

# New immunization schedule effectiveness against hepatitis B in liver transplantation patients

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**ABSTRACT – Background** – Although liver transplantation is considered to be a high-risk procedure, it is well-established as a treatment option for the cure and quality of life enhancement for individuals who suffer from diseases. Preventing an infection by hepatitis B virus through immunization schedules has been the most effective way to reduce complications, since it decreases the number of people who suffer from chronic hepatitis caused by the hepatitis B virus and eradicates its transmission. **Objective – 1.** Analyzing evidence in the literature on various schedules employed for immunization against hepatitis B in patients who have received a liver transplantation. **2.** Suggesting potential immunization schedules against hepatitis B in patients who suffer from liver cirrhosis, without previous verifying documentation, using the Child-Turcotte Pugh score, according to evidences found in the literature. **Methods** – Systematic review of the literature, conducted on the data bases MedLine, PubMed, and Lilacs, between September, 2017 and January, 2018, by using the following keywords: “Liver Transplantation, “Immunization Schedule”, “Hepatitis B Vaccines”. In order to analyze the articles, a summary figure was especially designed and both the results and discussion were presented in a descriptive way. **Results** – We included 24 studies; among them, eight had accelerated immunization schedules, 13 followed the conventional schedules, and three had super accelerated schedules. Regarding immunization, 21 studies were conducted with patients in the pre-transplant period, one with a transplanted patient, one with a pre-transplant group, and one with a post-transplant group. Found articles suggest that, disregarding the chosen immunization schedule, seroconversion rates tended to be lower as the liver disease advanced, compared to the healthy population. **Conclusion** – The studies did not find seroconversion superiority between the different immunization schedules (conventional and unconventional). However, since candidates to liver transplantation are usually very vulnerable, results show that super accelerated immunization schedules are possibly recommended for such group of patients; serologic test results will be higher when the immunization schedule is completed in the pre-transplant period.

**HEADINGS** – Hepatitis B vaccines. Liver transplantation. Immunization schedule.

## INTRODUCTION

Although liver transplantation is considered to be a high-risk procedure, it is well-established as a treatment option for the cure and quality of life enhancement for individuals who suffer from diseases, e.g., end-stage liver disease, acute liver failure, and hepatocellular carcinoma; most of them are linked to the hepatitis B virus (HBV). On the other hand, transplantations may bring about a risk of disease transmission by the HBV in the periods before, during, or after the procedure<sup>(1,2)</sup>.

Preventing an infection by HBV through immunization schedules has been the most effective way to reduce complications, since it decreases the number of people who suffer from chronic hepatitis caused by the HBV and eradicates its transmission. It is considered to be the first vaccine with an impact against cancer taking into account that HBV prevention reduces the risk of cancer linked to that virus; besides, it is the first vaccine against a sexually transmitted infection (STD)<sup>(3-6)</sup>.

The HBV vaccine is highly effective in healthy individuals, whereas it is little immunogenic in immunocompromised individu-

als, including those who have not been transplanted, but who have advanced liver diseases, such as chronic hepatitis C (HCV); thus, specific immunization schedules are recommended for specific groups<sup>(7)</sup>.

This study aims to analyzing available evidence in the literature about the different used schedules for immunization against hepatitis B in patients before and after they have received liver transplantation; and suggesting potential immunization schedules against hepatitis B in patients who suffer from liver cirrhosis, without previous verifying documentation, using the Child-Turcotte Pugh score, according to evidences found in the literature.

## METHODS

It consists of a systematic exploratory review of the literature, for which the following steps were adopted: identification of the issue, search in scientific literature, article classification, results evaluation, and overview of the evidences. The guiding question was “Which immunization schedules against hepatitis B were used in patients before and after liver transplantation and which results were obtained?”.

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The search was conducted on the data bases Medical Literature Analysis and Retrieval System Online (MedLine), US National Library of Medicine National Institutes of Health (PubMed), and *Literatura Latino-Americana e do Caribe em Ciências da Saúde* (Lilacs), between September, 2017 and January, 2018, using the following keywords: “Liver Transplantation, “Immunization Schedule”, “Hepatitis B Vaccines”. The articles were selected for their titles, abstracts, and keywords, disregarding their publication date and language.

