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Is prevention of acute pesticide poisoning effective and efficient, with Locally Adapted Personal Protective Equipment? A randomized crossover study among farmers in Chitwan, Nepal

Anshu Varma, Dinesh Neupane*, Jens P.E. Bonde**, Erik Jørs***

Department of Occupational and Environmental Medicine, Copenhagen University Hospital, Denmark; Department of Occupational and Environmental Medicine, Odense University Hospital, Denmark; NGO Dialogos/International Center for Occupational, Environmental and Public Health, Denmark

* Center for Global Health, Aarhus University, Denmark; NGO Nepal Development Society, Nepal; NGO Dialogos, Denmark

** Department of Occupational and Environmental Medicine, Copenhagen University Hospital, Denmark

*** Department of Occupational and Environmental Medicine, Odense University Hospital, Denmark

NGO Dialogos/International Center for Occupational, Environmental and Public Health, Denmark

Key words

Farmers; organophosphate; plasma cholinesterase; acute pesticide poisoning; personal protective equipment; randomized crossover study; Nepal

Parole chiave

Agricoltori; organofosfati; colinesterasi plasmatica; intossicazione acuta da pesticidi; mezzi di protezione individuale; studio crossover randomizzato; Nepal

Summary

Background: *Farmers' risk of pesticide poisoning can be reduced with personal protective equipment but in low-income countries farmers' use of such equipment is limited.* **Objective:** *To examine the effectiveness and efficiency of Locally Adapted Personal Protective Equipment to reduce organophosphate exposure among farmers.* **Methods:** *In a crossover study, 45 male farmers from Chitwan, Nepal, were randomly allocated to work as usual applying organophosphate pesticides wearing Locally Adapted Personal Protective Equipment or Daily Practice Clothing. For seven days before each experiment, each farmer abstained from using pesticides. Before and after organophosphate application, an interview surveys and blood tests were carried out, and analyzed with paired t-test, frequencies and percentages.* **Results:** *The difference between follow-up mean for acute organophosphate poisoning symptoms in the two groups was 0.13 [95% CI -0.22;0.49] and for plasma cholinesterase (U/ml) -0.03 [95% CI -0.11;0.06]. The difference between follow-up mean minus baseline mean for acute organophosphate poisoning symptoms in the two*

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Corrispondenza: Anshu Varma, Department of Occupational and Environmental Medicine, Bispebjerg Hospital, Bispebjerg Bakke 23, 2400 Copenhagen NV, Denmark - Tel. +4535316061, +4565414990

E-mail: anshu.dialogos@gmail.com, anshuvarma1985@gmail.com

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groups was 0.29 [95% CI -0.26;0.84] and for plasma cholinesterase (U/ml) -0.01 [95% CI --0.08;0.06]. Wearing the Locally Adapted Personal Protective Equipment versus Daily Practice Clothing gave the following results, respectively: comfort 75.6% versus 100%, sense of heat 64.4% versus 31.3%, other problems 44.4% versus 33.3%, likeability 95.6% versus 77.8%. **Conclusion:** *We cannot support the expectation that our farmers in Chitwan, Nepal working with Locally Adapted Personal Protective Equipment would have fewer acute organophosphate poisoning symptoms, higher plasma cholinesterase (U/mL) and find it more efficient to work with the equipment than farmers working with their Daily Practice Clothing. Based on the farmers' working behavior, compounds used, intensity and exposure duration we conclude that Locally Adapted Personal Protective Equipment does not provide additional protection during usual work practices. However, our Locally Adapted Personal Protective Equipment might offer protection from (certain) accidental overexposure. Trial Registration NCT02137317.*

