

Utilization of Dichlorvos and Trichlorfon in Salmonid Farming in Norway during 1981-1988

By K. Grave, M. Engelstad and N. E. Søli

Department of Pharmacology and Toxicology, Norwegian College of Veterinary Medicine, and Norwegian Medicinal Depot, Oslo, Norway.

Grave, K., M. Engelstad and N. E. Søli: Utilization of dichlorvos and trichlorfon in salmonid farming in Norway during 1981-1988. Acta vet. scand. 1991, 32, 1-7.

The main objectives of this investigation were to quantify the use of dichlorvos and trichlorfon in the treatment of salmon lice infestations, to evaluate the prescribing of these drugs, and to estimate possible changes in the salmon lice problem by use of drug statistics. This study has shown that the use of trichlorfon increased from 4.9 tons in 1981 to 28.3 tons in 1985. This figure declined to 3.2 tons in 1988. The use of dichlorvos increased from 0.3 tons in 1986 to 3.2 tons in 1988. The change in the prescribing from trichlorfon to dichlorvos has dramatically reduced the pollution caused by these substances in the marine environment. Moreover, if necessary safety rules are observed, this change reduces the exposure of the workers on fish farms to these drugs, and also reduces the possibilities of intoxications of the fish during the treatment procedure. The sales figures of dichlorvos and trichlorfon, related to the calculated biomass of farmed salmonids in the sea, indicate a dramatic increase in the salmon lice problem.

drug statistics; organophosphorus compounds; fish farming; morbidity; seasonal variations; salmon louse; pollution.

Introduction

The salmon louse, *Lepeophtheirus salmonis*, has become the major ectoparasitic problem in the marine farming of atlantic salmon (*Salmo salar*) and rainbow trout (*Oncorhynchus mykiss* Walbaum) in Norway. Untreated infestations cause significant damage to the fish when the parasite is present in large numbers. This may lead to considerable economic losses. The organophosphorus drug trichlorfon (Neguvon®), a weak inhibitor of cholinesterase (Nordgren *et al.* 1978, Ecobichon 1979), was introduced in 1974 for the treatment of salmon lice infestations (Anon. 1974, Håstein & Bergsjø 1976). In 1980 Neguvon® was registered by the Norwegian Medicines Control Authority for use in fish. Until recently, treatment with trichlorfon has been carried out using a me-

thod developed by Brandal & Egidius (1979).

In 1985, heavy mortalities occurred among salmonids after a controlled routine trichlorfon treatment (Salte *et al.* 1987). Furthermore, 3 incidents with high mortality in Atlantic salmon were reported (Røttereng *et al.* 1986, Horsberg *et al.* 1989), probably due to extensive formation of dichlorvos, a much more potent organophosphorous drug than trichlorfon (Ecobichon 1979, Samuelsen 1987). As a consequence of these events, the recommended dosage regime for trichlorfon was changed (Anon. 1987, Tørisen 1988).

In 1986, dichlorvos (Nuvan®) was introduced for the treatment of salmon lice infestations (Horsberg *et al.* 1986), and Nuvan® was approved for use in Norway in 1988.

The main objectives of the present study were to quantify the use of dichlorvos and trichlorfon in the treatment of salmon lice infestations, to evaluate the prescribing of these drugs, and to estimate possible changes in the salmon lice problem during 1981–1988 by use of drug statistics.

Materials and methods

Drugs used in fish farming in Norway have to be prescribed by a veterinarian and dispensed from a pharmacy. The pharmacies are supplied by a state-owned drug monopoly, Norwegian Medicinal Depot (NMD). Monthly sales figures of Neguvon[®] powder, containing 97 % trichlorfon, in 2.5 kg packages approved for fish were recorded by NMD during 1981–1988. The annual sales figures of Nuvan[®] emulsion, containing 500 mg dichlorvos/ml, were recorded in 1986, whereas monthly sales figures were recorded in 1987–1988. Annual and monthly sales figures expressed as kilogrammes of active substance of dichlorvos and trichlorfon were then calculated, and the results were defined as the annual and monthly use, respectively, of these drugs in salmonid farming.

