revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

INTOXICATION BY USE OF IVERMECTIN: AN INTEGRATIVE REVIEW

DOI: 10.16891/2317-434X.v12.e4.a2024.pp4611-4621 *Received in: 19.06.2024 | Accepted in: 20.11.2024*

Daniele Vasconcelos Cerqueira Meneses[a], Eloisa Portugal Barros Silva Soares de Souza[b]*, Matheus Silva Assis[a], Gustavo Hardman Batista[a], Paula Santos Nunes[a], Adriano Antunes de Souza Araujo[a]

Federal University of Sergipe – UFS, Aracaju – SE, Brazil[a]
Universidade Estadual de Feira de Santana, UEFS, Departamento de Saúde, Feira de Santana - BA[b]
****E-mail: eloisaportugal@gmail.com***

ABSTRACT

Ivermectin was the medicine most used for both prophylaxis and treatment during the COVID-19 pandemic period in many countries. Its use was evaluated in patients simultaneously with a race to produce vaccines and reduce mortality from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). As it is a prescription-free medicine in Brazil, and given the fear of contagion among a large part of the population, its use as a prophylactic alternative against SARS-CoV-2 was widely observed. The objective of this review is to survey scientific studies around the world that report the toxicity of ivermectin and its risks to the various systems of the human body. A search was carried out in the PubMed, Web of Science, Scopus and Embase databases using the keywords: "ivermectin" and "intoxication". After analyzing the search based on the strategy we outlined, we identified eight studies that addressed ivermectin toxicity. The data obtained from the articles reflect the toxic effects caused by the off-label use of ivermectin, and reports of its toxicity were more serious following the pandemic period than those previously reported. One hypothesis to explain this would be the indiscriminate use of the medication during this period.

Keywords: Medication; Toxicity; Covid-19.

revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

INTRODUCTION

Ivermectin was the medicine most used as prophylaxis and treatment during the COVID-19 pandemic period in many countries. Its use was evaluated in patients simultaneously with a race to produce vaccines and reduce mortality from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). This medication demonstrated immunomodulatory and anti-inflammatory action in preclinical models, by reducing the production of inflammatory mediators (POPP *et al.*, 2022); (AHMED *et al*., 2021).

The medication was designed as a broad-spectrum anthelmintic for veterinary and human use against nematodes and arthropods, and was the treatment of choice against *Onchocerca volvulus* and *Strongyloides*, including parasitic diseases such as scabies and pediculosis. Its mechanism of action consists of paralysis by hyperpolarization of chloride channels in the parasites' neuromuscular junction (JOHNSON-ARBOR, 2022).

As it is a prescription-free medicining Brazil, and given the fear of contagion among a large part of the population, its use as a prophylactic alternative against coronavirus (SARS-CoV-2) was widely observed. Many patients, even without showing symptoms, used it due to fear of being infected by the coronavirus (MARQUES *et al*., 2024). Although there was no evidence of its clinical efficacy in the treatment of COVID-19, at that time, it was considered relatively safe; however, its rampant and excessive use may have resulted in a range of serious adverse effects (QUINCHO-LOPEZ *et al*., 2021).

According to Lind *et al.* (2021), there was an increase in ivermectin prescriptions in the United States, from 3589 to 39102, between 2019 and August 2021, representing a 989% increase. At Poison Control Centers, the number of calls in respect of ivermectin increased five-fold. In addition to doctors' prescriptions, some patients self-medicated, while others used veterinary formulations (LIND *et al.*, 2021).

Even when used at the recommended doses, ivermectin can cause adverse effects such as itching, lymphadenitis, arthralgia and even the Mazzoti reaction, which consists of the appearance of skin rashes, hives, fever, enlargement and sensitivity of the lymph nodes, especially in the armpits (BOMZE; SPRECHER; GELLER, 2022). Yang *et al.* (2012), showed in their study that many organs and systems can be affected, with signs and symptoms that include: coma, convulsions, diarrhea, vomiting, respiratory failure, hypotension, visual disturbances and metabolic acidosis (YANG; SHEN; HOU, 2022).

The study by Lind *et al*. (2021), reported that adverse effects in cases of ivermectin overdose included gastrointestinal symptoms, such as nausea, vomiting and diarrhea, and was also associated with hypotension and neurological effects, such as decreased consciousness, confusion, hallucinations, seizures, coma and death (LIND *et al*., 2021).

