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Contents

Kombucha tea

Kombucha tea has become increasingly popular in recent years because it has been claimed to have a large number of beneficial effects including the prevention of cancer, relief of arthritis, treatment of insomnia, stimulation of the immune system and even the regrowth of hair. The tea is brewed from the Kombucha mushroom which is actually a symbiotic yeast and bacteria aggregate surrounded by a permeable membrane. The "mushroom", which grows like a round flat gray fungus about the

size of a dinner plate, is fermented in sugared tea to obtain the Kombucha tea. The mushrooms are sold or distributed by naturopaths and other alternative practitioners and are often passed on from person to person. The tea has been described to contain a mixture of many substances including alcohol, glucuronic acid, acetic acid, heparin and lactic acid.

In the last year, ADRAC has received two reports of hepatotoxicity in association with Kombucha tea. There have also been reports of both hepatotoxicity and lactic acidosis in the United States. [1,2] In one Australian report, a woman presented with rash, fever, rigors, nausea and vomiting after drinking Kombucha tea for a month. Investigations revealed abnormalities in liver function tests, white blood cells, and ESR. She recovered after treatment with steroids. The other report was of a 35 year old female who developed severe hepatitis after prolonged ingestion of the tea.

ADRAC is concerned that these reports suggest that Kombucha tea may be toxic and is keen to learn of the extent of the problem. Any patient who develops unexplained hepatotoxicity or other severe illnesses should be assessed not only for a drug history but also ingestion of herbal and other alternative treatments such as Kombucha tea.

References

1. Perron AD, Patterson JA, Yanofsky NN. Kombucha "mushroom" hepatotoxicity. *Ann Emerg Med* 1995; 26: 660-1.

2. Centers for Disease Control. Unexplained severe illness possibly associated with consumption of Kombucha tea - Iowa, 1995. *MMWR* 1995; 44: 892-900 (*JAMA* 1996; 275: 96-98).

Clozapine induced neuroleptic malignant syndrome

Clozapine (Clozaril) is an antipsychotic drug used in the treatment of schizophrenia resistant to other therapies. From 1993 to April 1997, ADRAC has received a total of 436 reports in association with clozapine. The drug is systematically monitored because of the risk of agranulocytosis, and therefore the proportion of adverse events detected is probably higher than with other drugs. The product information indicates that the incidence of extrapyramidal reactions with clozapine is less than with other antipsychotics. However, in common with other antipsychotic drugs, the use of clozapine has been associated with neuroleptic malignant syndrome (NMS). Common clinical features of NMS are fever, rigidity, autonomic instability and altered consciousness.

ADRAC has received 11 reports describing NMS in males aged 14 to 52 (median 40) years with clozapine being the only suspected drug cause in all but one case. Onset occurred as early as 6 days and as late as 9 months after commencing clozapine with most cases developing in the first two weeks. Daily doses of clozapine ranged from 75 to 600 (median 400) mg. Presenting clinical features included fever, confusion or disorientation, profuse sweating, tachycardia, and delirium. Significant rigidity does not seem to occur in many cases of NMS related to clozapine. Leukocytosis was noted in 7 cases and elevated creatine kinase levels (230 to 12,800 units/litre) were observed in 10 cases. All 11 patients required hospital admission. One case was complicated by pulmonary oedema and in another, the onset of acute renal failure was followed by cardiac arrest and death. All the remaining patients recovered.

The product information for clozapine states that neuroleptic malignant syndrome is estimated to occur with an incidence of less than 0.1%, but reports to ADRAC would suggest that the incidence is considerably higher. Prescribers should be aware of this rare but life threatening complication of clozapine therapy.

The Achilles heel of fluoroquinolones

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One of the more unusual adverse reactions known to be associated with the fluoroquinolone antibiotics is the occurrence of tendinitis. This is a serious effect since it may progress to tendon rupture with many weeks of disability as a result. Over 200 cases have been reported in the literature with the majority from France. Most members of the class including ciprofloxacin, enoxacin, ofloxacin, and norfloxacin have been implicated. The Achilles tendon is most often involved.

In Australia, there have been 25 reports of tendinitis in association with fluoroquinolones. Most (22) have been with ciprofloxacin and the other three with norfloxacin. The majority of the patients involved were elderly, ranging in age from 46 to 91 (median 69) years and the sex distribution was equal. For ciprofloxacin, daily dosages ranged from 750 mg to 2250 mg although most (13) patients were taking 1000 mg daily. For norfloxacin, all three patients were taking the usual dose of 800 mg daily. Time to onset ranged from the same day that the drug was commenced (in two patients) to two months although in 13 of the 24 reports which provided the information, the reaction occurred within the first week. Almost all (23) of the reports specified the Achilles tendon as the site of the tendinitis. Tendinitis was described as bilateral in 11 cases. Only 8 patients had recovered at the time the report was submitted and the other patients were being treated with rest and/or physiotherapy. There have been no reports of tendon rupture in Australia although in one severe case, the patient required a plaster cast up to the mid thigh.