To allow comparisons in the present and in future studies of the use of drugs against salmon lice infestations, m³ treatment solution was chosen as a unit of measurement. This unit was defined as g active substance (treatment dose) used in one m³ of a theoretical, standardized treatment solution. The treatment doses were chosen according to recommendations in the literature. The treatment dose for dichlorvos was set to 1 g/m³ water at temperatures ranging from 5–15°C (Horsberg et al. 1987, Tørisen 1988). For trichlorfon the treatment dose was set to 291 g/m³ water in 1981–1986, representing all temperatures (Brandal & Egidius 1979, Tørisen 1980, 1982, 1984, 1986). In 1987–1988 the

trichlorfon dose was set to 73 g/m³ water, representing a temperature range of 6–14°C (Anon. 1987, Tørisen 1988). Annual and monthly amounts in m³ of treatment solution were then calculated.

The annual treatment intensity against salmon lice was defined as the calculated amount in m³ treatment solution of dichlorvos and trichlorfon in year Y/calculated biomass of farmed salmonids in year Y. The corresponding monthly figures were defined as the calculated amount in m³ treatment solution of dichlorvos and trichlorfon each month in year Y/calculated biomass of farmed salmonids in year Y. The total biomass of the farmed salmonids in the sea 1981–1988 was calculated according to a model developed by Grave et al. (1987a).

Results

The amounts of trichlorfon and dichlorvos used to control salmon lice infestations in Atlantic salmon and rainbow trout during 1981–1988 are shown in Table 1.

Expressed as the calculated amount in m³ treatment solution used each year, dichlorvos was the most frequently prescribed drug during 1986–1988, increasing from 77 % in 1986 when the drug was introduced, to 99 % in 1988 (Fig. 1). The calculated amount treatment solution increased 190-fold from 1981–1988.

The annual treatment intensity defined as the calculated amount in m³ treatment solution of dichlorvos and trichlorfon in year Y/calculated biomass of farmed salmonids in year Y, increased 30-fold from 1981 to 1988 (Fig. 2).

The monthly variations in the treatment intensity of salmon lice infestations during 1981–1988 are shown in Table 2. In the period 1981–1985 and in 1988, treatment against salmon lice was most frequent in

Table 1. Use of dichlorvos (Nuvan® 500 mg/ml emulsion) and trichlorfon (Neguvon® 97 % powder, 2.5 kg) in kg active substance in salmonid farming in Norway during 1981–1988.

Drug	Year							
	1981	1982	1983	1984	1985	1986	1987	1988
Trichlorfon	4920	6300	9810	14820	28260	24860	7390	3190
Dichlorvos						250	1310	3200
Total	4920	6300	9810	14820	28260	25110	8700	6390

September or October, whereas in 1986–1987 a peak was recorded in August. NMD did not, however, record the monthly sales

figures of dichlorvos in 1986, and dichlorvos is therefore not included in Table 2 that year.

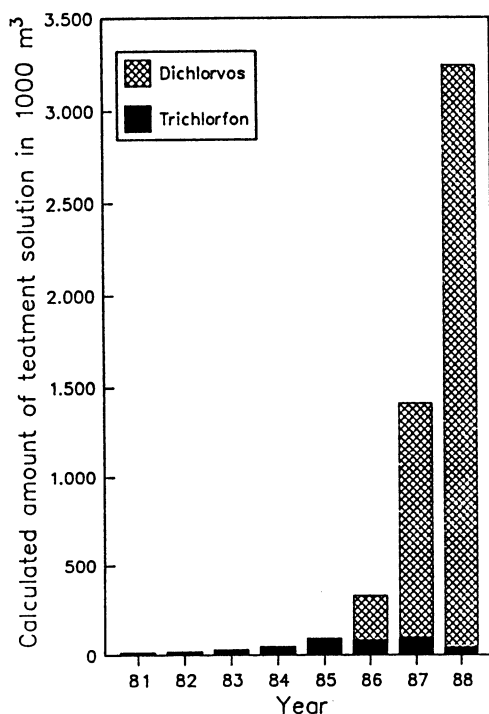


Fig. 1. The calculated amount in 1000 m³ treatment solution of dichlorvos (1 g/m³ water) and of trichlorfon (291 g/m³ water in 1981–1986; 73 g/m³ water in 1987–1988) used in the treatment of salmon lice infestations in salmonid farming in Norway during 1981–1988.