Bomze *et al*. (2022), used the FDA Adverse Event Reporting System (FAERS) to look at the association between severe cutaneous adverse reactions (SCARs), which are a group of rare but serious skin disorders that can occur in response to certain medications, and ivermectin use (BOMZE; SPRECHER; GELLER, 2022). Some scientific studies have reported toxic effects of ivermectin associated with increased self-medication and the use of high doses that go beyond those described in the leaflet.

In a recent study by Marques *et al*., a potential mechanism of action for ivermectin was suggested related to the inhibition at the nuclear level of viral proteins mediated by IMPα/β1, but the study emphasizes that controlled studies are needed to confirm this hypothesis, given that only one in vivo study has been published that reported any positive effect for the drug, with evidence of a lower mortality rate in individuals who needed ventilatory support (MARQUES *et al*., 2024). According to Marques *et al*., the use of ivermectin, in general, has been considered to be safe, but its indiscriminate use as a prophylactic measure, with, for example almost 60% of individuals interviewed in 10 cities in Mato Grosso (Brazil) reporting having used it preventively (most of them with high income and education) may change this picture (MARQUES *et al*., 2024).

When discussing the adverse effects of ivermectin, it is important to distinguish between the adverse effects that are common to several medicines, such as abdominal pain, nausea, diarrhea or constipation, from the more serious effects reported in more in-depth studies in the area that can pose serious risks to patients' health. It is possible to conceptualize an adverse reaction as any harmful and unintentional event that occurs during the use of a medication, at a standard dose for humans, with therapeutic, prophylactic or diagnostic purposes (VARALLO; MASTROIANNI, 2013). An adverse event is an unfavorable event that may occur during the use of medication, but has no causal relationship with this treatment (OMS, 2005).

revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

In contrast, intoxication is a process characterized by a physiological imbalance resulting from biochemical changes. It therefore consists of the manifestation of toxic effects evidenced by a series of signs and symptoms or laboratory tests (OLGA; CAMARGO; BATISTUZZO, 2021). They are classified as acute or chronic and each drug presents a set of specific signs and symptoms, according to its characteristics, including its toxicokinetic (MALAMAN *et al.*, 2009). Therefore, the objective of this review is to identify scientific studies from around the world that report on the toxicity of ivermectin and its risks to the various systems of the human body.

METHODOLOGY

Search Strategy

A search was carried out in the PubMed, Web of Science, Scopus and Embase databases using the keywords: "ivermectin", "intoxication" and "clinical trials". In PubMed, additionally, a search was carried out using the terms "ivermectin[Title] AND covid-19" selecting the "Case Reports" filter. An additional search was carried out to update the search but did not change the results.

Eligibility Criteria

The inclusion criteria were complete articles published in the last 20 years (from 2003 to 2023) that addressed the topic of poisoning in patients due to the use of ivermectin to treat any disease. The exclusion criteria were articles in respect of veterinary use of the drug, incomplete articles or those unrelated to the topic (Figure 1). Only studies which included calls from patients to drug poisoning centers, and reports and case studies that portrayed a potential risk to life or serious possible sequelae (such as injuries) were considered to describe poisoning (rather than general, milder side effects). However, to prepare the table and graph included in this study, the general adverse effects that are contained in the medication leaflet were also described. The therapeutic range was also included in the table when mentioned in the article, but was not used as an inclusion or exclusion criterion.

