پیشرفت‌های اخیر در درمان مسمومیت با حشره‌کش‌های فسفدار آلی

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چکیده:

سوموم فسفدار آلی به میزان وسیعی در دفع آفات نباتی و هم به عنوان عوامل اعصاب در جنگلهای شیمیایی مورد استفاده قرار گرفته‌اند. حشره‌کش‌های فسفدار به‌طور فراوان وارد کشور را وارد کنترل در دسترس افراد قرار می‌دهند. به‌همین دلیل مسمومیت حاد با این سوموم بیشتر نوع عمده بیماری بسیار شایع بوده به نحوی که 350 نفر (2/18) از مسمومی‌های درمانی امام رضا(ع) مشهد در سال 1377 شام گردیده‌اند.

سوموم فسفدار آلی با مهار آنزیم کولین استراز و موجب وقفه هیدروپراتیل کولین و در نتیجه احتمال این ماده در پایانه‌های عصبی می‌گردد که این خود به‌صورت تحریک گیرنده‌های موسکارینی و نیکوتینی می‌شود. آثار تحریک گیرنده‌های موسکارینی بسیار ناپذیر و تحریک گیرنده‌های نیکوتینی با اکسیمیا مانند پلاژیدوکسین و اپیدوکسین درمان می‌شود. با وجود تجویز و نوع پادزهر یادشده مرم و میر ناشی از سوموم فسفدار آلی نسبتاً زیاد (حدود 10/).

گزارش شده‌است.

در مورد اثر درمانی سولفات آنیوم در مسمومیت با سوموم فسفدار آلی از قدمی اتفاق نظر وجود داشته‌است اما در خصوص میزان و نحوه تجویز این پادزهر از اولات دهه هشتاد میلادی با توجه به تجربیات درمان مسمومین مشهد و تأیید آن از سوی جامعه علمی بین‌المللی با تزریق مقدار زیاد آن در سه مسمومیت خفیف از میران مرگ و میر سوموم فسفدار آلی کاسته‌شده‌است.

اکسیمیا به عنوان فعال کننده آنزیم کولین استراز کنترل آثار نیکوتینی مسمومیت با حشره‌کش‌های فسفدار آلی مورد افتاده‌بوده واقع شده‌اند. تجربیات بالینی در درمان مسمومیت با حشره‌کش‌های فسفدار آلی مسمومین مشهد و گزارش آمیخته‌ای از سری لالوکا (مجله لاهت شماره 32 سال 1992) مؤید عدم تأثیر اکسیمیا درسری بهبودی این مسمومیت می‌باشد. پروکسید بالینی 314 بیمار مسموم با حشره‌کش‌های فسفدار آلی که طی سالهای 1371-1372 در بخش بیمارستان بستره شده بودند مطالعه قرار گرفت. در بیمارستان که اکسیمیا دریافت کرده بودند یک‌ویستگی P<0/0735 و میزان مرگ و میر 0/01 و میزان مرگ و میر 0/01 مشاهده گردید. این نتایج نشانگر اثرات سوء و عدم تأثیر درمانی اکسیمیا در درمان مسمومیت حشره‌کش‌های فسفدار آلی می‌باشد. تأیید نهایی این نتایج مستلزم انجام یک تحقیق آینده‌گیر کنترل شده بالینی قرار می‌گیرد.

کلید واژه‌ها: ۱- مسمومیت با آفت‌آکثر
۲- ترکیب اورگانیک
۳- اکسیمیا
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RECENT ADVANCES IN TREATMENT OF
OP PESTICIDE POISONING

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ABSTRACT

Organophosphate (OP) compounds have largely been used as
pesticides and also as nerve agents in Chemical Wars. OP pesticides
have frequently been imported and freely available to the public
without usage control. Therefore, OP poisoning, mainly intentional
type, is very common; and accounts for 21.8% (250 patients) of the
total admission to the hospital between 21 March 1994 and 20
March 1995.

OP compounds induce accumulation of acetyl choline by
inhibition of acetyl cholinesterase leading to the stimulation of
muscarinic and nicotinic receptors. Muscarinic effects are
counteracted successfully by atropine sulfate, but the therapeutic
effects of oximes on nicotinic receptors and cholinesterase
reactivation have not been observed in clinical practice. Clinical
observations of the author and a report from Sri Lanka (Lancet
339, 1992), indicates no therapeutic effects of oximes in OP
poisoning. Case notes of 317 Treatment Centres between 21 March
1993 and 20 March 1995 were studied.

There were significant positive correlations between the oxime
doses and either hospitalization days (r = 0.625, p < 0.001) or
mortality rate (r = 0.718, p < 0.01).

It seems that oximes had no therapeutic effects on OP pesticide
poisoning. However, a prospective investigation is currently
undertaken to confirm this hypothesis.

Key Words: 1) Pesticide Poisoning 3) Acetylcholinesterase
2) Organophosphate (OP) compound 4) Oxime

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INTRODUCTION

Organophosphates (OP) have been used mainly as pesticides and also as nerve agents in chemical wars. OP pesticides have been imported, distributed and used in this country without proper control. Therefore, poisoning particularly suicidal attempts with these chemicals are very common and accounted for 250 (21.8%) admissions to the Poisons Treatment Centre and 25 (38%) deaths in the year of 1994.

