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Potential Risk of Respiratory Secretions in the Transmission of HBV Infection: A Review of the Literature

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Authors' contributions

This work was carried out in collaboration between all authors. Authors NK and MTK designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors NK and ET managed the literature searches, analyses of the studies performed previously. Authors MTK and YB analyzed the data and revised the article. All authors read and approved the final manuscript.

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ABSTRACT

Hepatitis B virus (HBV) infection is a significant health problem around the world and may cause serious morbidity and mortality. The most common transmission routes are parenteral, sexual, perinatal and horizontal way. Identification of the risk factors for viral hepatitis transmission is the main rule to reduce the spread of this infection. The aim of this study was to review the possible occupational risk factors for nanparenteral transmission of Hepatitis B virus for health care workers, especially for otorhinolaryngologists. The Medline / PubMed, Google Scholar, and Cochrane databases were searched by using different combinations of MeSH terms for HBV, transmission routes, and risk factors. The results were collected from articles published between January 2000 and July 2015. There were no language restriction during searching the data, whether the abstracts of the studies contain sufficient data were analysed. All searchable relevant

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data was evaluated and reviewed. The presence of viral particles, including HBsAg and / or HBV DNA in body secretions such as saliva, tears and cerumen may suggest the possibility of horizontal transmission of HBV infection. Therefore, the healthcare workers, particularly otorhinolaryngologists, ophthalmologists or other surgeons, audiologists, dentists, pulmonologists, intensive care specialists and nurses should pay special attention while applying the standard infection control precautions in order to prevent HBV infection in themselves and their patients.

Keywords: Hepatitis B virus; saliva; tears; cerumen; transmission risk.

1. INTRODUCTION

Hepatitis B virus (HBV) infection is a significant global health problem. It may cause life threatening liver diseases with high morbidity and mortality [1]. The World Health Organization (WHO) has estimated that approximately one-third of the world's population has been infected with HBV and more than 350 million people have cronic HBV infection. Patients chronically infected with HBV are at significant risk of developing cirrhosis, liver failure and hepatocellular carcinoma [1-4]. It is estimated that chronic HBV infection is leading cause of death over one million people each year [1,2].

The common transmission routes of HBV infection are vertical (from an infected mother to her child), sexual transmission (unprotected sex, multiple partners), parenteral (intravenous drug use, medical procedures; e.g., surgery, dialysis and accidental needle stick injuries), and horizontal way (child-to-child in one household) [1-5]. In some endemic areas transmission route of HBV infection cannot be identified in several patients with HBV infection. Therefore, in addition to vaccination, the only practical way of HBV infection prevention is to determine and control the probable routes of transmission [5].

The potential infectivity of saliva, tears, cerumen and other body secretions may provide an explanation for the 20% of infection caused by horizontal transmission. The aim of this study was to review the role of some body secretions in HBV transmission.

2. METHODS

We searched the Medline/PubMed, Google Scholar, and Cochrane databases by using a different combination of MeSH terms, such as "Hepatitis B virus, HBV, oral secretions, saliva, tears, cerumen, transmission and risk factors". The following types of studies were considered suitable for review: case control studies, review articles, investigative studies, observational studies, surveys and reports on HBV transmission. The results were limited with articles that were published between January 2000 and July 2015. There was no language restriction while searching the data whether the abstracts of the studies contain sufficient data were analysed. All searchable relevant data was evaluated and reviewed.

3. RESULTS AND DISCUSSION

Forty-nine articles were collected for the study from the online literature search. Twenty articles were included in the analysis according to our inclusion criteria. Full texts were available for 16 articles.

Health care workers always have a risk for transmission of some infectious diseases such as HBV infection. Although parenteral transmission is the most common transmission route for this kind of infectious diseases, some other body secretions, such as saliva, tear, or cerumen may cause transmission of virus. Health care workers such as otorhinolaryngologists are always in contact with this kind of body secretions. If they are not conscious about it, they can be easily infected with these secretions. Moreover, they can transmit the infection to other patients. In the current study, we focused on the possible occupational risk factors for nonparenteral transmission of HBV infection in health care workers, especially in otorhinolaryngologists and we reviewed the literature.