The inclusion criteria were: articles that covered the chosen subject through studies on employing different immunization schedules against hepatitis B in adult patients with cirrhosis before or after liver transplantation, or adult patients with a chronic liver disease previously negative for HBV.

The exclusion criteria were: literature review articles, guidelines, studies that tested immunization schedules as a treatment option for patients who were positive for HBV, studies concerning children and adolescents, studies with samples in which there were other groups of immunocompromised patients other than pre- or post- liver transplantation, studies which were not available in full; studies with immunization associated with hepatitis A/B.

In the analysis and subsequent summary of the included articles, a summary figure was especially designed for this study, which contains the following aspects considered appropriate: author, year, immunization schedule, dose, researched sample, and obtained results. Results were presented and the obtained data were discussed in a descriptive way aiming at a better understanding and an increase in the knowledge on the subject.

## RESULTS

We identified 52 studies; from them, 18 were excluded according to the aforementioned criteria; there was then a total of 24 studies included for the analysis, among them 23 were published in English and 1 in Spanish (FIGURE 1).

Regarding the employed immunization schedules, there were schedules classified as conventional/standard (0, 1, and 6 and/or 0, 1, 2, and 6 months between doses), accelerated (0, 1, and 2 months between doses), and super accelerated (0, 7, and 21 days/ 0, 7, 28 days; 0, 10, and 21 days; 0, 10, and 28 days between doses); some researchers even included a fourth booster dose after 12 months, especially when using shorter intervals.

Among the included studies shown in FIGURE 1, eight of them were identified as being accelerated immunization schedules, 13 were conventional schedules, and three were super accelerated ones. Regarding immunization periods, 21 studies were conducted with patients in the pre-transplant period, one in a transplanted patient, one with a pre-transplant group, and one with a post-transplant group. The clinical diagnosis that determines candidates for transplantation and/or who have already received transplantation was cirrhosis, mainly due to the HCV and to alcohol.

Seroconversion rates after immunization were analyzed through anti-HBs tests after the immunization schedule was completed. Variables, such as weight, height, body mass index (BMI), sex, albumin levels, total bilirubin, among others, when tested, did not present any connection to seroconversion rates and were not included in this study's scope<sup>(8-10)</sup>.

## DISCUSSION

It is known that the immune response depends on various factors related to the vaccine itself, its production, storage, route of

administration, besides a personal response. Thus, authors find that the immunological levels are lower especially in individuals who suffer from cirrhosis from different origins, among them the hepatitis C virus and alcohol<sup>(7-25)</sup>.

The immunological capacity also varies in the healthy population, i.e., vaccines will not provide full protection since not every organism will satisfactorily respond to certain antigenic stimuli<sup>(3)</sup>. Therefore, immunocompromised patients stand out among individuals in general due to a failure in responding to antigenic stimuli. Therefore, different immunization schedules concerning vaccine dose, route, and intervals of administration may be necessary for risk groups<sup>(3,26)</sup>.

According to the literature, the conventional immunization schedule, with doses being administered between 0, 1, and 6 months, has a seroconversion rate above 90% in healthy adults. On the other hand, in individuals who suffer from advanced liver diseases it is expected a protection between 44% and 54%<sup>(5,8,21)</sup>.

The test used for analyzing the protective index is the anti-HBs antibody; values above 10 UI/mL are considered to be responders<sup>(5,6)</sup>.

### Immunization before and after transplantation

During the pre-transplant period, i.e., when the immunization schedule has been completed before the surgical procedure, the protection tends to be higher than when the immunization schedule is completed after the transplantation, even though it is lower if compared to the healthy population.

Studies using unconventional immunization schedules (accelerated or super accelerated) in pre-transplant patients at an advanced stage of the disease obtained seroconversion rates between 16% and 44%<sup>(7,8,11,12,15,17,27)</sup>.

However, in studies with the conventional schedule, seroconversion rates were higher, between 40% and 67%<sup>(9,21,22,25)</sup>, but still lower than rates found in healthy patients, which are above 90%<sup>(10,13,25,27)</sup>.