Riassunto

«E' efficace e efficiente la prevenzione di avvelenamento acuto da pesticidi con una Attrezzatura Protettiva Personale Adattata Localmente? Uno studio crossover tra agricoltori di Chitwan, Nepal». **Introduzione:** *Il rischio di avvelenamento da pesticidi per gli agricoltori può essere ridotto con un'attrezzatura protettiva personale, ma nei paesi in via di sviluppo l'utilizzo di tale attrezzatura è limitato.* **Obiettivi:** *Scopo del presente lavoro è stato di esaminare la capacità dell'Attrezzatura Protettiva Personale Adattata Localmente al fine di ridurre l'esposizione a pesticidi organofosforici negli agricoltori.* **Metodi:** *In uno studio crossover, a 45 agricoltori maschi di Chitwan, Nepal, è stata fornita una Attrezzatura Protettiva Personale Localmente Adattata oppure un normale abito da lavoro mentre utilizzavano pesticidi organofosforici. Per i sette giorni prima dell'esperimento ciascun agricoltore è stato esonerato dall'impiego di pesticidi. Prima e dopo l'utilizzo di pestidici è stata effettuata un'intervista per la raccolta dei sintomi da intossicazione e un prelievo di sangue per la determinazione della colinesterasi plasmatica.* **Risultati:** *La differenza media tra i sintomi di avvelenamento acuto da organofosforici nel gruppo che indossava la Attrezzatura Protettiva Personale Localmente Adattata e quello che indossava un normale abito da lavoro era di 0.13 [95% CI -0.22;0.49] e tra i livelli di colinesterasi plasmatica (U/ml) era di -0.03 [95% CI -0.11;0.06]. La differenza media prima e dopo l'applicazione del pesticida per i sintomi da avvelenamento acuto era di 0.29 [95% CI -0.26;0.84] e per i livelli di colinesterasi plasmatica (U/ml) era di -0.01 [95% CI -0.08;0.06]. L'uso dell'Attrezzatura Protettiva Personale Adattata Localmente in confronto con l'uso del normale abito da lavoro ha mostrato meno comfort (75.6% contro il 100%), maggior sensazione di calore (64.4% contro 31.3%), generici problemi (44.4% contro 33.3%), e maggior gradimento (95.6% contro 77.8%).* **Conclusioni:** *Non possiamo avvalorare l'attesa che l'Attrezzatura Protettiva Personalizzata Adattata Localmente abbia portato ad una diminuzione dei sintomi da avvelenamento da organofosforici o ad un aumento della attività della colinesterasi plasmatica (U/mL) e neppure che i lavoratori preferiscano lavorare con questa attrezzatura rispetto ai normali abiti da lavoro. Da quanto riscontrato in questo studio l'Attrezzatura Protettiva Personale Adattata Localmente non offre protezione particolare durante le normali condizioni lavorative. Ciò non esclude che tale attrezzatura possa offrire maggiore protezione in caso di sovraesposizione accidentale.*

Abbreviations

AOPS, acute organophosphate poisoning symptoms; PPE, personal protective equipment; PChE, Plasma Cholinesterase

Background

Widespread use of pesticides and their ability to cause an estimated three million pesticide poisonings each year is a public health concern (14, 20, 43). In the short term, pesticide poisoning can lead to adverse health effects such as: headache, dizziness, bradycardia, weakness, anxiety, excessive sweating, fasciculation, vomiting, diarrhea, abdominal cramps, dyspnoea, miosis, paralysis, salivation, tearing, ataxia, pulmonary oedema, confusion, and acetyl cholinesterase inhibition. In the long term, carcinogenesis, developmental abnormalities, neurological and reproductive difficulties are seen (43). Farmers have a particularly high risk of pesticide poisoning because

their work directly involves pesticide use for crop protection (8). In low-income countries, where populations are largely agriculturally based and there is inadequate regulation, enforcement, surveillance, training, information access and use of personal protective equipment (PPE), the annual incidence rates of acute pesticide poisoning are expected to be much higher than in low-income countries (18.2 per 100.000 full time agricultural workers in low-income countries) (10).

Reducing farmers' use of pesticides significantly in low-income countries requires that secure and cost-effective alternatives be readily introduced (19). This is an ongoing and lengthy process, which should undoubtedly be supported. However, we also believe it is important that the numerous farmers, who are still using health hazardous pesticides and are expected to do so in the near future, can protect themselves. Since pesticides enter the body through dermal, oral and inhalation routes, PPE can minimize this exposure and consequently reduce the farmers' risk of pesticide poisoning (8). Unfortunately, in low-income countries recommended PPE is not widely used by farmers (2, 4, 11, 12, 15, 16, 18, 23, 28-31, 33, 35, 36, 39, 40-42, 45) for several reasons: unawareness (12, 39, 40), heat and humidity discomfort (31, 40, 41, 45), considered unnecessary (23, 41, 45) and unaffordable (23, 39, 45), unavailable (4, 23, 45) and belief that it causes illness (31).

To our knowledge, only a few studies have examined the effect of PPE among farmers using health hazardous pesticides in low-income countries with hot and humid climates (6, 17, 21, 22, 37, 38), moreover such studies were poor because: i) sample size calculations were not reported (6, 17, 21, 22, 37), ii) pesticide exposure time from handling, mixing, loading to spraying was not reported (6, 22, 37, 38), iii) none/few potential confounders were taken into account (6, 17, 21, 22, 37), iv) full body protection was not tested (6, 21, 37, 38), v) no efficiency factors were considered post trial (21, 22, 37) and vi) no comparison with another PPE solution was made (22, 37).

Our study's main purpose was to examine the effectiveness and efficiency of Locally Adapted PPE to reduce farmers' organophosphate exposure in Chitwan District, Nepal. It was expected that farmers working in Locally Adapted PPE would have fewer Acute Organophosphate Poisoning Symptoms (AOPS), higher Plasma Cholinesterase (PChE) U/mL and find it more efficient to work with the equipment than farmers working in their Daily Practice Clothing.