Op inhibits cholinesterase enzyme and thus acetylcholine accumulates at nerve ending and stimulates muscarinic and nicotinic receptors. Muscarinic stimulation is reduced by atropine sulphate. Oximes have been used for relief of nicotinic stimulation and cholinesterase reactivation\(^{(2)}\), but the mortality rate is still around 10%\(^{(3)}\). The effects of atropine sulphate have long been established, although the dosing regimens were different. Based on clinical experience, the proposed high doses of atropine by Mashhad Poisons Treatment Centre are now universally approved. The following mechanisms for oximes have been reported\(^{(4)}\):

1) Dissociation of phosphorylated binding of the enzyme and OP.
2) Direct attack of oxime at free molecule of OP.
3) Antimuscarinic effects

Based on clinical experience at Mashhad Poisons Treatment Centre and a report from Sri Lanka\(^{(5)}\), oximes revealed no significant therapeutic effects on OP poisoning. Over the past few years, there has been shortage of oximes and thus most of the OP cases were treated by atropine alone. It was aimed to compare the cases treated by atropine with those who have received oxime as well. Therefore, the case notes of the OP patients who were treated at the centre between 21 March 1992 and 21 March 1995 were investigated.

PATIENTS & METHODS

Case notes of all patients with OP pesticide poisoning who were hospitalised for more than three days were reviewed. Relevant parameters such as age, sex, clinical features, serum cholinesterase activity (estimated spectrophotometrically using Behring kit), atropine and oxime doses, hospitalisation days and outcome of treatment were recorded. The data were processed by FoxPro program and analysed by Statistical Package for Social Sciences (SPSS). Comparisons were made by Student-t, Pearson and Chi-Square tests.

RESULTS

A total of 317 case notes of OP poisoning including 114 males (36%) and 203 females (64%) with a mean±SD age of 25±14(1-80) years were reviewed. Apart from accidental cases in seven children (2.2%), the remainder were self-poisoning. The most
frequent age group was 16-20 years (107 cases) as shown in figure 1. Seasonal
distribution revealed 32% in spring, 22% in
summer, 25% in autumn and 21% in winter
with no significant differences between
them. Based on oxime therapy, 185(58%)
patients were treated by atropine and
oximes and 132 (24%) were treated by
atropine alone. There were no age and sex
differences between the two groups. Main
clinical conditions on admission were
pulmonary edema, coma and convulsions
that were observed in 28, 28, and 16
patients of the oxime group compared with
16, 15 and 13 patients of the atropine alone
group, respectively. There were no
statistically significant differences between
them.

Oximes were given as obidoxime (158
patients), pralidoxime (24 patients) and
mixture of both (three patients) with a dose
of 0.25 to 38g (3.5±4.2g) based on severity
of poisoning (Fiurre 2). Atropine was given
based on the severity of intoxication in the
doses ranging from 16 to 4650 (314±567)
mg in the oxime group compared with 13 to
1685(205±214) mg in the group receiving
atropine alone. The atropine dose difference
between the two groups was significant
(P<0.05).

Serum cholinesterase (SChE) activities of
the patients were all lower than normal on
admission and were less than 200U/L in
46% of the patients (Normal value>2000U/L). There was a good
relationship between the clinical severity and

reduction of SChE. Reactivations of the
enzyme during treatment were different in
each group as shown in figures 3 and 4.
SChE reactivation was even quicker in the
group receiving atropine alone compared to
the oxime group, although the difference
was not statistically significant (figure 5).

Hospitalization days in the oxime group
were 4 to 19 (6.7±2.9) days. There was a
significant positive correlation between the
hospitalisation days and oxime doses
(r=0.5149, P<0.001) as shown in figure 6.

Mortality rate in the group of atropine
alone was 6(4.5%), whereas in the oxime
group was 15 (98.1%) patients. The
mortality rate in the obidoxime subgroup
was 12(7.6%) and in the pralidoxime
subgroup was 3(13%) as shown in figure 7.
However, there were no statistically
significant differences between the groups.
There was a small number of patients in the
pralidoxime subgroup, thus, statistical
analysis between the subgroups was not
carried out.

DISCUSSION & CONCLUSION

Since the clinical finding on admission of
the oxime group was not significantly
different from the group of atropine alone,
thus the two groups were comparable
clinically. However, atropine doses used in
the oxime group were significantly higher
than the group of atropine alone. It seems
that first of all the oxime group patients were
more severely intoxicated than the group of
atropine alone, secondly the use of oximes
did not reduce the atropine doses as previously reported\textsuperscript{(4)}. Similar hospitalisation days of the two groups suggest similar severity of intoxication. The significant positive correlation between the hospitalisation days and oximes particularly the obidoxime group may also have two different explanations: First, those patients who had received more obidoxime were more intoxicated. Second, the adverse effects of obidoxime have more morbidity and thus more hospitalisation days.

SChE reactivations were similar in both groups. It appears that oximes did not increase the reactivations previously reported\textsuperscript{(6, 7, 8)}.

The dose and duration of oxime therapy in Sri Lanka\textsuperscript{5} Study were evaluated in sufficient by the European colleagues\textsuperscript{9}. In the present study, we did not find any significant difference between the low and high doses of oximes.

Mortality rate was slightly higher in the oxime group than in the atropine alone. It can be concluded that oximes particularly obidoxime had no therapeutic effects on acute OP poisoning. However, a prospective double blind clinical trial is currently undertaken to investigate more carefully about the therapeutic effects of oxime in OP poisoning.

\textbf{REFERENCES}