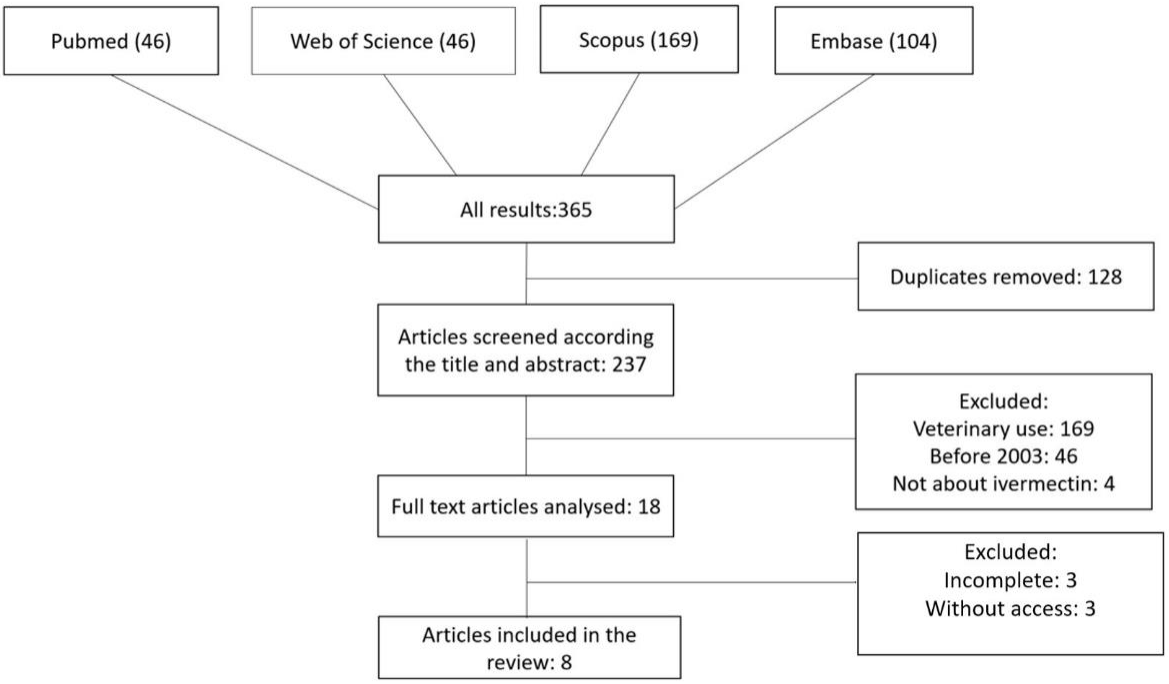
Data extraction

The search was conducted in November 2023 and generated 365 articles that were organized using Rayyan software (OUZZANI *et al.*, 2016). Two blinded researchers (A. M. and H. G) read the titles and, after evaluation, a high level of agreement was observed. Five articles generated disagreement, and these were evaluated by the third participant (S. E. P. B. S. S.), who conducted the research.

After preliminary analysis to exclude duplicates and select works by title, the abstracts were read for further evaluation and finally 18 articles were selected for full reading. Of these, works that only consisted of abstracts, articles from non-scientific newspapers and those whose access was blocked were excluded.

revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

Figure 1. Flowchart of article selection and inclusion methodology.



RESULTS AND DISCUSSION

Following the strategy outlined above, we identified eight studies that met our selection criteria, which were categorized according to whether they took place before or after the start of the COVID-19 pandemic, with seven articles addressing the toxicity of ivermectin after the start of the COVID-19 pandemic, and only one before. Among the studies that we found, only one was described in humans before the pandemic, in 2018, which was based on reports of community health campaigns in Africa for the treatment of onchocerciasis, a parasitic disease.

The increase in studies on this topic post-pandemic underscores a rising concern over ivermectin's potential toxicity, especially given its indiscriminate use during this period. Such usage patterns may result in more severe adverse effects than previously documented.

The entire discussion on the topic arose after the publication of a work that points out the ability of ivermectin to act on SARS-CoV-2, in a similar way, with SARS-CoV, demonstrating inhibitory activity on nuclear transport. This happens because the SARS-CoV virus proteins have a relationship with IMPα/β1 (CALY *et al.*, 2020). During the infection process, when the cytoplasmic nucleus closes, it is signal-dependent on the core capsid protein. With the administration of ivermectin, this transport signaling to the nucleus for the replication of new viruses would be blocked (CALY *et al*., 2020).

Furthermore, the SARS-CoV host accessory protein ORF6 is an antagonist of the antiviral activity of the transcription factor STAT1, thus sequestering IMPα/β1, through the drug, which is presented on the membrane of the Golgi complex. Therefore, the antiviral response generates a reduction in the viral load of SARS-CoV-2 in the host cell (CALY *et al.*, 2020).

The discussion will be based, initially, on clinical trials that raise the issue of the use of ivermectin, and subsequently, on patient reports, followed by the relationship with what was observed in animal models and a critical analysis on the topic.

