Toxicity of Lipid Nano Particles (causing liver damage)

By Craig Paardekooper

What are Cationic Lipids ?

Cationic and ionizable cationic lipids are small molecules with a positive charge. They form electrostatic bonds or complexes with negatively charged molecules such as nucleic acids and cell membranes. Consequently, they are utilized to improve cellular membrane permeability – by merging with a cell membrane, they can then release their payload.

The Lipids in the COVID-19 Jab are Ionizable Cationic Lipids

> *"Current prominent examples are the **ionizable cationic lipids ALC-0315** [[(4-hydroxybutyl)azanediyl]di(hexane-6,1-diyl) bis(2-hexyldecanoate))] and Lipid H (**SM-102**) (9-heptadecanyl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate) **that are used for coronavirus disease 2019 (COVID-19) mRNA vaccines BNT 162b and mRNA-1273, respectively**.[1]"*
>
> *References :*
> *https://onlinelibrary.wiley.com/doi/10.1002/smll.202206968*
> *https://pubmed.ncbi.nlm.nih.gov/34811367/*

The Dangers of Cationic Lipids

> *"The use of cationic and ionizable cationic lipids in pharmaceutical products, however, is a double-edged sword, as these excipients are of **considerable safety concerns**. Because of their permanent or pH-dependent cationic nature, they perturbate cellular and nuclear membranes, trigger the release of degrading enzymes from lysosomes, cause mitochondrial permeabilization and dysfunction, generate reactive oxygen species (ROS), alter cytoplasmatic enzyme functions, and damage DNA.[3]*
>
> *References :*
> *https://onlinelibrary.wiley.com/doi/10.1002/smll.202206968*

The above quote says that cationic lipids have considerable safety concerns. This arises from the fact that they have either –

1. A permanent positive charge or
2. A positive charge that appears under certain pH condition

The effect of this positive charge is that it –

1. Disturbs cellular and nuclear membranes
2. Triggers the release of degrading enzymes from lysosomes
3. Causes dysfunction of mitochondria
4. Generates reactive oxygen species
5. Damages DNA

All these are effects of its positive charge.

These cationic lipids have been investigated for over 30 years since cationic lipid-based gene delivery (lipofection) was first published by Felgner's group in 1987, but have not found their way into general application because of their toxicity.

It is not just cellular biologists with experience of this field who state that cationic lipids are "very, very toxic". A peer-reviewed paper in Toxicology Research from April 2018 states in the opening sentence of its abstract: "cationic lipids still have the problem of toxicity, which has become one of the main bottlenecks for their applications.". This finding is reflected throughout the literature on cationic lipids, across the entire three decades. An article as recent as May 2019, "Lipid Nanoparticles for Delivery of Therapeutic RNA Oligonucleotides" says "A major drawback with the use of cationic lipids for gene delivery is the high net positive charge associated with the headgroup as well as induction of immune response ... Furthermore, particles of cationic nature are known to undergo accumulation in the liver, lung, and spleen."

Reference : 603f7c2bc3f872e7e67deb52_Potential_risk_of_cationic_lipid_in_the_Pfizer-BioNTech_vaccine.pdf (webflow.com)

Attempted Solutions?

A. **Ionizable**
   The lipid only becomes positively charged when it has been taken into a cell by the process of endocytosis. Within the endosome, the lipid is subjected to a low pH environment, and this triggers the lipid to become cationic. The pH has to be quite low (pH=5) for this to happen. Then the cationic lipid releases its payload. However, a question arises as to what becomes of the cationic lipid afterwards.

B. **Biodegradable** alternatives have been introduced that are rapidly degraded in vivo, so that the toxic effects are "short-lived". How is this done?

   A cationic lipid consists of 3 parts

   1. A polar head (the charged part)
   2. A fatty hydrophobic tail (the lipid part)
   3. A bond linking the above two parts (either an ester or an amide bond)

   The bodies enzymes attack the ester or amide bond breaking it – so the cationic lipid breaks up into a charged head and a lipid tail – it degrades. However, a question arises as to how fast this degradation takes place.