Indices obtained for patients immunized after the transplantation were even lower, between 8% and 28%<sup>(7,8,13)</sup>. The hypothesis for such a difference in immunological response is the possible association with immunosuppressant, a prophylactic measure taken in view of the possibility of organ rejection, which in turn decreases the immunization effects capacity<sup>(8)</sup>.

### Seroconversion at the different stages and origins of the liver disease

Found articles suggest that, disregarding the chosen immunization schedule, seroconversion rates tended to be lower as the liver disease advanced, compared to the healthy population<sup>(7-11,15,17,18,21-25,27)</sup>.

Case-control studies which analyzed the risk between sick patients (case) and healthy individuals (control) are found in TABLE 1. The obtained results show the low immunization effectiveness in immunocompromised patients due to liver diseases in comparison to healthy individuals<sup>(10,11,13-15,17,19,25,27-29)</sup>.

The ideal scenario would be completing the immunization of all potential candidates for transplantation at an early stage of the disease, since studies show that patients with a better medical condition tend to have better responses, including long term ones<sup>(9,10,12,13,18,21,22,25)</sup>; also, non-responder patients, even receiving high vaccine doses, suffered from severe liver disease in general<sup>(15,18,23)</sup>. On the other hand, studies that selected patients who suffered from HCV at an earlier stage of the disease had a higher protective index, between 50%–89%, after completing the immunization schedule<sup>(14,16,19,20,24,28-30)</sup>.

Authors/Year	Immunization schedule	Route of administration	Sample	Vaccine doses / quantity per dose	Seroconversion rates
Van TD et al. (1992)	<b>Accelerated</b>	IM	Pre-transplant	3 doses Not informed.	30 days after the immunization schedule was completed: 44 to 54%
Chalasanani N et al. (1998)	<b>Accelerated</b>	IM	Pre and Post-transplant	Pre-transplant: 3 doses – 20 mcg Post-transplant: non responder to the first immunization schedule. A new immunization schedule was conducted with three monthly doses with 20 mcg each.	30 days after the immunization schedule was completed Pre-transplant: 16% Post-transplant: 6.7%
Kallinowski B et al. (1998)	<b>Super Accelerated</b>	IM	Pre-transplant	3 doses – 20 mcg	3–8 weeks after the immunization schedule was completed: 36%
Lee SD et al. (1999)	Conventional	IM	Pre-transplant	3 doses – 20 mcg	30 days after the immunization schedule was completed: 88.5%
Domínguez M et al. (2000)	<b>Accelerated</b>	IM	Pre-transplant	3 doses – 40 mcg	30 days after the immunization schedule was completed. Single dose immunization schedule: 44%. After the second immunization schedule: 62%
Villeneuve E et al. (2000)	<b>Accelerated</b>	IM	Post-transplant	3 doses – 20 mcg	30 days after the immunization schedule was completed: 28%
Wiedmann M et al. (2000)	Conventional	IM	Pre-transplant	3 doses – 40 mcg	3 months after the immunization schedule was completed: 51% – 100 UI/mL 17% – 10 UI/mL
Arslan M et al. (2001)	<b>Accelerated</b>	IM	Pre and Post-transplant	4 doses – 40 mcg	30 days after the pre-transplant immunization schedule was completed: 36%. 01 year after the transplantation: 11.6% 02 years after the transplantation: 8%
De Maria N et al. (2001)	<b>Accelerated</b>	IM	Pre-transplant	3 doses – 40 mcg	30 days after the last dose: 62% After revaccination: 94%
Engler SH et al. (2001)	<b>Super Accelerated</b>	IM	Pre-transplant	Group 1: 3 doses – 20 mcg Group 2: 3 doses – 40 mcg A 40 mcg booster dose in both groups 6 months before the transplantation.	Group 1 (conventional dose): 21% after 3 weeks; 31% after 8 weeks. Group 2 (double dose): 16% after three weeks; 26% after 8 weeks
Arbizu EA et al. (2003)	<b>Super Accelerated</b>	IM and ID	Pre-transplant	3 doses – 20 mcg	60 days after the immunization schedule was completed. IM Group: 72% ID Group: 36%
Mattos AA et al. (2004)	Conventional	IM	Pre-transplant	3 doses – 20 mcg	30 days after the immunization schedule was completed: 37%
Aziz A et al. (2006)	<b>Accelerated</b>	IM	Pre-transplant	3 doses – 80 mcg after an immunization schedule with a previous complete double dose in non-responder individuals.	3 months after the immunization schedule was completed: 72%
Elefsiniotis IS et al. (2006)	Conventional	IM	Pre-transplant	3 doses – 20 mcg	3 months after the immunization schedule was completed: Group without treatment: 82.85%. Group with treatment: 90.9%
Daryani NE et al. (2007)	Conventional	IM	Pre-transplant	3 doses – 20 mcg	3 months after the third dose: 73.7%
Bonazzi PR et al. (2008)	Conventional	IM	Pre-transplant	3 doses – 40 mcg	30 days after the immunization schedule was completed: 67.5%
Pascasio JM et al. (2008)	Conventional	IM	Pre-transplant	4 doses – 40 mcg	30 days after the fourth dose: 31.3%. After revaccination: 41.2%
Varaza TA et al. (2009)	Conventional	IM	Pre-transplant	3 doses – 20 mcg	30 days after the last dose: 57%. After revaccination: 74%
Dhillon S et al. (2012)	Conventional	ID	Pre-transplant	3 doses – 40 mcg	30 days after the last dose: 69%
Domingo G et al. (2012)	Conventional	IM	Pre-transplant	4 doses – 40 mcg	30 days after the fourth dose: 40.7%. After revaccination: 51%
Roni DA et al. (2013)	<b>Accelerated</b>	IM	Pre-transplant	3 doses – 20 mcg	30 days after the last dose: 19% – 10 UI/mL 60% – 100 UI/mL
Khokhar N et al. (2014)	Conventional	IM	Pre-transplant	3 doses – 20 mcg	30 days after the last dose: 89%
Minakari M et al. (2014)	Conventional	IM	Pre-transplant	Group 1: 3 doses – 40 mcg Group 2: 3 doses – 20 mcg	30 days after the last dose. Group 1: 65.6% Group 2: 62.5%
Al-Zahaby A et al. (2017)	Conventional	IM	Pre-transplant	3 doses – 20 mcg	30 days after the third dose: 42%