Rezai *et al.* (2022), in a clinical trial on the effectiveness of treatment with ivermectin that was carried out with 609 hospitalized individuals and 549 non-hospitalized individuals, reported no significant differences between the placebo group and the group that received ivermectin. Therefore, it was not indicated for the treatment of COVID-19. However, in relation to the

revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

current study it is interesting to note that no serious adverse effects were observed due to the use of ivermectin. However, the authors did highlight a reported increase in visits to poison control centers in respect of ivermectin compared to the pre-pandemic period (REZAI *et al.*, 2022).

The findings of a review by Romam *et al*. (2022) of randomized clinical trials on the use of ivermectin to treat COVID-19 agree with the study by Rezai *et al*. (2022), with the authors reporting that ivermectin did not improve the patients' condition in all aspects evaluated, such as mortality, length of hospitalization and the adverse events caused by the disease (REZAI *et al*., 2022; ROMAN *et al.*, 2022).

In the Tables below, we present the results of the articles that were included in this review and the main types of toxicities that the studies found with the use of ivermectin when used for the treatment or prophylaxis of COVID-19. Table 1 shows toxic effects of ivermectin used for the treatment or prophylaxis of COVID-19 in patients. Table 2 shows the same parameters for the only article found on the topic before the COVID-19 pandemic.

Table 1. Toxic effects of ivermectin used for the treatment or prophylaxis of COVID-19 in patients.

Authors, year	**Country**	**Sample**	**Sex (age)**	**Type of study**	**Dose**	**Results**
Temple *et al*., 2021	USA	21	11 men, 10 women (20-81 years old)	Case series	21 mg 2x/week	gastrointestinal discomfort (4), Confusion (3), ataxia (2), hypotension (2), seizure (1), visual symptoms, rash 4 hospitalizations in ICU.
Lorente *et al*., 2022	South Africa	Total: 65 Period 1: 19 Period 2: 46	Period 1: 9 boys, 10 girls (average: 4 years) Period 2: 24 boys, 22 girls (average: 2 years)	Retrospective	12mg to 300mg (oral, intramuscular and subcutaneous)	CNS (26): altered level of consciousness, ataxia, dizziness, blurred vision, nystagmus, hallucinations, involuntary movements; Gastrointestinal (18): abdominal pain, diarrhea, vomiting; skin reactions (5), respiratory depression (2), acute kidney (2) and liver injury (1).

revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

Porubcin *et al*., 2022	Slovakia	1	Woman (50 years old)	Case report	45mg/day 20mg/mL	Neurological symptoms: Glasgow 3, quadriparesis with myoclonic spasms of upper and lower limbs, signs of extrapyramidal syndrome, ptyalism, both pupils were mydriatic and no signs of neck rigidity. Elevation of transferases, gamma glutamyl transpeptidase, C-reactive protein, lactic dehydrogenase and low levels of albumin. Hemoglobin, platelet count and leukocyte count were normal. Coagulation tests: D-dimer level of 1.39 mg/L and fibrinogen of 6.54 g/L.
Bomze *et al.*, 2022	Israel	517	54.2% men 46.8% women (median: 54 years old)	Retrospective	Average dose: 9mg	Severe Cutaneous Effects (25): Stevens–Johnson Syndrome, Toxic epidermal necrolysis, DRESS syndrome, oral ulcer, Erythema multiforme, Acute generalized exanthematous pustulosis, Bullous dermatitis, exfoliative dermatitis, Pemphigoid, symmetric intertriginous and flexural exanthema, skin rash. Non-severe skin effects (81): Pruritus, Skin irritation, Angioedema, Acarodermatitis, Erythema, Alopecia, Eczema, Herpes zoster, Skin pain, Skin disorder. Non-cutaneous (411): Altered mental status (26), Visual disturbances (23), Nausea and vomiting (21), Balance disturbance (20), Headache (20), Encephalopathy (18), Coma (17), Elevated liver enzymes (17), Psychiatric disorders (17), Dizziness (13).

revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

Farah *et al*., 2022	USA	40	21 men 19 women (39–65 years old)	prospective case series	oral: 3mg, topical: cream 1%, solution 5 mg/mL, paste 1.87% parenteral: 1%	Gastrointestinal (13): nausea, vomiting, diarrhea, anorexia. Neurological: confusion (11), CNS depression (8), visual hallucinations (6), seizure (4), sedation (4), dizziness (7), headache (4), delirium (4), paresthesia (2), tremor (2), agitation (2), syncope (1). Cardiovascular: hypotension (4), bradycardia (3), tachycardia (3). pruritus (2), dyspnea (2), metabolic acidosis (3). 33 emergency visits, 19 hospitalizations.
Bhardwaj *et al.*, 2023	USA	1	Not reported	Case report	60mg	Ataxia, blurred vision, changes in peripheral vision, dizziness and loss of balance.
Goyal *et al.*, 2022	USA	2	Men (45, 51 years old)	Case report	High dose (not reported)	Auditory hallucinations, delusions and paranoia.

Below, we discuss the eight texts identified by our review of the literature. The text by Temple *et al*. was in the form of a letter and highlighted the increase in calls in respect of ivermectin related to COVID-19 to the Oregon Poison Center, which more than doubled between 2020 and 2021. In August 2021, 21 people called the center, 11 who used the drug to prevent COVID, and 10 to treat the disease. Six of these people were hospitalized due to ivermectin poisoning, four of whom were treated in ICUs (TEMPLE; HOANG; HENDRICKSON, 2021).

During this period, the Center for Disease Control and Prevention issued a warning about the risks associated with the unrestrained use of ivermectin given the high number of prescriptions. The study by Farah *et al.* was a prospective case series of adverse events related to ivermectin in a pharmacovigilance project at 15 medical centers. Forty cases of adverse effects were reported over one year and three months. Of these, 33 patients went to a hospital emergency room and 19 were admitted. Neurotoxicity was the most commonly reported adverse reaction, and there were a number of cases of self-medication with ivermectin in the formulation for veterinary use (FARAH *et al.*, 2022).

Lorente and Voigt *et al.* (2022) reported an increase in calls to toxicovigilance centers in South Africa related to exposure to ivermectin. They highlighted extensive off-label use of ivermectin against COVID-19. The study described human toxicity to ivermectin with involvement of the central nervous, gastrointestinal and dermatological systems. In their study, they concluded that these toxic effects on organs and systems potentially reflect the use of high doses of ivermectin, the lack of appropriate formulations and inappropriate use of veterinary formulations (LORENTE *et al.*, 2022).

Porubci and Rovnakova *et al.* (2022) published details of a serious case of neurotoxicity in the form of encephalopathy due to the use of ivermectin. A 50-year-old woman with no history of serious illness ingested 5

revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

tablets of 3 mg of ivermectin every 8 hours, that is, 45 mg/day. The day before the hospital assessment, she received an intravenous ivermectin infusion which, in her country (Slovakia), was approved for veterinary use only, consisting of a dose of 20 mg/mL of ivermectin. The patient had to be admitted to an intensive care unit (ICU) (PORUBCIN *et al.*, 2022).

Bomze *et al*. (2022), observed allergic skin reactions including tissue necrosis. This retrospective study was based on patient-reported data in the FDA Adverse Event System. In it, allergic and systemic symptoms were reported, including 4 deaths and 12 hospitalizations (BOMZE *et al.*, 2022).

Goyal *et al*. (2022) described episodes of psychosis following the use of ivermectin in patients with COVID-19 pneumonia, due to neuroinfection and complications of the inflammatory condition (NIRISHA *et al.*, 2022), or even due to vaccination (GOYAL *et al.*, 2022)

Based on the data obtained from the articles mentioned in table 1, a graph was created containing the symptoms and incidence (figure 2). This data reflects only a small part, without considering underreporting and difficulty in categorizing and classifying articles in table form. One way or another, it was possible to observe that the toxic effects reported after the pandemic period were more serious than those previously known, and one hypothesis for this fact would be indiscriminate use of the medication in question.

Figure 2. Symptoms and incidence in patients who used ivermectin during the covid-19 pandemic. Data extracted from articles cited in Table 1.