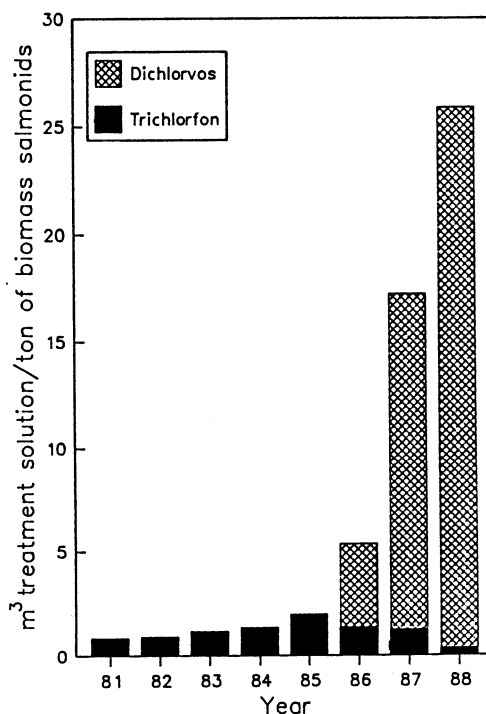


Fig. 2. The annual treatment intensity against salmon lice defined as the calculated amount in m³ treatment solution of dichlorvos and trichlorfon in year Y/calculated biomass of farmed salmonids in year Y in Norwegian salmonid farming during 1981–1988.

Table 2. Monthly variations in the treatment for salmon lice in salmonid farming in Norway during 1981–1988, defined as: calculated monthly amount in m³ treatment solution of dichlorvos (D) and trichlorfon (T) in year Y/calculated biomass of farmed salmonids in 1000 tons in year Y.

Drug	Year	Jan.	Febr.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sept.	Oct.	Nov.	Dec.
T	1981	6	1	4	29	10	105	83	74	104	284	142	40
T	1982	12	9	6	3	12	62	83	175	207	136	166	67
T	1983	31	8	25	31	104	143	66	160	156	323	117	37
T	1984	10	20	2	22	20	120	109	224	361	269	180	45
T	1985	56	28	6	29	32	115	273	341	516	381	186	39
T	1986	51	27	3	22	47	104	208	385	205	208	75	31
T	1987	0	8	8	2	0	81	300	169	322	152	112	86
D	1987	293	0	488	1403	73	391	1599	3270	2050	2916	2306	1208
T	1988	26	3	0	10	19	37	64	40	76	42	34	0
D	1988	1038	631	295	271	1293	663	5021	4422	5675	4135	1732	391

Discussion

Expressed as the calculated m³ treatment solution/calculated biomass of farmed salmonids, it is likely that the salmon lice problem increased 30-fold during 1981–1988. A part of the calculated 30-fold increase in the treatment intensity against salmon lice may be explained by a change in the treatment procedure used.

The recommended treatment method described by *Brandal & Egidius (1979)* involves transporting fish into a treatment unit consisting of a net-pen of 50–100 m³ capacity surrounded by a tarpaulin bag containing the treatment solution of trichlorfon. After the treatment period the fish are transported back to the original net-pen. By floating the treatment unit from net-pen to net-pen, the treatment solution can be used 8–10 times a day. This procedure can also be used to delouse with dichlorvos. However, this is a time- and labour-consuming process that needs 4–5 people a day to treat 8–10 pens, the equivalent of 25–40 tons of fish (*Brandal & Egidius 1979*).

During the last years there has been a tendency to change the treatment procedure (*Horsberg, T. E. personal communication,*

1989). Instead of using treatment units consisting of a net-pen surrounded with a tarpaulin bag (*Brandal & Egidius 1979*), the net-pen is surrounded by a plastic-skirt and a concentrate of dichlorvos or trichlorfon is added directly into the net-pen containing seawater. This method entails the treatment solution being used once, not 8–10 times as described by *Brandal & Egidius (1979)*. This change in the treatment procedure may explain as much as about 27-fold of the increase in the calculated m³ treatment solution/biomass of farmed fish during 1981–1988.

