Biologic Material in Needles and Cartridges After Insulin Injection With a Pen in Diabetic Patients

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OBJECTIVE — To evaluate the frequency of non-inert material, including cells, in needles and cartridges after insulin injection with pen-like devices in diabetic patients.

RESEARCH DESIGN AND METHODS — A prospective study was conducted in 120 insulin-treated diabetic patients who used pen-like devices. The patients, 46 women and 74 men, were 20–77 years old; 60% had type 1 diabetes, and 38% were overweight. Duration of diabetes ranged from 1 month to 40 years, and insulin therapy ranged from 1 month to 30 years. Insulin injection was performed by a trained nurse, using the patient's usual pen and cartridge. A cytopathological examination was performed on the material obtained from the needle and found in the cartridge after centrifugation. All slides were read by a single investigator.

RESULTS — In 62% of the patients, non-inert material was found, including squamous (32%) and epithelial (58%) cells. Biologic material was found in 30% of the needles and 58% of the cartridges, and in both needle and cartridge in 25% of the population. Biologic material was found more frequently in patients who had a longer duration of diabetes, who were treated with insulin for a longer time, and who performed injection in the thighs or upper arms ($P < 0.05$). In multivariate analysis, the presence of biologic material was associated with the duration of diabetes ($R^2 = 0.09$; $P < 0.01$).

CONCLUSIONS — Our data suggest that biologic material can be trapped in the delivery system, including the cartridge, after an insulin injection with a pen-like device. Our results emphasize the strict need for individual use of insulin delivery systems, including cartridges and nonrefillable pens, especially in clinics and hospitals.

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Recommendations for the prevention of external contamination, including viral acquired infection, have emphasized the strict need for individual use of disposable materials for insulin injection (1). To improve the accuracy and convenience of insulin administration, patients can use pen-like devices and insulin-containing cartridges (1,2). However, pen-like devices may require special care because of such particular elements as removable needles and cartridges. For instance, it has been suggested that air can enter the cartridges after injection unless the needle is removed, leading to reduced delivery of insulin. Immediate removal of the needle has been proposed (3,4).

The fact that air bubbles can enter the cartridge suggests that other materials, including non-inert material, could do the same. The aim of this study was to determine whether biologic material was present in needles and cartridges from pen-like devices after insulin injection in diabetic patients.

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

RESEARCH DESIGN AND METHODS

— A prospective study was conducted in 120 consecutive insulin-treated diabetic patients during one of their regular ambulatory visits to the department. Patients were included if they used pen-like devices for their insulin injection and cartridges and needles as recommended by the pen manufacturer. Informed consent was obtained. The patients, 46 women (38%) and 74 men (62%), were 20–77 years old (mean ± SEM, 53.7 ± 1.3 years). On average, diabetes had been present for 12.7 ± 0.9 years (range, 1 month to 40 years). A clinical history of type 1 diabetes was found in 60% of the patients, whereas obesity (presumed type 2) was found in 38% of the population. Insulin therapy had been used for 6.4 ± 0.7 years (1 month to 30 years).

During the visit, each patient's insulin injection was performed by a trained nurse, using the patient's own pen and cartridge and a new needle. It was done without prior use of topical alcohol (5) and according to the usual procedures. The site of injection was determined by the patient's usual site rotation (6). After injection, the needle was drained off with 2 U of insulin, and a cytological slide was made. Slides were dried, and May-Grünwald-Giemsa staining was performed using an automated technique. Cartridges were centrifuged (4,000 rpm for 5 min). The same technique was then applied to the platelets. All slides were read by a single investigator.

To study external or prior contamination, 10 control cytological examinations were performed on new cartridges, using the same procedure except for the patient's injection.

Results are expressed as means ± SEM or %. Comparisons were done with Student's *t* test or the χ^2 test. A stepwise multiple logistic regression was performed to study the factors associated with the presence of non-inert material.

RESULTS

— Injection sites were the deltoid area in 8% of the patients, the upper arms in 56%, the thighs or buttocks in 5%, and the anterior wall of the abdomen in 31%. None of the patients had

Table 1—*Squamous and epithelial cells in needles and cartridges from 120 diabetic patients after a single insulin injection using pen-like devices*

	Squamous cells		Epithelial cells	
	Needle	Cartridge	Needle	Cartridge
No material	73	47	79	53
<5 elements per slide	10	16	11	14
5–20 elements per slide	14	33	7	28
>20 elements per slide	3	4	3	4

Data are %.

lipoatrophy, hypertrophy, or any cutaneous change. The BD-Pen was used with Umuline cartridges and BD-Microfine needles in 42% of the patients, the Omnipen was used with Insuman and Disetronic needles in 17%, the Novolet and Novopen3 was used with NovoNordisk insulin and Novofine needles in 37 and 4%, respectively. Short (8-mm) needles were used by 32% of the patients. Air bubbles were found in 45% of the cartridges. The remaining volume of the insulin solution in the cartridge was <25% in 30% of the patients, 25–50% in 25% of the patients, 50–75% in 32% of the patients, and >75% in 13% of the patients. Because of their usual habits, 54% of the patients had a cutaneous skinfold performed. Injection was performed at a 45° angle.

In 62% of the patients, non-inert material was found: squamous cells (32%) and/or epithelial cells (58%). Cells were found in 30% of the needles and in 58% of the cartridges; in 25% of the study population, cells were found in both the needle and cartridge (Table 1). Blood cells were not found. No material was found in the control cartridges.