2 Weeks Later

But, as we shall see, the cationic lipids associated with the COVID-19 mRNA jabs do not degrade fast enough. They have been found in the circulatory system more than 2 weeks after the shot.

> *After **ester cleavage** of ALC-0315, the **doubly de-esterified** metabolite **still exhibits a lipophilic ionizable cationic character** that is further metabolized by **glucuronidation**, followed by urinary excretion.[53] Nonetheless, **considerable amounts of ALC-0315 were found in the liver two weeks after administration**, whereas SM-102 and its degradation products were more rapidly eliminated via the renal and biliary route.[53, 54] This might be explained by the linear fatty alcoholic tail of SM-102 that contributes to a higher accessibility for enzymatic cleavage of the first ester bond and subsequently also the second as a result of a reduced steric hindrance.*
>
> *References* : *https://onlinelibrary.wiley.com/doi/10.1002/smll.202206968*
> https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf

2 weeks later high concentrations of the lipid ALC-0315 were found in the liver.

PK studies with the two novel LNP-excipients ALC-0315 and ALC-0159*: Wistar Han rats were IV bolus injected with LNP formulated luciferase-encoding RNA at 1 mg/kg and ALC-0315 and ALC-0159 concentrations at 15,3 mg/kg and 1,96 mg/kg respectively. ALC-0315 and ALC-0159 levels in plasma, liver, urine and faeces were analysed by LC-MS/MS at different time-points up to 2-weeks.*
ALC-0315 and ALC-0159 were rapidly cleared from plasma during the first 24 hours with an initial t½ of 1.62 and 1.72 h, respectively. 24 hours post-dosing, less than 1% of the maximum plasma concentrations remained. A slower clearance rate was observed after 24 hours with ALC-0315 and ALC-0159 terminal elimination t½ of 139 and 72.7 h, respectively. ***Following plasma clearance, the liver appears to be to major organ to which ALC-0315 and ALC-0159 distribute****.* ***The applicant has estimated the percent of dose distributed to the liver to be ~60% for ALC-0315 and ~20% for ALC-0159.*** *The observed liver distribution is consistent with the observations from the biodistribution study and the repeat-dose toxicology, both using IM administration.* ***For ALC-0315 (aminolipid), the maximum detected concentration in the liver (294 µg/g liver) was reached 3 hours after IV injection. ALC-0315 was eliminated slowly from the liver and after 2-weeks the concentration of ALC-0315 was still ~25% of the maximum concentration indicating that ALC-0315 would be eliminated from rat liver in approximately 6-weeks.*** *For ALC-0159 (PEG-lipid), the maximum detected concentration in the liver (15.2 µg/g liver) was reached 30 minutes following IV injection. ALC-0159, was eliminated from the liver faster than ALC-0315 and after 2-weeks the concentration of ALC-0159 was only ~0,04% of the maximum detected concentration. The applicant was asked to*

discuss the long half-life of ALC-0315 and its effect, discussion on the comparison with patisiran, as well as the impact on the boosts and post treatment contraception duration. The applicant considered that there were no non-clinical safety issues based on the repeat dose toxicity studies at doses (on a mg/kg basis) much greater than administered to humans; this was acceptable to the CHMP."

"While there was no detectable excretion of either lipid in the urine, the percent of dose excreted unchanged in faeces was ~1% for ALC-0315 and ~50% for ALC-0159"

Reference :
https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf p 45/6

The takeaway from this is that the cationic lipids remain in your body for up to 6 weeks and will cause damage during this time. In particular, ALC-0315 does not seem to be excreted.

60% of the initial dose becomes concentrated in the liver. Should we expect liver damage?

Liver Damage

If 60% of the LNPs end up in the liver, and if these LNPs readily merge with the liver cells and become cationic, then we might expect liver damage.