Methods

Area

Chitwan District was selected specifically because it is one of the highest vegetable growing districts in Nepal (13), a country where pesticide use among farmers suggests hazardous exposures and poisonings (3, 32). Furthermore, vegetable farmers from Chitwan reported a higher number of AOPS and lower acetyl cholinesterase levels than a control group of blood donors (28). Chitwan's District Agricultural Office identified ten pocket villages with pesticide issues. Based on seasonal crop type, logistics and infrastructure, local experts advised us to focus on four pocket villages.

Inclusion and Exclusion Criteria

Male farmers, minimum 18 years old, growing crops reaching a maximum height up to the abdomen, willing to spray with organophosphate pesticides for approximately 1.5-3 hours, involved in farming for a minimum of two years, experienced in organophosphate spraying at least once in two weeks on average, and using a hand pressured backpack sprayer were included. Farmers were excluded if they: had a helper, had experienced liver disease/damage, alcoholic/viral hepatitis, acute infection, chronic malnutrition, heart attack, metastasis, obstructive jaundice, inflammation pyridostigmine drug use, abnormal PChE (≤ 1.04 U/ml) (7, 24), or were unwilling to comply with study conditions.

Design and Sample Size

A randomized crossover study design was applied (figure 1). Sample size calculations were based on a study measuring AOPS pre/post a spraying session

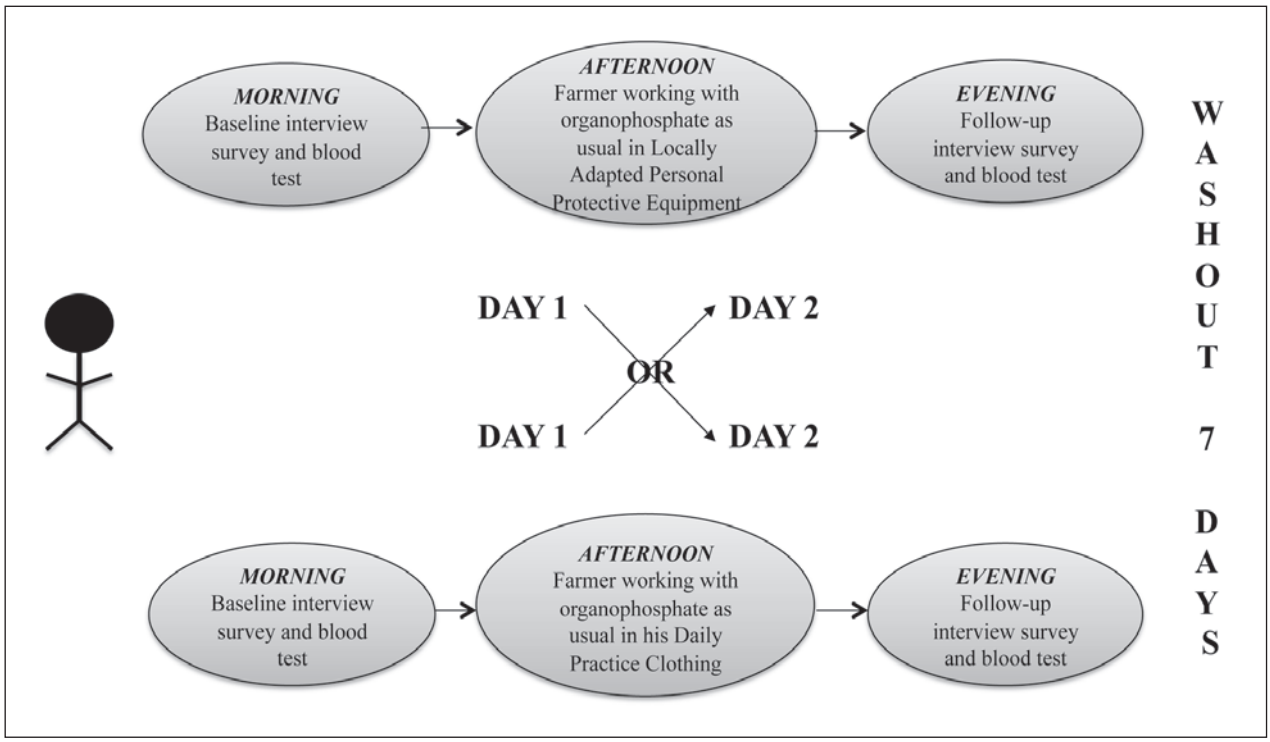

Figure 1 - Randomized crossover study design. Each farmer is randomized to partecipate in the first experiment on the first experiment day working with organophosphate wearing Locally Adapted PPE or their Daily Practice Clothing. Seven days before each experiment day each farmer stays pesticide free