The presence of cells was associated with a longer duration of diabetes (Table 2 and Fig. 1). It was found more frequently *1*) in patients treated with insulin for >15 or <2 years ($P < 0.05$) and 2) when the injection was performed in the thighs or buttocks (Table 2). The presence of cells was not significantly associated with whether a skinfold was made; the nature of the pen, insulin cartridge, or needle; the size of the needle; the presence of air bubbles; or the remaining volume of insulin solution in the cartridge (Table 2). Similar results were observed when different nurses performed the insulin injection. Among the six patients using a new cartridge for the first time, biologic material was found in four cartridges (67%, NS versus the others).

In multivariate analysis, the presence of biologic material was associated only with the duration of diabetes ($R^2 = 0.09$; $P < 0.01$).

CONCLUSIONS — Our data show that biologic material, including epithelial cells, can be found in needles and cartridges after an insulin injection in diabetic patients. Because external or prior contamination was not observed, these results indicate that biologic material can be aspirated from the skin or subcutaneous tissue, through the needle, and into the cartridge. This capture is not infrequent (two out of three patients in our study) and is often associated with a considerable number of cells.

Cells were found more frequently in cartridges than in needles. This finding could be due to total aspiration into the cartridge. Another possibility is contamination from a previous injection. However, the antiseptic products contained in the cartridge make previous contamination unlikely (7). Among the six patients using a new cartridge for the first time, the presence of cells had a similar frequency. However, a definite conclusion cannot be made, and a study designed to evaluate the length of time in which epithelial cells remain in the cartridges should be performed.

The capture of cells into the cartridge could be related to an increased pressure in the needle after puncture and before injection, to a reduced internal pressure in the cartridge after (versus during) the injection, and/or to temperature changes, causing cells to be drawn through the needle by the contracting insulin solution (3). In any case, rapid removal of the needle appears to be the appropriate action to prevent cells from entering the cartridge.

Table 2—*Factors associated with the presence of squamous or epithelial cells in needles and cartridges*

	Squamous or epithelial cells		Material in needles		Material in cartridges	
	No	Yes	No	Yes	No	Yes
Age (years)	53.5 ± 2.0	53.9 ± 1.7	53.0 ± 1.5	55.4 ± 2.5	55.7 ± 1.9	52.3 ± 1.7
Women	33	41	35	44	41	41
Obesity	28	30	26	35	34	25
Duration of diabetes (years)	10.1 ± 1.2	14.6 ± 1.3*	11.0 ± 1.1	16.5 ± 1.7*	10.2 ± 1.5	14.9 ± 1.2*
Duration of insulin therapy (years)	6.3 ± 0.8	6.5 ± 1.0	6.0 ± 0.7	7.3 ± 1.5	6.1 ± 0.8	6.6 ± 1.0
Injection site						
Arms/shoulders	32	68	67	33	39	61
Thighs/buttocks	0	100	20	80	20	80
Abdominal wall	54	46*	84	16*	51	49
Skinfold	42	50	65	50	55	53
Refillable pen	42	35	48	42	46	33
Air bubbles	59	52	44	50	38	51
Volume in insulin cartridge						
<50%	44	56	76	24	42	58
50–100%	49	51	61	39	43	57

Data are means ± SEM or %. *$P < 0.05$.

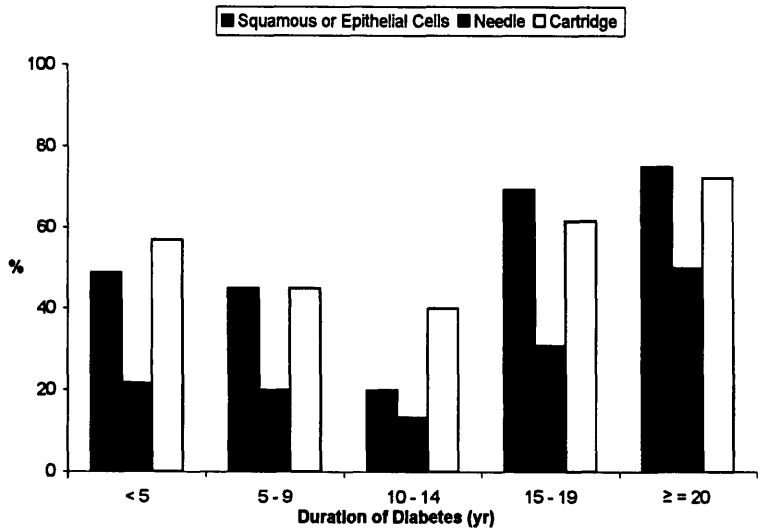

Figure 1—*Frequency (%) of non-inert material (squamous or epithelial cells) in needles and cartridges in 120 diabetic patients depending on the duration of diabetes.*

Evidence of biologic material was associated with a longer duration of diabetes and insulin therapy. Micro- and macroangiopathy could involve the skin and induce its progressive degradation (8,9). In addition, skin tends to toughen after its long-term use for injection. Our results might indicate that alteration of the skin facilitates the aspiration of epithelial cells into the cartridge. The reason for the elevated frequency of cells found in newly treated patients remains unclear. The elevation might suggest that these patients were treated with insulin because of severe complications, including those of the skin, but other confounding factors cannot be excluded. Injection in thighs or buttocks was more frequently associated with the presence of cells, and injection in the abdomen was more frequently associated with negative results. Skinfold, needle size, and the remaining volume of insulin solution in the cartridge do not seem to significantly influence the capture of cells.

Our results concern both health care professionals and patients (10). Information on the risk related to the presence of cells in disposable materials should be obtained because hepatitis and HIV disease have been associated with cross-contamination with cells from infected individuals (11). Although it is clear that the needle is strictly for individual use and should be changed after each injection, our results underline the need for removing it promptly after injection. Evidence of cells in devices emphasizes that the same cartridge or the same nonrefillable pen must not be used for different patients, especially in clinics and hospitals. Individual reuse of disposable materials (12) and the precise impact of repeated self-administration of non-inert material remains to be studied.

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