Theoretically, there is still a 3-fold increase in the treatment of salmon lice infestations that cannot be explained on the basis of a change in the treatment procedure. Part of the reason for this may be a tendency on the fish farms to treat more actively against salmon lice infestations. Still the calculated figures indicate that the salmon lice problem has increased dramatically. One explanation may be that the increasing number of fish farms has enhanced the frequency of transfer of salmon lice between farms. It is, however, important to realize that these figures are indirect measurements of the salmon lice

problem. Thus our results should be used as a basis for further investigations, not as the final conclusion on the development of the salmon lice problem in Norway.

The estimates of the monthly variations in treatment of salmon lice infestations (Table 2) showed that the problem existed throughout the year. The most intense treatment periods were, however, in August, September and/or October, as reported in Scottish salmonid farming (Wotten *et al.* 1982).

In this investigation, the treatment dose, i. e. the amount of drug as g active substance in one m³ of a theoretical, standardized treatment solution, was used to define "m³ treatment solution" as a unit of measurement. The treatment dose is not the real prescribed dose, and should be seen as a technical aid in the interpretation of drug statistics (Lunde *et al.* 1979). Because dichlorvos and trichlorfon are only used for one disease in salmonid farming, the prescribed dose may therefore be close to the recommended dose. The treatment dose for dichlorvos was chosen for temperatures ranging from 5–15°C, and for trichlorfon for temperatures ranging from 4–15°C. According to Wotten *et al.* (1982), the greatest numbers of *L. salmonis* occur on Scottish farmed salmon between May and October, with temperatures ranging from 9–14°C. As can be seen from Table 2 most of the delousing process takes place in late summer and autumn. The treatment doses chosen therefore cover most of the actual treatment situations.

When dissolved in seawater, trichlorfon is relatively rapidly transformed into the much more potent organophosphorus compound dichlorvos. Dichlorvos is responsible for the main part of the insecticidal effect of trichlorfon, and trichlorfon acts mainly as a slow-release formulation for dichlorvos (Ecobichon 1979, Nordgren *et al.* 1978, Hofer 1981, Samuelsen 1987). The degrada-

tion in seawater of trichlorfon is dependent on temperature, pH and aeration rate. At a temperature of 13.5°C, pH of 8.0 and a high aeration rate, the half-life of trichlorfon is reported to be 29 h (Samuelsen 1987). When using the treatment method described by Brandal & Egidius (1979), highly toxic concentrations of dichlorvos may be reached during the 8 to 10 h period the trichlorfon solution is recommended used. Dichlorvos is, however, transformed to nontoxic metabolites in sea water, the half-life is reported to be 93 h at a temperature of 13.5°C, a pH of 8.0 and a high aeration rate (Samuelsen 1987). This makes dichlorvos safer to use than trichlorfon, thus the change in the prescribing from trichlorfon to dichlorvos is preferable from a clinical point of view.

The molecular weights of trichlorfon (257.5) and dichlorvos (221), result in 1 kg of trichlorfon producing on average 0.85 kg dichlorvos. In clinical practice, 1 g of dichlorvos (5–15°C) corresponds to 73 g of trichlorfon (6–14°C), (Horsberg *et al.* 1987, Tørisen 1988). The change in the drug of choice from trichlorfon to dichlorvos has dramatically reduced the pollution caused by these substances in the marine environment.

Trichlorfon is only slightly soluble in water and has to be dissolved in a small amount of water by stirring vigorously for about 15 min before being added to the treatment unit or net-pen (Brandal & Egidius 1979). This process may expose the fish farmers to trichlorfon dust, and the drug may be absorbed through the skin or by inhalation. Of 141 prescriptions of Neguvon[®], the mean amount of prescribed drug was 36.5 kg (range 2.5–250 kg (Grave *et al.* 1987b), which is a relatively large amount to handle. As a liquid, Nuvan[®] is easier to handle, and the concentrate may be added directly to the treatment unit or net-pen. If the drug is handled correctly, the change of drug of

choice from trichlorfon to dichlorvos can therefore reduce the exposure of the workers on fish farms to organophosphorous drugs. However, due to its higher toxicity, the possibility of a fatal outcome in case of oral intake or other serious accidents with the concentrate would be higher. Thus, observation of safety rules in handling of Nuvan[®] concentrate is imperative.