on the same day during daily practice conditions, among 25 farmers from Chitwan - mean (standard deviation): pre-spraying=1.08(1.32), post-spraying=2.4(1.87), p-value<0.01) (27). We expected the pre/post spraying results to indicate AOPS experienced among farmers wearing Locally Adapted PPE and Daily Practice Clothing, respectively. In SAS 9.3, PROC POWER estimated 34 pairs (paired mean=1.08,2.4; paired standard deviation=1.32,1.87; correlation=0; sides=1,2; alpha=0.05; power=0.9). Considering dropouts, technical issues and co-variables, 25% of the sample size was added, rounded off to 45 pairs.

Recruitment

Farmers are usually organized in cooperative groups at village level in Chitwan. Thus, each cooperative's management has an overview of the farmers' crops in their respective village. Based on participation criteria, 45 farmers were identified by the management in the farmers' cooperatives of the four pocket villages. The principal investigator, a local nurse and a local mobilizer visited each farmer before data collection to verify his participation criteria, trade name of his usual organophosphate pesticide, and his willingness to comply with the study conditions and to gain informed consent.

Randomization Schedule and Allocation Concealment

Prior to data collection, each farmer's participation on the first of two experiment days was randomized to wearing Locally Adapted PPE or his Daily Practice Clothing. The principal investigator prepared 45 physical cards numbered 1 to 45. All cards had back and front covered and were placed in one main bucket. Under the principal investigator's supervision, a person uninvolved in the study stood in front of the main bucket and two similar empty buckets unaware of what was written on the underside of the

two empty buckets (Locally Adapted PPE/Daily Practice Clothing schedule or Daily Practice Clothing/Locally Adapted PPE schedule) (personal communication Saroj Adhikari). Blindfolded, the uninvolved person decided in which of the two empty buckets the first card from the main bucket should be placed. The next card from the main bucket was placed in the other empty bucket and so on. Upon completion the identity of both filled buckets with a 49/51 card partition was disclosed. The uninvolved person wrote the given schedule on each card, covered the front and back, and placed it in an opaque sealed envelope (DaklaPack CoverPlus Kuvert A5/C5) writing the card number on the envelope. All sealed envelopes were kept in a box supervised by the principal investigator.

Locally Adapted PPE

The Locally Adapted PPE was defined based on guidelines from the World Health Organization (8), Food and Agricultural Organization (9) as well as on informal input from local/international agronomists [personal communication Erik Jørs, Mette Jørgensen, Lars Jørgensen, Per Gummer Andersen, Erik Kirknel, and Sundar Tiwari], local PPE/textile retailers and farmers. As a result, for inner body protection the farmer wore over his underwear: a tailored cotton shirt and trousers, cotton socks, cotton handkerchief covering the forehead, cotton mask and cotton gloves. For outer body protection the farmer wore: a bamboo hat, transparent paper face shield fixed with elastic band, rainproof cape, calf height unlined rubber boots and latex gloves, and supplied with a 20 ml syringe with which to draw organophosphate. All items were available at the main market in Chitwan and purchased at a total cost of 1.890 Nepali Rupees (approximately 20 US dollars) per set of Locally Adapted PPE (38). A new commonly used hand pressured backpack sprayer (Shakti 16 liter Compact Knapsack Sprayer) was lent to each farmer.

Data Collection

During the winter season 2014/2015 the principal investigator and local nurse visited each farmer in his home over two full experiment days. The farmer was instructed to abstain from working with pesticides for seven days before each experiment day, because according to the World Health Organization "*An acute pesticide poisoning is any illness or health effect resulting from suspected or confirmed exposure to a pesticide within 48 hours*" (43). In the seven days prior to each experiment day, the farmer was contacted regularly by the local nurse, reminding him to abstain from using pesticides. Based on the chronological date of the farmer's first experiment day, the numbered sealed envelope was chosen and brought to the farmer's home on his first experiment day. The local nurse opened the envelope in front of the farmer before initiating data collection and then carried out a baseline interview survey and blood test. The principal investigator and local nurse instructed the farmer to wear either Locally Adapted PPE or his Daily Practice Clothing, according to the already disclosed randomization schedule. Once ready, the farmer was given a newly purchased container of organophosphate matching what he usually used (Dichlorvos, Triazophos, Chlorpyrifos or Dimethoate) and he was observed applying it in the dose/dosages that he usually found necessary (average 0.9-2.6 ml per liter water) (See online Supplementary file 1 and 2). Thereafter, his usual work during spraying was observed. A minimum of 2 h 30 min after the farmer's work had been completed the local nurse carried out a follow-up interview survey and blood test. By the end of the second experiment day, the local nurse and farmer signed a document stating that the sealed envelope had been opened in front of the farmer and that he participated as per the designated randomization schedule (See online Supplementary file 3).