The primary function of the liver is to filter and purify the blood, so liver damage may result in blood poisoning, septicaemia, liver disease or liver failure.

Effect on Liver Cells

A detailed analysis of the effect of cationic lipids on liver cells from December 2017 explains the mechanism as follows - cells were disturbed in amino acid metabolism, energy and lipid supply when cationic lipid exposure-induced injury occurred.

It is concluded that cationic lipids may ***induce cytotoxicity*** *by enhancing reactive oxygen species in vitro, affect the normal process of* ***energy metabolism****,* ***disturb several vital signalling pathways and finally induce cell death****.*

Reference :
Metabolomics revealed the toxicity of cationic liposomes in HepG2 cells using UHPLC-Q-TOF/MS and multivariate data analysis - PubMed (nih.gov)

Effect on Animals

In an animal trial, submitted as evidence for authorisation of the vaccine by BioNTech to the EMA, this resulted in **high elevations** of liver enzymes GGT – "**exposure generated increased levels of GGT (>200%) – indicative of liver damage,** and AST, which rises in liver and cardiac inflammation.

Given that 60% of the Lipid Nano Particles end up in the liver, merge with liver cells, and become positively charged, we would expect liver damage to occur, which is what the animal study showed.

Reference :
http://radio.rumormillnews.com/pdfs/20201130-BioNTech-Vaccine-Document.pdf

Speeding up Degradation

With ALC-0315, the cationic lipid found in the Pfizer jab, even after it has been doubly de-esterified, it still exhibits a positive charge. A second stage of glucuronidation is required so it is metabolized and excreted in the urine.

SM-102, the cationic lipid found in Moderna jabs, degrades more readily.

It follows that there are 2 ways of speeding up the degradation of the cationic lipids found in the Pfizer jab –

1. Increase the rate of breaking of the ester bonds
2. Increase glucuronidation

Here is a link to how to boost glucuronidation - Glucuronidation: Detox, Balance Hormones, & Genes - SelfHacked

A Simple Conclusion

Premise 1 : Cationic (positively charged) lipids are highly toxic

Premise 2 : The COVID-19 jab is made of lipids that become cationic when in contact with human cells

Deduction : Therefore, the COVID-19 jab has a degree of toxicity / it cannot be completely safe.

The question then becomes, how dangerous is it ?

CONFIRMED: COVID-19 mRNA Vaccines Can Cause Severe Liver Damage - Dr. Rath Health Foundation (dr-rath-foundation.org)

Immune-mediated liver injury following COVID-19 vaccination

Georgios Schinas [1], Eleni Polyzou [2], Vasiliki Dimakopoulou [2], Stamatia Tsoupra [2], Charalambos Gogos [2], Karolina Akinosoglou [3]

Affiliations + expand

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Free PMC article

Abstract

Liver injury secondary to vaccination is a rare adverse event that has recently come under attention thanks to the continuous pharmacovigilance following the widespread implementation of coronavirus disease 2019 (COVID-19) vaccination protocols. All three most widely distributed severe acute respiratory syndrome coronavirus 2 vaccine formulations, *e.g.*, BNT162b2, mRNA-1273, and ChAdOx1-S, can induce liver injury that may involve immune-mediated pathways and result in autoimmune hepatitis-like presentation that may require therapeutic intervention in the form of corticosteroid administration. Various mechanisms have been proposed in an attempt to highlight immune checkpoint inhibition and thus establish causality with vaccination. The autoimmune features of such a reaction also prompt an in-depth investigation of the newly employed vaccine technologies. Novel vaccine delivery platforms, *e.g.*, mRNA-containing lipid nanoparticles and adenoviral vectors, contribute to the inflammatory background that leads to an exaggerated immune response, while patterns of molecular mimicry between the spike (S) protein and prominent liver antigens may account for the autoimmune presentation. Immune mediators triggered by vaccination or vaccine ingredients per se, including autoreactive antibodies, cytokines, and cytotoxic T-cell populations, may inflict hepatocellular damage through well-established pathways. We aim to review available data associated with immune-mediated liver injury associated with COVID-19 vaccination and elucidate potential mechanisms underlying its pathogenesis.