A number of risk factors have been identified with regard to this adverse reaction. These include old age, renal dysfunction, and concomitant corticosteroid therapy. Of the patients reported to ADRAC, 72% were older than 60 years. Nine of these patients were taking corticosteroids as were three of the younger patients.

Prescribers are reminded that tendinitis, especially involving the Achilles tendon, is a rare adverse effect of the fluoroquinolones. It is more likely to occur in association with the risk factors referred to above. The antibiotic should be withdrawn immediately to reduce the risk of tendon rupture.

Paraesthesia with NSAIDs

A recent report to ADRAC described an 88 year old female with insulin dependent diabetes who began taking diclofenac (Voltaren) for back pain. After a few days, she developed paraesthesiae in the arms and the legs which became of such severity as to keep her awake at night. Diabetic neuropathy was suspected but there were no objective signs of this pathology and median nerve conduction studies were also normal. After some months, the patient ceased diclofenac and all symptoms resolved within 24 hours.

Paraesthesia is reported as a possible adverse reaction in the product information for most NSAIDs (diclofenac, diflunisal, ibuprofen, indomethacin, ketorolac, ketoprofen, piroxicam, sulindac, tiaprofenic acid) but not all (mefenamic acid, naproxen, tenoxicam). Reports to ADRAC appear to indicate that paraesthesia (including the related symptoms of hypoaesthesia and hyperaesthesia) is a class effect of NSAIDs as there have been cases with all NSAIDs ranging from naproxen with 28 reports to diflunisal with one report. Except for diflunisal (0.2%), reports correlate with the total number of adverse reports received for each drug with reports of paraesthesia for all the other NSAIDs within the range of 1% to 3%.

Of the total of 120 reports, the NSAID was the only suspected drug in 101 cases. Ages of the patients ranged from 13 to 88 (median: 47) years with a majority of them (87:32) female. Of the 86 reports for which the information is available, a rapid onset was documented in

58 patients who developed paraesthesiae within a week, although the onset in two cases was greater than 2 years. Thirty seven patients developed the reaction on the same day that the drug was started. Most (86) had recovered at the time the report was submitted and in 11 patients, the reaction recurred on rechallenge. Prescribers should be aware that paraesthesia is a rare, but reversible adverse effect of most NSAIDs.

Drugs of current interest

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Please report **all** suspected reactions to these **Drugs of Current Interest**

- Alendronate (Fosamax)
- Azithromycin (Zithromax)
- Cabergoline (Dostinex)
- Cilazapril (Inhibace)
- Dicloxacillin (Diclocil)
- Enoxacin (Enoxin)
- Famciclovir (Famvir)
- Fexofenadine (Telfast)
- Fluvastatin (Lescol, Vastin)
- Gestrinone (Dimetriose)
- Losartan potassium (Cozaar)
- Nafarelin (Synarel)
- Nefazodone (Serzone)
- Olanzapine (Zyprexa)

- Pantoprazole (Somac)
- Salmeterol (Serevent)
- Sevoflurane (Sevorane)
- Tacrine (Cognex)
- Ticlopidine (Ticlid)
- Valaciclovir (Valtrex)
- Venlafaxine (Efexor)
- Zopiclone (Imovane)

What to report?

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(you do not need to be certain, just suspicious!)

ADRAC encourages the reporting of all **suspected** adverse reactions to medicines, including vaccines, OTC medicines, herbal, traditional or alternative remedies. ADRAC particularly requests reports of:

- ALL suspected reactions to **new drugs** (see **drugs of current interest**)
- ALL suspected drug interactions
- Suspected reactions causing
    - Death
    - Admission to hospital or prolongation of hospitalisation
    - Increased investigations or treatment
    - Birth defects

For blue cards

Reports of suspected adverse drug reactions are best made by using a prepaid reporting form ("blue card") which is available from the website or from the Office of Medicines Safety Monitoring (02 6232 8744).

Reports can also be submitted electronically, by clicking on "Report a problem" on this website, by fax: 02 6232 8392, or email: ADR.Reports@tga.gov.au .

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All correspondence to be addressed to: The Secretary, ADRAC, PO Box 100, Woden ACT 2606