The World Health Organization's definition of AOPS was applied, in some cases with explanations: bradycardia (extreme tiredness, weakness, dizziness), fasciculation (trembling hands), abdominal cramps (abdominal pain), dyspnoea (respiratory difficulties), miosis (blurred vision), ataxia (lack of coordination), pulmonary oedema (respiratory difficulties) (43). Based on local health care experience, skin irritation and dry mouth were added. Due to AOPS' broad nature, teeth pain, nasal bleeding, voiding urge, low back pain, elbow pain and ankle pain were added as

"fake" AOPS. Data on AOPS were collected with the following item in the interview survey, previously applied in other surveys (15,27): "*Do you have any of the following symptoms? (Yes/No)*".

PChE (U/mL) activity is considered a useful indicator of immediate organophosphate exposure (24). Dichlorvos, Triazophos, Chlorpyrifos and Dimethoate are expected to inhibit PChE (U/mL) (34). Data on PChE (U/mL) were collected with blood tests using a self-contained and portable Test-Mate Che Cholinesterase System (Model 400) following the instruction manual (7). All blood tests were conducted in an air-conditioned vehicle under 15-30°C, and retaken if any errors were detected.

Efficiency was defined by comfort, heat, other problems and likeability (6). Data on efficiency were collected with the following items, based on a previous study (6) with minor changes: "*Was it comfortable?*", "*Did it feel hotter?*", "*Any problem when spraying?*", "*Did you like the garments?*" all with yes/no response categories.

Background information was age, marital status, ethnicity, education, farming experience, pesticide experience, crop type, spraying surface, alcohol, smoking, chronic illness, height, weight, temperature, humidity, and work practice. Data on background information were collected with open and closed items, based on previous surveys (25,27), checklist observations from experts [personal communication Erik Jørs, Mette Jørgensen, Lars Jørgensen, Per Gummer Andersen] and previous studies (5), and online weather forecast monitoring (1).

The Locally Adapted PPE (figure 2), informed consents (See online Supplementary file 4) and interview survey (See online Supplementary file 5) were all pre-tested on five farmers fitting the inclusion and exclusion criteria. The blood test procedure was pre-tested 20 times on volunteers from the research team, relatives or volunteers from the Nepal Red Cross Society Blood Bank Laboratory Assistants' Team.

Figure 2 - A volunteer modeling how each farmer wore the Locally Adapted PPE

Data Preparation

Data was entered twice in Microsoft Excel, by the principal investigator and local nurse. The former matched both databases in SAS 9.3 with PROC COMPARE. A 'phone number digit and word spacing differed for two respondents. Otherwise, no missing or unrealistic values were found, text lengths covered all text and cross checks did not warrant corrections. New variables were created for efficient data interpretation and their construction is explained based on item numbers in the interview survey: body mass index (b10/(b11*b11)), organophosphate hazard category (manual classification of e16's common name based on World Health Organization's Hazard Classification (44)), randomization order (c1<f1 or f1>c1), total organophos-

phate dose (sum of d4 or g10), total liters of water (sum of d4 or g10), exposure time (d7-d3 or g7-g3), follow-up time (e1-d7 or h1-g7), crop type (number of each crop based on e11 or h11), crop height (sum of e12 or h12), humidity (d2+d9), temperature (d1+d8). An overall work practice sum score from 1-15 was constructed; the higher the sum score the higher the number of poor work practices observed/reported. The sum score was based on 15 work practice items with yes/no response categories (d5, d6, e15 or g5, g6, h15). An overall AOPS sum score from 1-19 was constructed; the higher the sum score the higher the number of AOPS reported. The sum score was based on 19 AOPS items with yes/no response categories excluding "fake" AOPS (c4, e2 or f4, h2). Further details on variable editing can be obtained upon request to the main author.

Data Analysis

In SAS 9.3, analyses were conducted with frequencies (PROC FREQ), percentages (PROC UNIVARIATE) and Paired T-tests (PROC TTEST). A 5% statistical significance level and 95% confidence interval were set. The normality assumption was checked. Sensitivity analyses were conducted on farmers without known medical conditions or "fake" AOPS.

Ethics

Prior to the start of the study, approval was obtained from Nepal Health Research Council [Reg. no.: 99/2013], the Danish Ethics Committee [Case no.: 1402439] and Chitwan District Offices of Agriculture and Public Health [personal communication Kamal Wagle and Kehar Singh Godar]. The study was registered at ClinicalTrials.Gov [Identifier: NCT02137317]. Informed consent was obtained from each farmer before data collection. Completed interview surveys were stored confidentially, analyzed in anonymized formats and shredded upon study completion. Anonymized data on the Test Mate ChE Cholinesterase System (Model 400) was automatically deleted after power switch-off. The Nepal Red Cross Society Blood Bank provided disposal facilities for the used blood test materials.