Some studies demonstrated several markers of HBV in body secretions of head and neck region and suggested possible transmission routes of infection (Table 1). These studies are mainly focused on saliva, cerumen and tear.

Saliva and oral secretions are the most studied body secretions in the head and neck region. The results of these studies have showed that

serum HBV level has high correlation with HBV level in saliva and oral secretions. Zhevachevsky et al. [6] studied HBsAg, HBeAg, and HBV DNA in the serum and saliva samples of 109 patients with acute HBV infection. In that study HBsAg positivity was found 85.7% in the saliva and 83.3% in the serum of the patients. Moreover, HBV DNA positivity was found 84.6% in the serum and 46.2% in the saliva. However, during the early convalescence phase, HBsAg was found to be significantly more frequent in the serum samples of the patients than the saliva samples (59.5% and 23.8%, respectively). The frequency of HBeAg in saliva was significantly higher than serum in the acute phase (84.3% and 28.1%, respectively) and the convalescence phase (56.2% and 3.1%, respectively). Hutse et al. [7] performed a study with 73 HBsAg-negative and 43 HBsAg-positive serum and oral secretion paired samples. They found significant correlation between the serum and oral secretion HBsAg level, with 90.7% sensitivity and 100% specificity. Similarly, Cruz et al. [8] found HBsAg positivity in 40 (85.1%) of 47 oral secretion samples and 44 (93.6%) of the 47 saliva samples. Additionally, Van der Eijk et al. [9] evaluated the quantitative levels of HBV DNA in saliva and serum. They found that 85% (23 of 27) of the HBsAg-positive patients had HBV DNA in their serum. Also, 80% of the HBeAg-positive patients and 42% of the HBeAg-negative patients had HBV DNA in their saliva. In that study, the median HBV DNA levels in serum and saliva were 2.10×10^5 and 2.27×10^4 genome equivalents (GEQ) per milliliter (GEQ/ml), respectively. In another study, HBV DNA levels in serum and saliva, Van der Eijk et al. [10] reported higher correlation than previous study. The rate of HBV DNA positivity in the serum of the HBeAg-positive patients was 100%, and 76% in the saliva. Similarly, Heiberg et al. [11] studied the HBV DNA levels in plasma and saliva of 43 children with chronic HBV. Fifty-eight percent of the children were found positive for HBeAg in the plasma. According to their results, the HBV DNA levels in the saliva were 39 times higher in the HBeAg-positive children than in the HBeAg-negative. The HBV DNA levels of saliva were higher than 10^4 IU/ml in 60% of the samples collected from the HBeAg-positive children and it was higher than 10^5 IU/ml in 33% of those children, similar results were reported by Zhang et al. [12]. They noted that high levels of serum HBV DNA could be correlated with the saliva levels. According to all these study results, significant correlation between the HBV DNA levels of serum, saliva and oral secretion might be suggested. In the other study, Quoilin et al. [13] investigated the sensitivity of HBsAg in oral secretion and saliva in 2036 participants and they noted higher HBsAg sensitivity in serum rather than oral secretion. As a result of this study, it can be considered that oral secretions have a lower risk of contamination compared to saliva.

There are also some case reports about this topic in the literature. Marie-Cardine et al. [14] noticed the horizontal transmission of HBV infection by eating food with hands from a common bowl. In another case report, Hui et al. [15] reported in a 43-year-old man with acute HBV infection who had no history of sexual activity, surgical operation or transfusion. However, it was also noticed that he was bitten by another patient with chronic hepatitis B. Both of the men had genotype B and the similar sequences of HBV. These reports may support the infectivity of saliva in HBV patients. All of these studies may show us that HBV DNA in saliva and oral secretions are enough to make it an infective agent.