The sales figures of trichlorfon used in salmonid farming in Norway during 1981-1988 is reported on the basis of 2.5 kg packages of this preparation. Trichlorfon is sold for use in other animals as well. These packages (Neguvon[®], powder of 0.1 and 1 kg) may also be prescribed or dispensed to Atlantic salmon and rainbow trout. However, the total annual sales figures of these package sizes varied between 1800 and 3600 kg in the period 1981-1988. Even if part of this amount had been used in salmons, it does not change the prescribing patterns for trichlorfon and dichlorvos in the treatment of salmon lice infestations. Sales figures of dichlorvos and trichlorfon are wholesale figures recorded by Norwegian Medicinal Depot, and do therefore not represent the real sales figures from the Norwegian pharmacies. The pharmacies, however, keep stocks of drugs only on a short-term basis (Halvorsen et al. 1979). The wholesalers' figures during 1981-1988 may therefore give a good estimate of the real use of dichlorvos and trichlorfon in Norwegian salmonid farming in this period.

Acknowledgement

This work was supported by a grants from the Norwegian Medicinal Depot and the Norwegian Agriculture Research Council. The authors thank the Norwegian Medicinal Depot for providing statistical data on the drugs.

References

- Anonymous*: Nytt doseringsregime for Neguvon[®] ved behandling av laks mot lakselus. (A new dosage regime for Neguvon[®] used in the delousing of salmon). *Nor. Vet. Tidsskr.* 1987, 99, 598.
- Anonymous*: Annual Report. Norwegian College of Veterinary Medicine, 1974, 172 pp.
- Brandal PO, Egidius E*: Treatment of salmon lice (*Lepeophtheirus salmonis*, Krøyer, 1838) with Neguvon[®]-description of method and equipment. *Aquaculture* 1979, 18, 183-188.
- Ecobichon DJ*: The chemical stability of trichlorfon in fresh and salt water as measured by changes in anticholinesterase potency. *Toxicol. Lett.* 1979, 3, 117-120.
- Grave K, Engelstad M, Söli NE, Håstein T*: Forbruk av antibiotika og kjemoterapeutika til oppdrettsfisk fra 1980-1986. (The use of antibiotics and chemotherapeutics in the treatment of farmed fish in Norway 1980-1986). *Nor. Vet. Tidsskr.* 1987a, 99, 527-534.
- Grave K, Engelstad M, Söli NE, Uhlving M*: For- skrivning av legemidler fra apotek til bruk på oppdrettsfisk. (Prescription of drugs from pharmacies used in fish-farming in Norway). *Nor. Vet. Tidsskr.* 1987b, 99, 873-878.
- Halvorsen IK, Halse M, Lunde PKM, Baksaas I, Strømnes B, Øydvin K*: Data collection in Norway. WHO Regional Office Publications 1979, *European Series no. 8*, 59-71.
- Hofer W*: Chemistry of metrifonate and dichlorvos. *Acta Pharmacol. Toxicol.* (Copenhagen) 1981, 49, suppl. V, 7-14.
- Horsberg TE, Berge GN, Høy T*: Avlusning av fisk med et nytt ektoparasittmiddel. (Delousing of fish with a new ectoparasitic drug). *Nor. Vet. Tidsskr.* 1986, 98, 333.
- Horsberg TE, Berge GN, Høy T, Djupvik HO, Hektoen H, Hogstad IM, Ringstad R*: Dichlorvos som avlusningsmiddel for fisk. Klinisk utprøving og toksisitetstestning. (Dichlorvos as a fish delousing agent. Clinical trial and toxicity testing). *Nor. Vet. Tidsskr.* 1987, 99, 611-615.
- Horsberg TE, Høy T, Nafstad I*: Organophosphate poisoning of Atlantic salmon in connec-