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Drug-Induced Liver Injury After COVID-19 Vaccine

Monitoring Editor: Alexander Muacevic and John R Adler

Rupinder Mann,[1] Sommer Sekhon,[2] and Sandeep Sekhon[3]

New-onset and relapsed liver diseases following COVID-19 vaccination: a systematic review

Saad Alhumaid,[✉1] Abbas Al Mutair,[2,3,4] Ali A. Rabaan,[5,6,7] Fatemah M. ALShakhs,[8] Om Prakash Choudhary,[9] Shin Jie Yong,[10] Firzan Nainu,[11] Amjad Khan,[7] Javed Muhammad,[12] Fadil Alhelal,[13] Mohammed Hussain Al Khamees,[14] Hussain Ahmed Alsouaib,[15] Ahmed Salman Al Majhad,[15] Hassan Redha AL-Tarfi,[15] Ali Hussain ALyasin,[15] Yaqoub Yousef Alatiyyah,[16] Ali Ahmed Alsultan,[17] Mohammed Essa Alessa,[18] Mustafa Essa Alessa,[19] Mohammed Ahmed Alissa,[19] Emad Hassan Alsayegh,[19] Hassan N. Alshakhs,[19] Haidar Abdullah Al Samaeel,[20] Rugayah Ahmed AlShayeb,[21] Dalal Ahmed Alnami,[21] Hussain Ali Alhassan,[22] Abdulaziz Abdullah Alabdullah,[22] Ayat Hussain Alhmed,[23] Faisal Hussain AlDera,[24] Khalid Hajissa,[25] Jaffar A. Al-Tawfiq,[26,27,28] and Awad Al-Omari[29,30]

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Associated Data

▸ **Data Availability Statement**

Abstract

Go to: ▸

Background

Liver diseases post-COVID-19 vaccination is extremely rare but can occur. A growing body of evidence has indicated that portal vein thrombosis, autoimmune hepatitis, raised liver enzymes and liver injuries, etc., may be potential consequence of COVID-19 vaccines.

LIVER INJURY FOLLOWING COVID-19 mRNA VACCINE ADMINISTRATION: THE DILIN EXPERIENCE

Background: The COVID-19 mRNA vaccines have been associated with infrequent reports of liver injury. The aim of this study is to describe the presenting features, liver histology, and outcomes of 15 patients who developed liver injury following COVID-19 mRNA vaccine administration.

Methods: 15 patients with suspected COVID-19 mRNA induced liver injury were enrolled in the Drug-Induced Liver Injury Network (DILIN) prospective (n=5) or retrospective (n=10) studies from 3/ 21 to 5/22. Causality was scored using DILIN expert opinion (1= definite, 5= unlikely).

Results:: 9 had liver injury after the Moderna vaccine (med latency= 38 days;) and 6 following the Pfizer vaccine (med latency = 29 days). Amongst the 13 adjudicated cases to date, COVID-19 mRNA vaccine was scored as highly likely (4), probable (5), and possible (4). In 2 possible cases another medication was implicated as being more likely, and latency was prolonged (84 and 175 days) in the other 2. Among the 9 high causality cases, median age was 67 years (r: 25-74), 78% were female and 88% Caucasian. At DILI onset, median ALT was 364 U/L (r: 121-1199), ALP 206 U/L (r:58-383), and T. bilirubin 1.9 mg/dL (r: 0.3-5.6) with 56% hepatocellular, 33% mixed and 11% cholestatic. 11% had eosinophilia, 22% had rash, and 33% were hospitalized; 37% were ANA+ , 37% SMA+ and

Case Reports > Respir Med Case Rep. 2022;35:101568. doi: 10.1016/j.rmcr.2021.101568. Epub 2021 Dec 14.