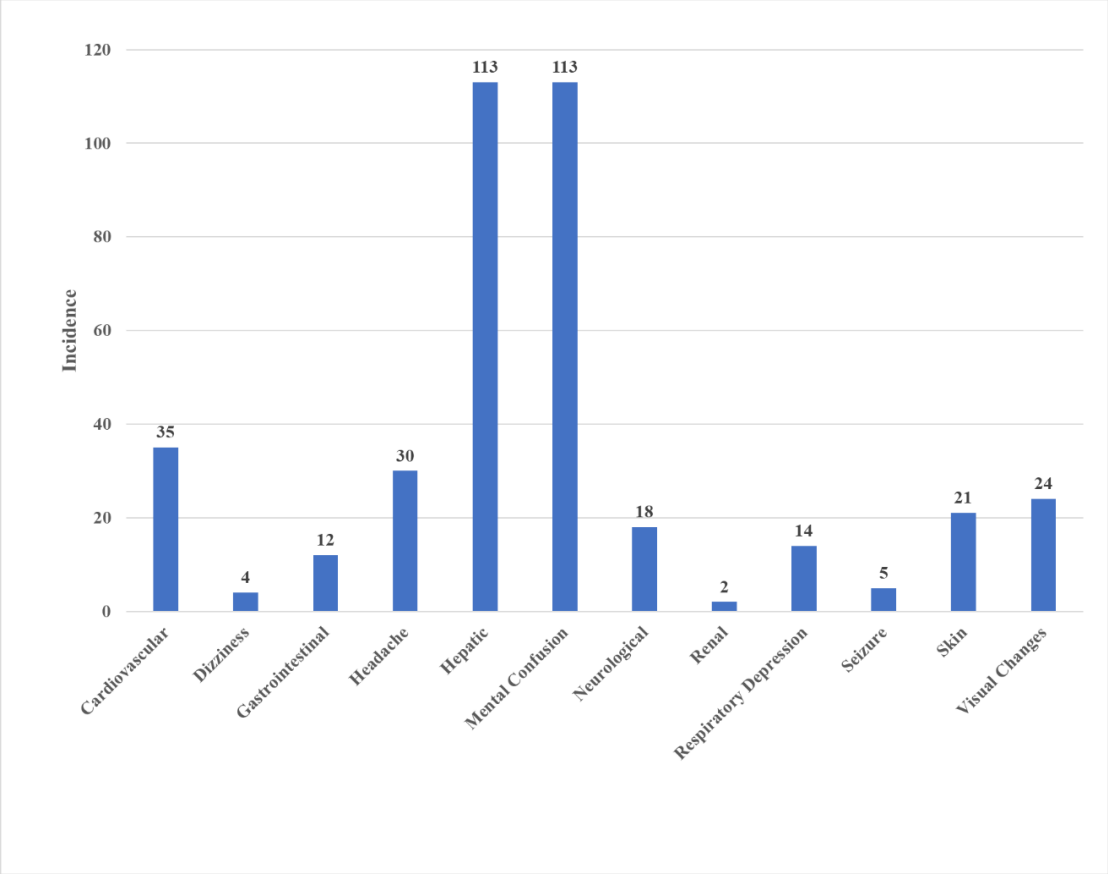


Figure 2 graphically represents the symptoms observed in patients who used ivermectin during the pandemic, whether for off-label use, medical prescription or prophylaxis. As observed, liver toxicity and mental confusion were the most frequent symptoms, together representing 57% of the total symptoms described in the

revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

graph. Headaches were less frequent, but they are a more nonspecific symptom and difficult to associate with the use of the medication. Symptoms such as cardiovascular, skin irritations and visual changes are more worrying and represented approximately 20% of the total. It is worth mentioning that symptoms such as dizziness and seizures could be classified within the neurological symptoms section, causing this incidence to increase considerably. However, the description according to the original of each article was maintained, paying attention to the common points.

Table 2. Toxic effects of ivermectin before the covid-19 pandemic.

Author, year	Country	Sample	Sex	Kind of study	Dose	Results
Chandler, 2018	Sweden	28	14 men 13 women 1 Gender not provided	Case series	3mg to 24mg (20 cases of concomitant medications)	Itching, headache, dizziness, inability to walk, decreased level of consciousness, convulsion, encephalopathy, coma and tremor. 2 deaths. Autopsy: high levels of ivermectin in brain tissue 14 days after the last dose (man, 64 years old).