Results

In general, the farmers were married (86.7%), belonged to upper caste (62.2%), had basic education (77.8%), had no medical conditions (93.3%), took no medicines (93.3%), did not smoke (80%) or drink (84.4%). On average the farmers were 40.9 years old (18-61 years), had body mass index 22.5 (17.7-30.7 kg/m^2), were in farming for 16.6 years (3-41 years), used pesticides for 14.8 years (3-35 years) and currently applied organophosphates that were highly (51.1%) or moderately (48.9%) hazardous. On the first experiment day 22 farmers wore Locally Adapted PPE and 23 Daily Practice Clothing (See online Supplementary file 1). All farmers wore the Locally Adapted PPE and, in general, the farmers did not protect all body parts with their Daily Practice Clothing (table 1). Work characteristics (dose, water in sprayer, exposure time, follow-up time, spraying surface, temperature, humidity, poor work practices, crop height and crop type) did not differ considerably between farmers while working wearing Locally Adapted PPE or their Daily Practice Clothing (See online Supplementary file 2). Fewer AOPS, higher PChE (U/mL) or more efficiency was not observed among farmers working in Locally Adapted PPE compared to farmers working in their Daily Practice Clothing; more problems were reported with the Locally Adapted PPE than with Daily Practice Clothing, however a burning and itching sensation was only reported when wearing the latter (table 2-4).

Discussion

Interpretation of AOPS, PChE (U/mL), Efficiency and Earlier Studies

Our study does not support the expectation that farmers working with Locally Adapted PPE would have fewer AOPS and higher PChE (U/mL) than farmers working in their Daily Practice Clothing. We propose six possible explanations. *i)* A Hawthorne Effect can make study participants change their behavior because they are being observed (26). Thus, the farmers may have been more cautious

Table 1 - Characteristics of Locally Adapted PPE[a] and Daily Practice Clothing for male farmers, Chitwan District, Nepal

	Locally Adapted PPE[a]		Daily Practice Clothing	
	n	%	N	%
Gloves				
- yes	45	100	5	11.1
- no	0	0	40	88.9
Boots				
- yes	45	100	12	26.7
- no	0	0	33	73.3
Mask				
- yes	45	100	22	48.9
- no	0	0	23	51.1
Hat/cap				
- yes	45	100	22	48.9
- no	0	0	23	51.1
Goggles				
- yes	45[b]	100	3	6.7
- no	0	0	42	93.3
Long sleeved shirt				
- yes	45	100	31	68.9
- no	0	0	14	31.1
Long trousers				
- yes	45	100	31	68.9
- no	0	0	14	31.1
Apron/clothing over shirt/trousers				
- yes	45[c]	100	14	31.1
- no	0	0	31	68.9
Local practice				
- yes	45	100	16[d]	35.6
- no	0	0	29	64.4

[a] Personal Protective Equipment; [b] Face shield; [c] Waterproof cape; [d] Towel/scarf around neck (n=5), borah/plastic/towel between back and sprayer (n=7), circular head clothing (n=2), head band (n=1), skirt around legs (n=1)

about avoiding major spilling accidents. Or ongoing training in Integrated Pest Management, even if in different villages, could have provided the farmers with pesticide safety knowledge prior to study participation. *ii)* Weather can influence clothes worn and pesticide absorption (8). Thus, the cooler than locally expected winter season might have made the farmers wear more/thicker clothes for their Daily Practice Clothing, and since hot and sweaty skin absorbs pesticides more quickly than cool skin (8), less organophosphate may have been absorbed by the farmers' skin. *iii)* A Healthy Worker Effect can exclude severely ill/disabled workers from working (26). Thus, the farmers' who became sick from pesticides might have left the field already or shifted to organic farming. *iv)* Acute pesticide poisoning can occur within 48 hours after confirmed exposure (43). Thus, the farmers' time window to experience AOPS and reduced PChE (U/mL) may have been too short. *v)* Self-reporting can make it difficult for laymen to respond (26). Thus, the farmers's memory might have been lacking, they became "mentally" immune to certain AOPS or confused AOPS with common illnesses. *vi)* Chance may be an explanation.