Acute liver failure after vaccination against of COVID-19; a case report and review literature

Masoudreza Sohrabi [1], Elham SobheRakhshankhah [1], Hosein Ziaei [1], Manizhe AtaeeKachuee [2], Farhad Zamani [1]

Affiliations + expand

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Free PMC article

Abstract

Background: Vaccination against COVID-19 remains as a main root of COVID-19 prevention. Few vaccines have been launched for this purpose recently with different side effects. Thrombotic events have been reported as a rare side effect after ChAdox1nCOV-19 vaccination that may cause death of recipient.

Case presentation: We report a case of hepatic artery occlusion after the first dose vaccination by ChAdOx1nCov-19. The patient was a health care worker, aged 34-year old. Past medical history was unremarkable and had not used heparin. Over the next couple of days after the vaccination, he reported headache, nausea, and dizziness as well as abdominal pain. His general status and the laboratories studies deteriorate quickly by increasing liver enzymes and severe coagulopathy. Clinically he had presented acute hepatic failure. He had been received blood products, prednisolone pulse along with broad antibiotics without benefit. He died on the sixth day.

JOURNAL OF HEPATOLOGY The Home of Liver Research EASL

Liver injury following SARS-CoV-2 vaccination: A multicenter case series

Hersh Shroff • Sanjaya K. Satapathy • James M. Crawford • Nancy J. Todd • Lisa B. VanWagner

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To the Editor:

In response to the COVID-19 pandemic, two novel mRNA-based vaccinations against the SARS-CoV-2 virus have been manufactured and distributed in an unprecedented fashion. In light of their rapid uptake, providers must remain vigilant in their monitoring of new adverse events. In early 2021, multiple providers, communicating on AST LICOP and AASLD online forums, shared strikingly similar experiences with patients who presented with liver injury following COVID-19 vaccination with no other clear precipitants. Given the pattern, we report herein on a multicenter cohort of patients with liver injury following COVID-19 vaccination. No personally identifiable information or protected health information was collected for any patient. The series was reviewed by the Northwestern University IRB and deemed not to be human subjects research.

Covid-19 Vaccines

Last Update: October 28, 2021.

OVERVIEW

Introduction

The Severe Acute Respiratory Syndrome Coronavirus type 2 (SARS-CoV-2) is the cause of the pandemic of coronavirus disease (COVID-19) that was first detected in December 2019 in Wuhan, China and subsequently spread globally. By March 2020, COVID-19 was declared a global pandemic and within a year it accounted for more than 100 million cases and 2 million deaths. Also, within a year of its detection, vaccines against SARS-CoV-2 were developed using several methodologies including mRNA-, adenoviral vector- and recombinant DNA-technology. Several of these vaccines have been evaluated in large, placebo-controlled trials and found to be both safe and effective. Adverse events have been mild-to-moderate local reactions and transient systemic symptoms such as fatigue, nausea and headache. After their release and widespread use, however, individual case reports and small case series of serious adverse events began to appear including thrombotic thrombocytopenia, that sometimes involved portal or hepatic vein thromboses and some degree of liver dysfunction, as well as acute liver injury, that often resembled autoimmune hepatitis. Both of these syndromes are rare and it is not clear whether they are coincidental with or a result of the recent COVID-19 vaccination.

A Case of Hepatotoxicity After Receiving a COVID-19 Vaccine

Muath M. Alqarni • Ammar Z. Faloudah • Amjad S. Alsulaihebi • Hassan K. Halawani • Abdulmajeed S. Khan

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COVID-19 vaccination and liver disease

Sotaro Ozaka [1] [2], Takashi Kobayashi [3], Kazuhiro Mizukami [1], Kazunari Murakami [1]