The only study identified that was published before the pandemic in response to reports of significant adverse neurological events following campaigns using ivermectin to treat Onchocerciasis volvulus in Africa. The study was based on pharmacovigilance data, and indicated the most common adverse effects of ivermectin were itching, headache and dizziness. It also highlighted the neurological effects of ivermectin such as confusion, depression and seizures in some patients (CHANDLER, 2018). Despite these data, Silva *et al.* (2023) suggest that a lower death rate from COVID-19 during the pandemic could have been related to its use for the treatment of onchocerciasis (SILVA *et al.*, 2023).

With the aim of evaluating the toxic effects of ivermectin due to accidental overdose and possible antidotes that could be used, Trailović and Nedeljković (2010) studied the neurotoxic effects of ivermectin. They observed CNS depression similar to anesthesia in rats, and increased tone and amplitude of contraction of the ileum isolated from guinea pigs, indicating a possible blockade of voltage-dependent Ca+2 channels. Thus, they confirm the central and peripheral GABAergic properties of ivermectin and suggest the involvement of the cholinergic system in toxicity. These studies pointed to a potential clinical application of atropine and flumazenil as antagonists that could neutralize the gastrointestinal and CNS depressant effects caused by ivermectin intoxication (TRAILOVIĆ; NEDELJKOVIĆ, 2011).

Articles that show toxicity in animal models with different doses and associations alert us to use greater caution when it comes to prescribing ivermectin off-label for purposes other than the already studied and known objectives of this drug. Idowu *et al*. (2015), suggested that there was a risk of toxicity with the associated the use of artemether-lumefantrine, albendazole and ivermectin. The study was carried out in Wistar rats at human therapeutic and subtherapeutic doses where hepatotoxic effects and oxidative stress were observed. Although the effect of ivermectin in conjunction with other drugs was only evaluated in this study, these data provide an indication of the possible toxicity of ivermectin in isolation (IDOWU *et al*., 2015).

Retrospective studies that reported toxicity in different systems of the human body and at different doses must be analyzed very carefully, some are patient reports and without clinical anamnesis, laboratory parameters and

revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

the exact dose that the individuals ingested. Pharmacovigilance data was scarce to correctly control the real adverse events of ivermectin at the doses used. Measures to raise public awareness about the importance of reporting the effects and risks of self-medication could have been implemented.

In this context, there is a need to clarify the population about the difference between treatment and prophylaxis. It is believed that this period of epidemiological misunderstandings will provide lessons for future health emergency situations that may arise and that do not have the appropriate tools for public health management.

CONCLUSION

It is evident that during the COVID-19 pandemic, ivermectin was used without guidance on proper dosing or duration. Furthermore, the only notable evidence supporting its efficacy came from in vitro studies, which were insufficient to establish its safe and effective use for COVID-19 prophylaxis and treatment in clinical practice.

There is still no clear evidence on its efficacy, and until there is it should not be used in the treatment of COVID-19. Additionally, a standardized treatment protocol for ivermectin intoxication should be established, a measure that was overlooked during the pandemic in the urgency to save lives, often without thorough evidence.

The studies reviewed are heterogeneous but collectively highlight the serious adverse effects associated with high doses of ivermectin and the use of veterinary formulations. Off-label use of this drug, for unapproved purposes beyond its known applications, significantly increases the risk of intoxication and may even lead to the death of patients.

ACKNOWLEDGMENTS

We are grateful for the financial support from CAPES and CNPq.

REFERENCES

AHMED, S. *et al.* A five-day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness. **International Journal of Infectious Diseases**, v. 103, p. 214–216, 2021.

BOMZE, D.; SPRECHER, E.; GELLER, S. Severe cutaneous adverse reactions associated with systemic ivermectin: A pharmacovigilance analysis. **Journal of Dermatology**, v. 49, n. 8, p. 769–774, 2022.

CALY, L. *et al.* The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. **Antiviral Research**, v. 178, 2020.

CHANDLER, R. E. Serious neurological adverse events after ivermectin-do they occur beyond the indication of onchocerciasis? **American Journal of Tropical Medicine and Hygiene**, v. 98, n. 2, p. 382–388, 2018.

FARAH, R. *et al*. Ivermectin associated adverse events in the treatment and prevention of COVID-19 reported to the FACT pharmacovigilance project. **Clinical Toxicology**, v. 60, n. 8, p. 942–946, 2022.