**FIGURE 1.** Studies included in the review according to used immunization schedules details and found immunization rates.

**TABLE 1.** Case-control researched articles and their respective seroconversion results according to patient classification.

Author/Year	Seroconversion rates after completed immunization schedule for hepatitis B		
	Case (sick patients)	Control (healthy individuals)	Patient classification
Van TD et al. (1992)	44–54%	93%	Cirrhotic patients
Kallinowski B et al. (1998)	36%	95%	Cirrhotic patients
Lee SD et al. (1999)	88.5%	91.4%	Liver disease at early stage
Villeneuve E et al. (2000)	28%	97%	Cirrhotic patients
De Maria M et al. (2001)	62%	92%	Liver disease at early stage
Engler SH et al. (2001)	20–30%	95%	Cirrhotic patients
Wiedmann M et al. (2001)	51%	74%	Liver disease at early stage
Mattos AA et al. (2004)	37%	84.8%	Cirrhotic patients
Elefsiniotis IS et al. (2006)	82.85–90.9%	92.56%	Liver disease at early stage
Khokar N et al. (2014)	89%	96%	Liver disease at early stage
Al-zahaby A et al. (2017)	58%	89%	Liver disease at early stage

Varaza et al. (2009) also found a significant difference in seroconversion when comparing the immunized group who had HCV (63.4%) and patients who suffered from cirrhosis, both by HCV and other origins (47%). Aziz et al. (2006) also obtained a protective index of 52% in individuals with cirrhosis and 83% without it, thus stressing the premise that the immunological response in patients with a history of their decompensated liver disease is considerably lower if compared to individuals who had an early diagnosis<sup>(18,23)</sup>.

It is relevant to note the causes for cirrhosis, mainly for alcoholic cirrhosis, in view of the interference that alcohol has on cellular immunity, as shown by De Maria et al. (2001), who found 12% protection in cirrhotic individuals due to alcohol and 54% in those who had the VHC, when comparing seroconversion in cirrhotic groups classified according to origins. In their study, Roni et al. (2013) evaluated the seroconversion of hepatitis B immunization with liver diseases; 44% of the seroconverted were patients with alcoholic cirrhosis, compared to 56% of liver disease from other origins<sup>(15,24)</sup>.

