, which have an unknown cause and occur throughout the world at the rate of approximately one per 1 million people, account for 85 of CJD cases. Familial cases are associated with a gene mutation and make up 5–10% of all CJD cases.[4] Iatrogenic cases result from the accidental transmission of the causative agent via contaminated surgical equipment or as a result of cornea or dura mater transplants, or the administration of human-derived pituitary growth hormones.[5] Less than 5% of CJD cases are iatrogenic.

In contrast to the traditional forms of CJD, vCJD affects younger patients (average age is 29 years, as opposed to 65 years), has a relatively longer duration of illness (median of 14 months, as opposed to 4.5 months), and is strongly linked to exposure, probably through food, to TSE of cattle called bovine spongiform encephalopathy.[3]

According to the CJD surveillance unit, Edinburgh, the total number of suspected and confirmed cases and deaths due to CJD in the UK up to May 2010 was 2617 and 1146, respectively.[2]

Iatrogenic CJD (iCJD) has affected at least 400 people worldwide.[7] The prion is acquired via cadaver-derived growth hormone, pituitary gonadotropins, dura mater homografting, corneal grafts, or inadequately sterilized intracerebral surgical equipment. Subsequent to understanding of the cause of iCJD and the methods used to avoid future disease, its frequency has fallen considerably.

Dental implications of prion disease

Oral manifestations

Oral manifestations of human prion disease comprise dysphagia and dysarthria due to pseudobulbar palsy. In patients with vCJD, there can be orofacial dysesthesia or paresthesia.[7,8] Recently, loss of taste and smell was reported as a feature of one patient with vCJD. The mouth would seem to be rarely affected in patients with prion disease.[1]

Infectivity and transmission risk from oral cavity

The prion's possible route of transmission from the brain to the oral tissues and *vice versa* was suggested on the basis of the observation of neuronal degeneration with probable prion protein accumulation in the trigeminal ganglia of patients with sCJD.[9] Since dental pulp originates from the richly-innervated tissue of the neural crest, theoretically, it is reasonable to presume that the dental pulp of people infected with vCJD, sCJD, and familial CJD might be infectious. There is evidence that infected laboratory animal models build up some level of infectivity in the oral tissues (including dental pulp, gingiva,

tongue musculature, salivary glands, and trigeminal ganglion).[10–14] Although, to date, there has been no confirmation in humans of the occurrence of PrP in dental tissues, nosocomial transmission of prions in the dental setting cannot be excluded.

There is little data to indicate that prions are transmitted within the dental clinic setting, mirroring knowledge of the transmission of HIV[15] and hepatitis C virus.[16] Oral tissues are considered to be of low infectivity, and people who are liable to acquire iCJD (e.g. recipients of dura mater, corneal transplants, and human pituitary hormones, and people who have undergone neurological procedures) are regarded by the World Health Organization (WHO) as being at low risk of developing prion disease (and thus require no additional infection-control measures).[17]

Potential of transmission in health-care workers

Community transmission

Until now, there has been no evidence to show that CJD or any other amyloidosis is transmissible from person to person by normal contact, airborne droplets, or sexual contact.[17,18] However, owing to the long incubation period of amyloidosis, such as vCJD, it is premature to infer that they are not transmitted from one person to another by social contact.[18]

Transfusion of blood

Past studies have not revealed any evidence of transmission of sCJD by blood or blood products. To date, there have been four instances of possible transmission of vCJD infection through blood transfusions. In these cases, the donors were at a preclinical phase of the disease at the time of donation.[19,20] It should be noted that the extended incubation period of prion diseases results in a long asymptomatic period in infected people.[21]

Occupational exposures and patient safety

There is no risk of transmission of TSE to health-care workers, relatives, or the community through normal social and clinical contact or non-invasive clinical procedures.[10] Up until 2005, a total of 24 cases of sCJD were reported in health-care workers.[18] Theoretically, it is possible that health-care workers might acquire TSE from patients through inoculation injuries.[10] However, so far, there has been no such case reported, and there is no epidemiological evidence that proves a relationship between the acquiring of sCJD and any occupational exposure.[21] In case of a needle stick injury while performing dental procedures on a TSE patient, the WHO common-sense actions are recommended:[10]

(**a**) Contamination of unbroken skin with internal body fluids or tissues: wash with detergent and abundant quantities of warm water (avoid scrubbing), rinse, and dry. Brief exposure (l min, to 0.1N NaOH or a 1:10 dilution of bleach) can be considered for maximum safety);
(**b**) Needle sticks or lacerations: gently encourage bleeding; wash (avoid scrubbing) with warm soapy water, rinse, dry, and cover with a waterproof dressing. Institute further treatment (e.g. sutures) as per the type of injury. Report the injury according to normal procedures for your hospital or healthcare facility/laboratory;
(**c**) Splashes into the eye or mouth: irrigate with either saline (eye) or tap water (mouth); report according to normal procedures for your hospital or health-care facility/laboratory;
(**d**) Health and safety guidelines mandate reporting of injuries, and records should be kept for no less than 20 years.