GOYAL, L. *et al*. Ivermectin-Induced Acute Psychosis in Patients Infected With COVID-19 Pneumonia. **Cureus**, 2022.

IDOWU, E. T. *et al*. Artemether-Lumefantrine treatment combined with albendazole and ivermectin induced genotoxicity and hepatotoxicity through oxidative stress in Wistar rats. **Egyptian Journal of Basic and Applied Sciences**, v. 2, n. 2, p. 110–119, 2015.

JOHNSON-ARBOR, K. Ivermectin: a mini-review. **Clinical ToxicologyTaylor and Francis Ltd**., 2022.

LIND, J. N. *et al*. Increase in Outpatient Ivermectin Dispensing in the US During the COVID-19 Pandemic: A Cross-Sectional Analysis. **Journal of General Internal Medicine Springer**, 2021.

LORENTE, V. P. F. *et al*. Ivermectin exposures reported to the Poisons Information Helpline in South Africa during the COVID-19 pandemic. **South African Medical Journal**, v. 112, n. 8, p. 522–525, 2022.

MALAMAN, K. R. *et al*. Perfil das intoxicações medicamentosas. **Infarma**, v. 21, 2009.

revista interfaces
Revisão de Literatura
V. 12, N. 4 (2024) | ISSN 2317-434X

MARQUES, L. L. M. *et al*. Ivermectin as a possible treatment for COVID-19: A review of the 2022 protocols. **Brazilian Journal of Biology**, v. 84, 2024.

NIRISHA, P. L. *et al.* First episode psychosis and COVID-19: A case series and mini review. **Asian Journal of Psychiatry** B.V., 2022.

OLGA, S.; CAMARGO, M. M. DE A.; BATISTUZZO, J. A. DE O. **Fundamentos de toxicologia**. 5ª ed. São Paulo: 2021.

ORGANIZAÇÃO MUNDIAL DA SAÚDE. **Importância da farmacovigilância**. Brasília: Organização Pan-Americana da Saúde, 2005.

OUZZANI, M. *et al*. Rayyan-a web and mobile app for systematic reviews. **Systematic Reviews**, v. 5, n. 1, 5. 2016.

POPP, M. *et al.* Ivermectin for preventing and treating COVID-19. **Cochrane Database of Systematic Reviews John Wiley and Sons Ltd**, 2022.

PORUBCIN, S. *et al*. Intravenous veterinary ivermectin in a COVID-19 patient causing neurotoxicity. **ID Cases**, v. 27, 2022.

QUINCHO-LOPEZ, A. *et al*. Self-medication practices to prevent or manage COVID-19: A systematic review. **PLoS ONE Public Library of Science**, 2021.

REZAI, M. S. *et al.* Non-effectiveness of Ivermectin on Inpatients and Outpatients With COVID-19; Results of Two Randomized, Double-Blinded, Placebo-Controlled Clinical Trials. **Frontiers in Medicine**, v. 9, 2022.

ROMAN, Y. M. *et al*. Ivermectin for the Treatment of Coronavirus Disease 2019: A Systematic Review and Meta-analysis of Randomized Controlled Trials. **Clinical Infectious Diseases**, v. 74, n. 6, p. 1022–1029, 2022.

SILVA, N. B. L. DA *et al*. Prevalence of Ivermectin use to prevent COVID-19 during the pandemic in Mato Grosso: cross-sectional home-based study. **Revista Brasileira de Epidemiologia**, v. 26, 2023.

TEMPLE, C.; HOANG, R.; HENDRICKSON, R. G. Toxic Effects from Ivermectin Use Associated with Prevention and Treatment of Covid-19. **New England Journal of Medicine**, v. 385, n. 23, p. 2197–2198, 2021.

TRAILOVIĆ, S. M.; NEDELJKOVIĆ, J. T. Central and Peripheral Neurotoxic Effects of Ivermectin in Rats. **J. Vet. Med. Sci.** ;v. 73, n. 5, p. 591-9, 2011.

VARALLO, F. R.; MASTROIANNI, P. C. **Farmacovigilância: da teoria à prática.** São Paulo: UNESP, 2013.

YANG, S.; SHEN, S.; HOU, N. Is Ivermectin Effective in Treating COVID-19? **Frontiers in Pharmacology**, v. 13, 21, 2022.