The best immunization response may be obtained in patients with a less compromised immunity. It is necessary, thus, to raise the awareness of health professionals to what immunization protocols are concerned for those patients who suffer from chronic liver diseases at an early stage of diagnosis, so that immunization can be completed before the transplantation and consequently generate better results regarding immunization seroconversion<sup>(9,15-17,19,20,22-24,28,30)</sup>.

### Interval between vaccine doses

Considering the intervals between which vaccine doses will be administered, there is no agreement among the researched articles on effectiveness when comparing the several found intervals (accelerated, super accelerated, and conventional); there were no evidences of one schedule being superior to others. Some studies obtained positive results by using unconventional schedules; they showed an increase in anti-Hbs antibody rates in the first months after completing the schedule, with seroconversion rates between 30% and 70%<sup>(10-12,15,16,18,27)</sup>.

However, the permanent protection duration might be inferior to that of the conventional schedule<sup>(7,8,10,12,13,18,27)</sup>. Engler et al. (2001) show that 67% of the candidates for transplantation who obtained the pre-transplant primary response by receiving the super accelerated immunization schedule, later had a decrease in antibodies, between 4 and 7 months after transplantation. Arslan

et al. (2001), by employing an accelerated immunization schedule in a group of post-transplant patients, obtained quick responses after its completion; however, the protective antibodies decreased in four weeks; after two years, only 8% still had protective antibodies<sup>(7,10)</sup>.

On the other hand, the need for high immediate protection in a short term may justify the choice of super accelerated schedules as the only option for cirrhotic patients who make it to the waiting list without immunization against hepatitis B, but with the proviso that the anti-Hbs antibody levels should be monitored after transplantation<sup>(9,16,27)</sup>. This option is less unsafe than the total lack of immunization in that period.

All the context in which patients find themselves in order to receive a transplantation makes them very susceptible to acquiring the HBV, either through exposure during invasive procedures, the potential presence of the latent virus in the donor's liver, which may be reactivated under immunosuppression, or the need for blood transfusions<sup>(5,9,10,12,13,18,21,22)</sup>. Given the data, unconventional schedules may be appealing and increase the immunization schedule completion rates<sup>(5,16)</sup>, thus providing protection for people under high contamination risks by hepatitis B in the peri-transplantation period (before, during, and immediately after surgery).

### Seroconversion after booster doses and/or revaccination

Studies that considered revaccination in non-responders to the primary immunization schedule obtained protective indices between 40% to 60%, except for De Maria et al. (2001), who obtained a 94% index after revaccination with high doses (80 mcg) in non-cirrhotic patients and 48% in cirrhotic ones<sup>(9,12,15,22,25)</sup>.

In Brazil, the Health Ministry recommends repeating the immunization schedule in high-risk patient groups, which include those who have received transplantation, with three more doses, following the conventional schedule. Those who are still negative for the anti-Hbs antibody after completing two immunization schedules must be considered non responders and susceptible in case of exposure<sup>(31)</sup>.

Using vaccine double doses (40 mcg) in immunocompromised patients is acknowledged and is the adopted practice by the Health Ministry, which recommends four doses, with twice its usual quantity. Researched articles reinforced such need<sup>(12,14,17,21,25,30,32)</sup>. Moreover, some results suggest that the alternative schedule effectiveness is enhanced with a high vaccine dose, prompting an early antibody response in these patients<sup>(9,12,18,22)</sup>.

### Route of vaccine administration

Intramuscular use is the most recommended one, whereas some articles suggest it should be intradermal instead in non-responder groups, both for healthy individuals and immunosuppressed ones, with satisfying immunological results<sup>(16,33-36)</sup>.

Studies with non-cirrhotic patients who have the HCV deserve special focus since they have satisfying results in a group of non-responder individuals with the primary and secondary schedules, with a double dose and intradermal administration: 69% obtained a positive immunological response; among them 51% of the responders had levels above 100 mUI/mL<sup>(34)</sup>.