In the other study, Chen et al. [16] examined HBsAg, HBcAg, and HBV DNA in the parotid tissues of 22 HBsAg-positive patients who had undergone surgery due to a kind of parotid tumor. The HBsAg and HBcAg positivity in the parotid cells was found to be 45.5% and 40.9%, respectively. The HBV DNA positivity rate was 58.3% in the samples in which HBsAg was detected. The authors suggested that HBV in saliva might originate from infected salivary glands. But, according to us, this comment is open to debate. It is well known that HBV has very high transmission risk with blood. Any tissue such as parotid has blood inside. It is not surprise to find high level of HBV DNA and other viral particles in any tissue, if the patient has HBV infections. But, on the other hand, it is well known that saliva includes secretions from salivary glands, bronchial tissue, and blood derivates [8]. HBV particles and genome in saliva can orginate from either salivary glands or any part of respiratory system or blood vessels. Chan et al.'s [16] study give rise to think about the role of salivary glands in HBV replication.

Table 1. Hepatitis B virus ınvestigations in different body secretions

Year	Authors	Secretion / Tissue in head and neck	n	Evaluated factors	Authors conclusions
2000	Zhevachevsky et al. [6]	Saliva	109	HBsAg, HBeAg, HBV DNA	Long-term persistence of HBeAg in saliva might play a possible role in HBV transmission. Saliva may have a role in HBV transmission
2004	Van der Eijk et al. [9]	Saliva	27	HBV DNA	High correlation between the HBV DNA levels in serum and saliva. It may pose a potential risk for HBV transmission
2004	Kalcioglu et al. [20]	Cerumen	40	HBV DNA	Cerumen is a possible source of HBV transmission
2005	Hutse et al. [7]	Oral secretion	43	HBsAg	Oral secretion may be important for HBV transmission
2005	Van der Eijk et al. [10]	Saliva	150	HBV DNA	HBV DNA level in saliva is high enough to make it an infective
2006	Kidd-Ljungrren et al. [17]	Saliva, Tears, Nasopharyngeal swabs	25	HBV DNA	Very high titers of HBV DNA in serum could go along with high titers of HBV DNA in saliva and in the nasopharyngeal swab
2007	Quoilin et al. [13]	Oral secretion	2036	HBsAg	HbsAg in oral secretion had lower sensitivity than the HbsAg in serum
2008	Zhang et al. [12]	Saliva	200	HBV DNA	When serum contains a highlevel of HBV DNA, the level of HBV DNA in the saliva could also be high
2008	Goh et al. [22]	Cerumen, Otorrhea	30	HBsAg, HBeAg, HBV DNA	Cerumen and otorrhea had a low risk for HBV infectivity.
2009	Chen et al. [4]	Parotid tissue	22	HBsAg, HBcAg, HBV DNA	HBV in saliva might originate from infected salivary glands
2010	Heiberg et al. [11]	Saliva	43	HBV DNA	Saliva might be a potential vehicle for the spread of HBV
2011	Gholami-Parizad et al. [21]	Cerumen	70	HBV DNA	A high level of HBV DNA in cerumen had a high risk for transmission of HBV
2011	Cruz et al. [8]	Saliva, Oral secretion	115	HBsAg	Oral secretions have a lower risk of contamination compared to all other forms of saliva
2012	Komatsu et al. [18]	Saliva, Tears, Sweat	47	HBV DNA	The tears of patients chronically infected with HBV might be highly infectious
2013	Eftekharian et al. [23]	Cerumen	30	HBV DNA	Cerumen can be a potential source of transmission of hepatitis B virus.