- tion with treatment against salmon lice. *Acta vet. scand.* 1989, *30*, 385–390.
- Håstein T, Bergsjø T: The salmon lice, *Lepeophtheirus salmonis*, as the cause of disease in farmed salmonids. *Ital. Piscic. Ittiopat.* 1976, *11*, 3–6.
- Lunde PKM, Baksaas I, Halse M, Halvorsen IK, Strømnes B, Øydvinn K: The methodology of drug utilization studies. WHO Regional Office Publications 1979, *European Series no 8*, 17–28.
- Nordgren I, Bergström M, Holmstedt B, Sandoz M: Transformation and action of metrifonate. *Arch. Toxicol.* 1978, *41*, 31–41.
- Røttereng PJ, Silset TO, Horsberg TE, Hektoen H: Massedød av laks etter avlusning. (High mortality in salmon after delousing). *Nor. Vet. Tidsskr.* 1986, *98*, 885–887.
- Salte R, Syvertsen C, Kjønnøy M, Fonnum F: Fatal acetyl-cholinesterase inhibition in salmonids subjected to a routine organophosphate treatment. *Aquaculture* 1987, *61*, 173–179.
- Samuelsen OB: Aeration rate, pH and temperature effects on the degradation of trichlorfon to DDVP and the half-lives of trichlorfon and DDVP in seawater. *Aquaculture* 1987, *66*, 373–380.
- Tørisen HM: The Norwegian Compendium of Veterinary Medicines 1980–1981, 6th. ed. I/S Farmainformasjon, Oslo, Norway 1980, 151 pp.
- Tørisen HM: The Norwegian Compendium of Veterinary Medicines 1982–1983, 7th. ed. I/S Farmainformasjon, Oslo, Norway 1982, 117 pp.
- Tørisen HM: The Norwegian Compendium of Veterinary Medicines 1984–1985, 8th. ed. I/S Farmainformasjon, Oslo, Norway 1984, 117 pp.
- Tørisen HM: The Norwegian Compendium of Veterinary Medicines 1986–1987, 9th ed. I/S Farmainformasjon, Oslo, Norway 1986, 118 pp.
- Tørisen HM: The Norwegian Compendium of Veterinary Medicines 1988–1989, 10th ed. I/S Farmainformasjon, Oslo, Norway 1988, 125 pp.
- Wotten R, Smith JW, Needham EA: Aspects of the biology of the parasitic copepods *Lepeophtheirus salmonis* and *Caligus elongatus* on farmed salmonids, and their treatment. *Proc. R. Soc. Edinb. [Biol.]* 1982, *81B*, 185–197.
- Sammendrag**
 Forbruk av dichlorvos og trichlorfon i norsk fiskeoppdrettsnæring i perioden 1981–1988. Målet med denne undersøkelsen var å kartlegge forbruket og å evaluere forskrivningen av dichlorvos og trichlorfon til behandling mot lakselusangrep i perioden 1981–1988. Videre var det ønskelig å estimere mulige endringer i lakselusproblemet i den samme perioden ved hjelp av disse forbrukstallene. Denne undersøkelsen viser at forbruket av trichlorfon økte fra 4,9 tonn i 1981 til 28,3 tonn i 1985 for så å reduseres til 3,2 tonn i 1988. Forbruket av dichlorvos økte fra 0,3 tonn i 1986 til 3,2 tonn i 1988. Denne forandringen i forskrivningsmønsteret har medført en dramatisk reduksjon i forurensningen av det marine miljøet med denne legemiddelgruppen. Så sant sikkerhetsregler blir etterlevet vil denne endringen i legemiddelvalg redusere yrkesmessig eksponering av disse stoffene. Den vil dessuten redusere faren for forgiftninger hos fisken. Salgstallene for dichlorvos og trichlorfon indikerer en dramatisk økning i lakselusproblemet i Norge.

(Received October 12, 1989; accepted February 21, 1990).

Reprints may be requested from: K. Grave, Department of Pharmacology and Toxicology, Norwegian College of Veterinary Medicine, P. O. Box 8146 Dep., N-0033 Oslo 1, Norway.