The authors say that the epidermis is rich in antigens, thus it is an inviting target for the administration of vaccines, because it is more immunogenic if compared to the intramuscular route in immunocompromised patients<sup>(33-36)</sup>.

### Adverse events after immunization

Most articles did not mention adverse events to the vaccine, but two of them, which report events around the place of administration (pain, redness, and swelling), of low intensity and spontaneous recovery both with the conventional schedule and the unconventional one; systemic events, such as temperature and fatigue, were statistically and clinically less significant after the first dose and decreased in the subsequent ones, reassuring the vaccine safety, even in immunocompromised patients<sup>(10,11,14-18,20,23,24,28-30)</sup>.

### IMMUNIZATION SCHEDULE PROPOSAL AGAINST HEPATITIS B FOR PATIENTS WHO SUFFER FROM LIVER CIRRHOSIS

Once the found studies did not corroborate among themselves regarding the effectiveness of the various immunization schedules, neither there was superiority for serologic tests of one over the other, our proposal for potential immunization schedules will highlight the choice of unconventional schedules for the group of patients who suffer from a liver disease (FIGURE 2).

This choice is explained by their need for urgent protection, which will be obtained with high protective rates in a short term; since they are more vulnerable to the risk of contamination by hepatitis B in the peri-transplant period, particularly those patients who make it to the waiting list for transplantation without previous immunization. Such strategy is therefore less unsafe than not receiving any immunization at all during this period.

In the literature, high serologic levels are obtained right after completing the super accelerated schedule, the permanent protection lasting less time than that of the conventional schedule. Such low levels must be continuously monitored and, if necessary, it is advisable to administer booster doses. These patients usually go to health service units very often due to their clinical presentation, so this monitoring is very feasible.

Since the intervals between doses in unconventional schedules are short, it is more likely they will be completed in the pre-transplant period, immediately after a cirrhosis diagnosis is established, when the immunity is less compromised and better results may be obtained in seroconversion, although they will be lower if compared to the healthy population.

The vaccine against hepatitis B is available in the public health services in Brazil for all the population, regardless of eligibility criteria. Thus, efforts must be made in order to increase the immunization coverage among healthy individuals, so the disease transmission pathways will be interrupted and the risk of contamination will decrease among groups categorized as at high-risk, mainly those who did not receive the vaccine against hepatitis B in their immunization schedule.

It is worth noting that in an ideal scenario, all the population should have the conventional immunization schedule, preferably in early childhood, since the vaccine is available and free at the health services across the country. If everybody received the immunization, it would not be necessary to make any proposals such as the present one, we would only be discussing the exceptions.

Score		Immunization schedule	Doses	Route of administration	Anti-HBs dosing
Child-Turcotte Pugh					
A	Clinically stable	Conventional (0, 1, 2, 6 months)	40 mcg	Intramuscular	15 days after the last dose. Repeat schedule when anti-HBs <10 UI/mL.
	Special Cases*	Super accelerated (0, 7, 21 days and 3 months)	40 mcg	Intramuscular	15 days after the last dose. Repeat schedule when anti-HBs <10 UI/mL.
B		Super accelerated (0, 7, 21 days and 3 months)	40 mcg	Intramuscular	15 days after the last dose. Repeat schedule when anti-HBs <10 UI/mL.
C		Super accelerated (0, 7, 21 days and 3 months)	40 mcg	Intramuscular	15 days after the last dose. Repeat schedule when anti-HBs <10 UI/mL.

\* Special cases described in Ordinance No. 2600, from October 21st 2009.

- The immunization strategy for patients who suffer from cirrhosis has better serologic results if started and completed in the pre-transplant period, when the patient still has their immunity less compromised. Thus, immunization protocols must be started right after the cirrhosis diagnosis is established.
- If revaccination is necessary, and because of the time, it should happen during the post-transplant period; it must be administered three months after the completion of the clinical discontinuation if the immunity is still being recovered after a careful medical evaluation.
- Individuals who do not respond appropriately as of antibody levels, must be revaccinated with a new schedule.
- After completing two schedules, with negative anti-HBs, they must be considered non responders and susceptible.
- Immunization schedules must be individualized, based on the clinical evolution of the patient.