Table 2 - PChE[a] (U/mL) and AOPS[b] for male farmers, Chitwan District, Nepal, by Locally Adapted PPE[c] and Daily Practice Clothing (SD=standard deviation; Min.=minimum; Max.=maximum)

			Baseline						Follow-up			
	n	%	Mean	SD	Min.	Max.	n	%	Mean	SD	Min.	Max.
PChE[a] (U/mL)												
- Locally Adapted PPE[c]	45	100	1.7	0.4	1	2.3	45	100	1.6	0.4	0.6	2.3
- Daily Practice Clothing	45	100	1.7	0.4	0.7	2.4	45	100	1.6	0.4	0.5	2.2
AOPS[b,d]												
- Locally Adapted PPE[c]	45	100	1.1	1.6	0	7	45	100	1.2	1.5	0	6
- Daily Practice Clothing	45	100	1.2	1.8	0	7	45	100	1.1	1.5	0	6

[a] Plasma Cholinesterase; [b] Acute Organophosphate Poisoning Symptoms; [c] Personal Protective Equipment; [d] Overall score from 1-19 (19 total AOPS with yes/no response excluding fake and non-pesticide poisoning related symptoms in the "other" category), the higher the score the higher the number of AOPS reported

Table 3 - Efficiency by Locally Adapted PPE[a] and Daily Practice Clothing for male farmers, Chitwan District, Nepal

	Locally Adapted PPE[a]		Daily Practice Clothing	
	n	%	n	%
Comfort				
- yes	34	75.6	45	100
- no	11	24.4	0	0
Hotter				
- yes	29	64.4	14	31.1
- no	16	35.6	31	68.9
Problems				
- yes	20[b]	44.4	15[c]	33.3
- no	25	55.6	30	66.7
Likeability				
- yes	43	95.6	35	77.8
- no	2	4.4	10	22.2

[a] Personal Protective Equipment; [b] Difficulties with sight (n=10); heat sensation (n=6); water absorption (n=4); breath (n=4); smell (n=3); syringe (n=2); sprayer (n=1); [c] Difficulties with smell (n=13); burning/itching sensation (n=2)

All earlier studies, except one where no comparison was made with another PPE solution (22), concluded a difference in pesticide exposure when examining the effect of cotton garments vs cotton garments with repellent finish (37, 38) or cotton garments vs Polypropylene Kleenguard/Comfitak Coveralls (6, 21). However, the contrast in these studies' PPE comparisons might be greater than in our study, since cotton with repellent finish or coveralls could be perceived as advanced materials. Furthermore, extraction methods quantifying pesticide by magnitude/time were used, and organophosphate was examined in only two of the studies (6,37).

Thus, despite the valid combination of AOPS and PChE (U/mL) as a biomarker for pesticide exposure it appears not to be sensitive enough since the difference between farmers wearing Locally Adapted PPE and Daily Practice Clothing was not considerable. Based on the farmers' working behavior compounds used, intensity and exposure duration we conclude that the Locally Adapted PPE does not provide additional protection during usual

Table 4 - Association between PChE[a] (U/mL) and AOPS[b] with Locally Adapted PPE[c] and Daily Practice Clothing for male farmers, Chitwan District, Nepal (CI=confidence interval)

			Paired T-test	
	n	%	Mean Difference	95% CI
PChE[a] (U/mL)				
- Unadjusted[d]	45	100	-0.03	(-0.11;0.06)
- Adjusted for baseline value[e]	45	100	-0.01	(-0.08;0.06)
- Locally Adapted PPE[c]/Daily Practice Clothing[d]	22	49	-0.01	(-0.11;0.10)
- Daily Practice Clothing/Locally Adapted PPE[c, d]	23	51	-0.05	(-0.19;0.10)
- Sensitivity[e, f]	42	93	-0.02	(-0.10;0.05)
- Sensitivity[e, f]	18	40	0	(-0.12;0.13)
AOPS[b, g]				
- Unadjusted[d]	45	100	0.13	(-0.22;0.49)
- Adjusted for baseline value[e]	45	100	0.29	(-0.26;0.84)
- Locally Adapted PPE/Daily Practice Clothing[d]	22	49	0.18	(-0.34;0.70)
- Daily Practice Clothing/Locally Adapted PPE[c, d]	23	51	0.09	(-0.43;0.61)
- Sensitivity[e, f]	42	93	0.29	(-0.27;0.84)
- Sensitivity[e, f]	18	40	0.40	(-0.23;1.01)