Optional precautions for major dental work

Possible safety measures that could prevent disease transmission include:[10]

(**a**) Use single-use items and equipment (e.g. needles and anesthetic cartridges;
(**b**) Reusable dental broaches and burs that might have become contaminated with neurovascular tissue should either be destroyed after use (by incineration) or alternatively decontaminated by a method recommended by the WHO;
(**c**) Schedule procedures involving neurovascular tissue at the end of day to permit more extensive cleaning and decontamination.

General measures for cleaning instruments and environment

Wide-ranging actions that should be followed in the dental operatory to clear up the instruments and surroundings include:[10]

(**a**) Instruments should be kept moist until cleaned and decontaminated;
(**b**) Instruments should be cleaned as soon as possible after use to minimize drying of tissues, and blood and body fluids on to the item;
(**c**) Avoid mixing instruments used on no detectable infectivity tissues with those used on high- and low-infectivity tissues;
(**d**) Recycle durable items for reuse only after TSE decontamination;
(**e**) Instruments to be cleaned in automated mechanical processors must be decontaminated before processing

through these machines, and the washers (or other equipment) should be run through an empty cycle before any further routine use;

(**f**) Cover work surfaces with disposable material, which can then be removed and incinerated; otherwise clean and decontaminate underlying surfaces thoroughly;

(**g**) Be familiar with and observe safety guidelines when working with hazardous chemicals, such as sodium hydroxide (NaOH, soda lye) and sodium hypochlorite (NaOCl, bleach);

(**h**) Observe manufacturers' recommendations regarding care and maintenance of equipment.

Dental management of patients at high risk for CJD

It is important that dental personnel obtain appropriate information regarding protection against CJD and its occupational risks and hazards. As a thumb rule, proper medical history (including a risk assessment for CJD) should be obtained from all patients before all dental procedures.

For practical considerations, it is important to differentiate between symptomatic patients (unambiguous or suspected CJD or vCJD cases) and asymptomatic patients (those with no clinical manifestations, but potentially at risk because of having a medical or family history). For a high-risk patient, dental procedures without the involvement of the neurovascular tissues, general infection control practices are sufficient.[10] However, when a dental procedure involves exposure to neurovascular tissues on a high-risk patient, more rigorous infection control should be followed. It is preferable to perform such a procedure in appropriate referral centres by personnel familiar with CJD safety measures.

While treating suspected or confirmed CJD patients, it is recommended that the patient should be appointed at the end of the day to prevent cross-infection and allow more extensive cleaning; disposable drapes and coversheets should be used to prevent environmental contamination, whenever possible;[10] all dental instruments must not be reused, but should be either discarded or decontaminated immediately after clinical use;[22,23] use a separate waterline (e.g. syringe) for cooling dental handpieces, a suction unit, and a separate disposable bowl instead of the spittoon of the dental unit.[18,24]

Proper infection control in treating high-risk patients

Prion agents, unlike infectious microorganisms, resist conventional sterilization methods, such as steam autoclaving, even at increased temperatures, or by ethylene oxide gas.[10,25] It has been reported that human sCJD prions were more than 100 000 times more resistant to inactivation than hamster prions, which have been historically used as the standard for assessing prion inactivation procedures. All non-disposable instruments should be mechanically cleaned and passed through stringent decontamination protocols before cleaning, terminal sterilization, and reuse.[10,26]

There are minor differences in transatlantic and European guidelines. According to the WHO, the most stringent protocol for heat-resistant instruments is to ''immerse the instruments in sodium hydroxide (1 N NaOH) and heat in a gravity displacement autoclave at 121°C for 30 min; clean; rinse in water and subject to routine sterilization''.[10] The Centers for Disease Control recommend cleaning ''instruments thoroughly and steam-autoclave at 134°C for 18 min'' in a vacuum autoclave, and in addition, repeat the standard cycle six times.[26] According to the chief dental officer for England, dental instruments used on patients with or ''at increased risk'' of CJD can be handled in the same way as those used in any other low risk surgery (i.e. these instruments can be reprocessed according to best practice and returned to use).[27] For those tissues where evidence suggests this risk is most pronounced, endodontic files and reamers should be single-use instruments in all cases. Other instrument or device types for which a reliable cleaning regime is not available should also be considered for replacement by single-use types or by the single use of reprocessible instruments. Although the Department of Health UK guidelines do not recommend any special protocols for prion decontamination, they do emphasize that an improved cleaning process and its ability to remove proteins in tandem with a validated steam sterilization procedure should be followed.[28]

For surfaces and heat-sensitive, reusable instruments, the WHO recommends ''Flood with 2 N NaOH or undiluted sodium hypochlorite; let stand for 1 h.; mop up and rinse with water''.[10]

Conclusion

Although there is no evidence to show that sCJD is transmissible, vCJD is transmissible during the preclinical stage of the disease. To date, there are no published definite or suspected cases of vCJD transmission arising from dental procedures, and there seems to be no correlation between dental treatment and prion diseases. Because there is a theoretical but real risk of transmission of prion disease from dental instruments, as a general rule, clinical sterilization and cleaning should be of the highest standard possible. Also, since the rapid disease progression produces physical and psychological dependency, these patients are worth special attention during dental treatment. Medical history should be obtained from all

patients before all dental procedures. Prion disease investigations regarding diagnosis, transmission, management, and decontamination of prion proteins are ongoing, and thus, dental professionals should maintain up-to-date standards of knowledge of infection control and decontamination protocols.

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