**FIGURE 2.** Immunization schedule proposal against hepatitis B for patients who suffer from liver cirrhosis, according to the Child-Turcotte Pugh score.

However, due to several reasons, there is still a large number of people who do not receive the vaccine, and/or do not have the records of it, thus being considered not immunized; therefore, this study is crucial as a way of encouraging reflection and discussions in the scientific community.

Hence the need for randomized, multicentric and controlled studies in order to support the proposed hypothesis herein and strengthen the discussion on novel immunization strategies for risk groups, such as liver transplantation patients.

## CONCLUSION

The searched studies did not find seroconversion superiority between the different immunization schedules (conventional and unconventional). However, since candidates to liver transplantation are usually very vulnerable, results show that unconventional immunization schedules (accelerated and super accelerated) may be recommended for such group of patients, and serologic test results will be higher when the immunization schedule is completed in the pre-transplant period.

The need for immediate serologic protection, with high protective rates in a short term, may justify employing unconventional

immunization schedules in patients who make it to a transplantation waiting list without previous immunization. Such strategy is therefore less unsafe than not receiving any immunization at all during this period.

## Authors' contribution

Rodrigues IC: main author; this article is part of the author's PhD thesis. Silva RCMA: active participant in the process, from sample selection, data collection, data analysis and interpretation, statistical calculations and final review. Felício HCC: active participant of the process, from the selection of the sample, data collection, preparation of the manuscript and final revision. Silva RF: PhD thesis advisor, active participant of the whole process, from the project to the final review as the research group leader.

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Rodrigues IC, Silva RCMA, Felício HCC, Silva RF. Eficácia de um novo esquema vacinal contra hepatite B em pacientes submetidos a transplante de fígado. *Arq Gastroenterol.* 2019;56(4):440-6.

**RESUMO – Contexto** – O transplante de fígado, apesar de ser um procedimento de elevado risco, está consolidado como recurso terapêutico para cura e melhoria da qualidade de vida de indivíduos acometidos por doenças. A prevenção da infecção pelo vírus da hepatite B através da vacinação tem sido a medida mais efetiva para reduzir complicações, diminuindo o número de pessoas com hepatite crônica pelo vírus da hepatite B e eliminando a transmissão. **Objetivo** – 1. Analisar as evidências na literatura sobre os diferentes esquemas utilizados para a vacina contra a hepatite B em pacientes submetidos a transplante de fígado. 2. Sugerir possíveis esquemas de vacinação contra hepatite B para pacientes com cirrose hepática, sem documentação comprobatória anterior, em relação à classificação de Child-Turcotte Pugh, segundo evidências encontradas na literatura. **Métodos** – Revisão sistemática da literatura, realizada nas bases de dados MedLine, PubMed e Lilacs, no período de setembro/2017 a janeiro/2018, com as seguintes palavras chaves: “Liver Transplantation”, “Immunization Schedule”, “Hepatitis B Vaccines”. Para análise dos artigos foi utilizado um quadro sinóptico especialmente construído para esse fim e a apresentação dos resultados e discussão foi feita de forma descritiva. **Resultados** – Foram incluídos 24 estudos, sendo oito com esquemas vacinais acelerados, 13 com esquemas convencionais e três com esquemas super acelerado. Quanto ao período da vacinação, 21 estudos foram realizados com pacientes no período pré-transplante, um em pacientes transplantados e um com um grupo pré e um grupo pós transplante. Os artigos encontrados sugerem que independente do esquema vacinal escolhido, as taxas de soroconversão tendem a ser menores conforme o avançar da doença hepática, em relação à população saudável. **Conclusão** – Os estudos não encontraram superioridade de soroconversão entre os diferentes esquemas de vacinação (convencional e não convencional). Entretanto, sabendo da vulnerabilidade que os candidatos a transplante de fígado estão expostos, os resultados demonstram que o esquema de vacinação superacelerado pode ser indicado para este grupo de pacientes, e que os resultados sorológicos são mais elevados quando o esquema de vacinação é completado no período pré-transplante.

**DESCRITORES** – Vacinas contra hepatite B. Transplante de fígado. Esquemas de imunização.

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