[a] Plasma Cholinesterase; [b] Acute Organophosphate Poisoning Symptoms; [c] Personal Protective Equipment; [d] Difference between follow-up mean in both groups; [e] Difference between follow-up mean minus baseline mean in both groups; [f] No medical conditions (n=42); No "fake" AOPS at baseline (teeth pain/nasal bleeding/voiding urge/low back pain/elbow pain/ankle/pain/other) (n=18); [g] AOPS[b] overall score 19 total AOPS[b] with yes/no response excluding "fake" AOPS[b], the higher the score the higher the number of AOPS[b] reported

work practices. However, our Locally Adapted PPE might offer protection from (certain) accidental overexposures. Based on the farmers' comments in open items (table 3) and informal observations of the principal investigator and local nurse, we highlight pros and cons of the Locally Adapted PPE to put into perspective the conclusion that our study does not support the expectation that farmers working with Locally Adapted PPE would find it more efficient to work than farmers working in their Daily Practice Clothing. The Locally Adapted PPE was reasonably priced, estimated to be a half-yearly total purchase. All materials were locally available and usually easy to find except for unlined boots. Nearly all farmers reported that they liked the Locally Adapted PPE, even more than their Daily Practice Clothing (table 3). The overall look and function of particularly the gloves, boots and tailored cotton shirt and trousers seemed to be appreciated from a cultural and heat perspective. Furthermore, a burning/itching sensation was only reported by farmers working in their Daily Practice Clothing (table 3). The face shield did not always afford enough breathing passage, which occasionally created mist inside the shield, also making it difficult to see. The dark color of the rainproof cape, farmers' habit of taking no/few breaks and overfilling the sprayer caused excessive heat sensation. Spraying low crops wearing calf-height rubber boots in some cases soaked the lower part of the farmers' cotton trousers making them heavy to walk with. Extra effort was needed when using a metal tool to open the organophosphate container while wearing gloves, using the syringe, or carrying the sprayer over unfamiliar clothes.

Only two earlier studies evaluated efficiency post trial and unlike our study, those farmers reported that both types of PPE solutions worn were equally comfortable (6, 38), there were no general difficulties with face shields except reflection occurring from white garments worn, and nitrile gloves were uncomfortable to wear (6). However, sweating made garments cling to the body (38), face shields were only worn during mixing/loading (6) and crops were at least double the height of our crops, and the PPE solutions were worn over several days (6, 38).

Modifications in our Locally Adapted PPE should be considered, and its pros and cons could afford some guidance. There may be scope for farmers to become used to some of the Locally Adapted PPE's limitations which seem conditional given, that its effectiveness and efficiency in protecting against acute organophosphate poisoning is scientifically proven and awareness of personal protection from pesticide exposure is widespread. Overall, PPE is only one aspect of personal protection, and to reduce pesticide exposure it should be used and maintained appropriately as well as accompanied by behavioral and spraying safety practices (8).

Major Study Strengths and Limitations

A realistic occupational health intervention was examined, by defining the Locally Adapted PPE based on a participatory approach and measuring its effect under the farmers' usual working conditions. Moreover, the influence of other factors was considerably reduced with randomization, farmers' acting as their own controls and observation of the farmers' work. However, our study is not without limitations. *i)* Blinding the principal investigator, local nurse or farmers was not considered practical. Thus, there is a genuine risk that not only the farmers' response, but also the active participation of the principal investigator and local nurse might have influenced the results. However, standardized experiment guidelines, an objective outcome measure and a predefined analysis strategy should have reduced this risk considerably. *ii)* Carry-over effects can never be completely removed. Thus, there is a risk of difference in the carry-over effect from wearing Locally Adapted PPE and Daily Practice Clothing and vice versa. However, the abstaining period of a minimum of seven days and baseline measurements mitigate any serious concern about potential differential carry-over effects. *iii)* Sampling with non-probability methods reduces the degree of generalization of the main results to farmers from other pocket villages, districts and countries. However, local and international experts in the farming and health field of low-income countries support the contention that the farmers in our study resembled some typical farmers using health hazardous pesticides in low-income countries at present [personal communication Erik Jørs]. *iv)* Efficiency was only tested once, which challenges our understanding of the Locally Adapted PPE's long-term potential. However, in general we observed that reasonably priced locally available materials are known to be of low quality, and therefore it would be essential to regularly replace parts of the Locally Adapted PPE.

Conclusion

The expected result that farmers working with Locally Adapted PPE would have fewer AOPS, higher PChE (U/mL) and find it more efficient to work than farmers working with their Daily Practice Clothing cannot be supported by our study, made among farmers in Chitwan, Nepal. Based on the farmers' working behavior, compounds used, intensity and exposure duration we conclude that the Locally Adapted PPE does not provide additional protection during usual work practices. However, our Locally Adapted PPE might offer protection from (certain) accidental overexposure. Difficulties with breathing, visibility, humidity and heat sensation should be taken into account when improving its efficiency. Thus, future research could consider efficiency modifications in our Locally Adapted PPE and re-test it to reduce current potential methodological issues, or fundamentally rethink the concept of Locally Adapted PPE.

Conflict of interest

All authors declare they have no competing interests. However, this publication may be influenced by our managerial and membership affiliations to the non-commercial NGOs, Dialogos, Nepal Development Society, and International Center for Occupational Environmental and Public Health.

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