Affiliations + expand

PMID: 36632314 PMCID: PMC9827578 DOI: 10.3748/wjg.v28.i48.6791

Free PMC article

Abstract

Various vaccines against severe acute respiratory syndrome coronavirus 2 have been developed in response to the coronavirus disease 2019 (COVID-19) global pandemic, several of which are highly effective in preventing COVID-19 in the general population. Patients with chronic liver diseases (CLDs), particularly those with liver cirrhosis, are considered to be at a high risk for severe COVID-19 and death. Given the increased rates of disease severity and mortality in patients with liver disease, there is an urgent need to understand the efficacy of vaccination in this population. However, the data regarding efficacy and safety of COVID-19 vaccination in patients with CLDs is limited. Indeed, several organ-specific or systemic immune-mediated side effects following COVID-19 vaccination, including liver injury similar to autoimmune hepatitis, have been recently reported. Although the number of cases of vaccine-related liver injury is increasing, its frequency, clinical course, and mechanism remain unclear. Here, we review the current findings on COVID-19 vaccination and liver disease, focusing on: (1) The impact of COVID-19 in patients with CLD; (2) The efficacy, safety, and risk-benefit profiles of COVID-19 vaccines in patients with CLD; and (3) Liver injury following COVID-19 vaccination.

J Hepatol. 2022 Mar; 76(3): 747–749. PMCID: PMC8491984

Published online 2021 Oct 5. doi: 10.1016/j.jhep.2021.09.031 PMID: 34619252

Immune-mediated hepatitis with the Moderna vaccine, no longer a coincidence but confirmed

Gloria Shwe Zin Tun,* Dermot Gleeson, Amer Al-Joudeh, and Asha Dube

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See "Autoimmune hepatitis developing after coronavirus disease 2019 (COVID-19) vaccine: Causality or casualty?" in *J Hepatol*, volume 75 on page 222.

We have read with interest the recent cases suggesting the possibility of vaccine-induced immune-mediated hepatitis with Pfizer-BioNTech and Moderna mRNA-1273 vaccines for the SARS-CoV-2 virus.[1], [2], [3], [4], [5], [6], [7] However, as the cohort of vaccinated individuals against COVID-19 increases, the previously reported cases could not exclude a coincidental development of autoimmune hepatitis, which has an incidence of 3/100,000 population per year.[8] Our case demonstrates conclusive evidence of vaccine-induced immune-mediated hepatitis with a rapid onset of liver injury after the first Moderna dose, which on re-exposure led to acute severe autoimmune hepatitis.

We might expect that –

1. If ionizable cationic lipids are toxic owing to their charge
2. If these lipids induce human cells to produce a foreign protein that causes auto-immune attack
3. If the foreign protein being produced (the spike protein) is intrinsically toxic, and known to cause harm
   And
4. If 60% of these lipids concentrate in the liver

then, liver damage will occur.

A Clear and Present Danger

Given that the World Health Organisation pushed so hard for these shots and promoted them as safe and effective, is it not dangerous that the same World Health Organisation seeks to amend International Health Regulations to allow it to mandate medical treatments for all future pandemics upon all 190 member countries – a medical tyranny?

It seeks not to advise, but to command medical policies for all 190 member states – come the next "pandemic" – and make these policies **binding and mandatory**.

It seeks not to allow open discussion, but to **suppress any alternative scientific view** – labelling such as "mis-information", and "info-terrorism" – and use constant monitoring and surveillance of subject populations to enforce this.

It should be noted that such regulations would **violate all constitutional rights** in all countries by imposing **medical treatment without informed consent**. Such regulations would also violate the sovereignty of all member countries by allowing **a foreign, unelected body** to decide who can travel, who can work, who should be put into isolation, and who can have access to resources.

These international Health Regulations will automatically come into effect by default, unless member governments explicitly opt out within a limited time frame. The default is this tyranny will happen.

What Can You Do?

Should this tyranny become reality –

1. Don't comply
2. Prepare now by developing greater independence of means
3. Share info and tell many
4. Get active with local groups
5. Support MPs who have been outspoken against the lies and have laid their careers on the line for the truth
6. Support doctors who have been outspoken against the lies and have laid their careers on the line for the truth
7. Support MPs who can push for direct democracy – and a restitution of your constitutional rights.