Some researchers have also studied in the other materials such as tears and sweat with or without saliva or oral secretion of HBV positive patients (Table 1). Kidd-Ljungrren et al. [17] studied with serum, saliva, tears and nasopharyngeal swabs in 25 chronic HBV carrier patients. They investigated the HBeAg and anti-HBe levels of those patients. All the patients had positive for HBV DNA in their serum. In that study, researchers found that five of the 23 nasopharyngeal swabs had detectable HBV DNA. All of them had positive for HBeAg in the serum. In addition, four of the 17 tear samples had positive for HBV DNA (but lower titers compared to the serum levels) with positive for HBeAg in their serum. The authors demonstrated that very high titers of HBV DNA in serum could go along with high titers of HBV DNA in saliva and in the nasopharyngeal swab. Komatsu et al. [18] studied the HBV DNA levels in serum, saliva, tears, and sweat samples from 47 patients who were chronically infected with HBV. According to their results, the highest levels of HBV DNA were in the serum, followed by the tear and saliva samples. They reported no significant differences between them. Then they injected a tear specimen (collected from a 10-month-old girl who had > 9.0 log copies/ml HBV DNA in her serum sample and 7.1 log copies/ml in her tear sample) into two human hepatocyte transplanted chimeric mice, intravenously. One week later they determined HBV DNA positivity in the serum of those mice. The positivity for HBV in the aqueous humour of a HBV positive patients was reported in an another case report in the literature [19]. According to these results, it is possible to say that the tear and sweat of patients chronically infected with HBV might be highly infectious.

Other body secretions in head and neck region are cerumen and otorhea. Especially otorhinolaryngologist and other health care workers always have contact with these samples. Therefore, some researchers focused on these samples to investigate possible transmission risk for HBV infection (Table 1). Kalcıoğlu et al. [20] studied HBV DNA in 40 cerumen samples collected from patients with positive HBV DNA in their serum. They found that 27.5% of these patients were also positive for cerumen. The authors noted a good correlation between serum HBeAg and cerumen HBV DNA positivity. They reported that patients who had positive HBV DNA in cerumen also had high quantities of HBV DNA in serum. In other similar literature, Gholami-Parizad et al. [21] studied cerumen and blood samples from 70 patients infected with HBV. All the patients were positive for HBsAg and anti HBc total. HBV DNA were positive in 82.1% (61/70) of cerumen samples ranging from 1.53×10^2 to 2.9×10^8. In that study, the HBeAg-positive patients showed a higher rate of HBV DNA positivity in the serum and cerumen samples. According to these results, it is possible to say that cerumen of patients with HBV infection may have a role in the transmission. On the other hand, HBeAg is very important for transmission of HBV infection. Goh et al. [22] conducted a study on 30 HBsAg-positive, chronic hepatitis B patients. They examined HBsAg, HBeAg, and HBV DNA levels in 30 cerumen and five otorrhea samples. They reported the HBV DNA positivity as 66.7% in the cerumen and 100% in the otorrhea. In cerumen, the HBV DNA and HBsAg levels were found to be significantly higher in patients whose serum was positive for HBeAg rather than HBeAg negative. In their study, HBeAg was not detected in any of the cerumen samples. According to this results, it can be considered that even though cerumen and otorrhea have HBV DNA, the risk for HBV infectivity of these samples is low.

Contrarily to these results, Eftekharian et al. [23] reported only 6.6% positivity of HBV DNA in cerumen of 30 patients who had chronic HBV infection. Contrasting these results still indicate the need of further studies on this issue.

Many HBV markers, such as HBsAg, HBeAg, and HBV DNA, had been studied to determine the presence of HBV in serum and other body secretions, such as saliva, tear and cerumen. There is not enough data to prove that some body secretions are infectious, but the risk of infectivity can not be ignored. Moreover, an experimental study showed the transmission of HBV infection from a child into 2 human hepatocyte-transplanted chimeric mice as mentioned above [18].

4. CONCLUSION

In this review article, the results of the researchs were summarised and focused on the possible transmission risk of some body secretions for HBV. Many reports have demonstrated that the presence of a high amount of HBV DNA in oral secretions, tears, saliva and cerumen suggest the possibility of transmission. Therefore, healthcare workers, particularly otorhinolaryngologists, ophthalmologists or other surgeons, audiologists, dentists, pulmonologists, intensive care specialists, and nurses should pay special

attention for applying standard infection control precautions to protect themselves and their patients from HBV infection.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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